RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE *DDR1* EN EL TRASTORNO MENTAL GRAVE

Beatriz García Ruiz

UNIVERSITAT ROVIRA i VIRGILI

Relación entre el estrés y la adversidad en la vida temprana con la metilación de *DDR1* en el trastorno mental grave

BEATRIZ GARCÍA RUIZ

TESIS DOCTORAL
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dirigida por la Dra. Elisabet Vilella Cuadrada

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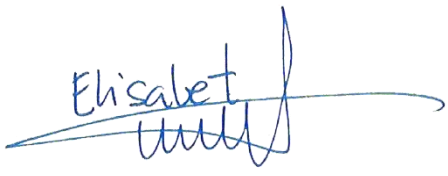
HAGO CONSTAR que este trabajo titulado **"Relación entre el estrés y la adversidad en la vida temprana con la metilación de *DDR1* en el trastorno mental grave"**, que presenta Beatriz García Ruiz, se ha realizado bajo mi dirección en el Departament de Medicina i Cirurgia de esta Universidad y que cumple todos los requerimientos necesarios para la obtención del título de Doctora.

Reus, 21 de abril de 2023.

La directora de la tesis doctoral



Dra. Elisabet Vilella Cuadrada

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A todas aquellas personas que sufren

«El mundo está lleno de sufrimiento, pero rebosa de personas que lo han vencido y en su lucha descubrieron algo valioso».

-Helen Keller

(*The World I Live In,* 1908)

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«Una ciencia privada de conciencia humanística es algo tan estremecedor como una conciencia que habla del mundo de espaldas a la ciencia».

-Edgar Morin

(*Science avec conscience,* 1982)

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Parte del contenido de esta tesis doctoral es confidencial y se indica como **"contenido confidencial**" donde corresponda.

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JUSTIFICACIÓN

Según la Organización Mundial de la Salud (OMS), los trastornos mentales son la primera causa de discapacidad en todo el mundo, y actualmente representan alrededor de un tercio de las diferentes discapacidades (física, sensorial, intelectual, y psíquica). Las personas con un trastorno mental sufren consecuencias debilitantes que impactan directamente en sus relaciones interpersonales y familiares, así como en los ámbitos educativo y laboral, viéndose reducida su esperanza de vida entre 10 y 15 años en comparación con la población general, en parte, debido a una elevada tasa de suicidio. Además, el desconocimiento social y su consecuente imagen negativa sobre las personas que padecen un trastorno mental dificulta su integración social y laboral, aumentando el riesgo de aislamiento y marginación. De ahí la importancia de llevar a cabo investigaciones encaminadas a lograr un mejor conocimiento de los trastornos mentales que proporcione una atención integral a las personas que los padecen, y que, a su vez, pueda ofrecer una imagen más ajustada de su realidad, sus capacidades potenciales de integración y aportación a la comunidad, y su condición de ciudadanos de pleno derecho.

En 2018, me incorporé al grupo de investigación en Genética y Ambiente en Psiquiatría (GAP) del Hospital Universitari Institut Pere Mata, el cual cuenta con una larga trayectoria en el campo de la psiquiatría genética y en la investigación del gen del receptor dominio discoidina 1 (*DDR1*). Este gen se ha involucrado en los procesos de mielinización y remielinización, y su expresión se ha encontrado correlacionada con la de genes y proteínas de mielina como *MBP*, *MAG* u *OLIG2.* Asimismo, sus variantes genéticas se han asociado a la esquizofrenia y a las alteraciones en la materia blanca cerebral y consecuente reducción de la velocidad de procesamiento cognitivo observadas en estos pacientes. Considerando estos resultados y el hecho de que la metilación del ADN tiene un papel importante en la regulación del proceso de mielinización, el grupo decidió abrir una línea de investigación para estudiar si *DDR1* se encontraba diferencialmente metilado en la esquizofrenia y el trastorno bipolar.

La presente tesis doctoral se enmarca en esta línea de investigación y estudia, desde un contexto multidisciplinar y multicéntrico, posibles alteraciones en la metilación de *DDR1* en pacientes con psicosis incipiente, esquizofrenia, y trastorno bipolar, así como su asociación con la expresión del gen y con factores ambientales como el estrés y la exposición a la adversidad en la vida temprana que podrían subyacer a la vulnerabilidad para el desarrollo de estos trastornos mentales y de sus fenotipos clínicos.

Incorporar el conocimiento de los estudios genéticos en psiquiatría nos permite tener una mayor comprensión de los trastornos mentales y desarrollar estrategias de tratamiento cada vez más personalizadas. Por tanto, la mejora en los diagnósticos y la identificación de individuos que presentan signos y síntomas sutiles, y aquellos con alto riesgo clínico, son las formas más prometedoras de reducir los altos costos personales, familiares, sociales, clínicos, y económicos que causan los trastornos mentales en todo el mundo.

ABREVIATURAS

2NPFF2: Neuropeptide FF Receptor 2

5HT1-7: 5-Hydroxytryptamine Receptors 1-7

5-HTT: Serotonin transporter

5mC: 5-metilcitosina

ADN: Ácido desoxirribonucleico

ADRA2: Adrenoceptor Alpha 2A

ADRA2B: Adrenoceptor Alpha 2B

AE: Abuso emocional

AKT1: AKT Serine/Threonine Kinase 1

ALS2: Alsin Rho Guanine Nucleotide Exchange Factor ALS2

ARNm: Ácido ribonucleico mensajero

AVT: Adversidad en la vida temprana

BDNF: Brain Derived Neurotrophic Factor

BH: Benjamini & Hochberg

CACNA1C: Calcium Voltage-Gated Channel Subunit Alpha1 C

CF: Corteza frontal

CH_3: Grupo metilo

CIE: Clasificación Internacional de Enfermedades

CLDN11: Claudin 11

CNP: 2',3'-Cyclic Nucleotide 3' Phosphodiesterase

CNV: Variación del número de copias (*copy number variants*)

CO: Corteza occipital

COMT: Catechol-O-Methyltransferase

CPF: Corteza prefrontal

CPFDL: Corteza prefrontal dorsolateral

CpG: Citosina-fosfato-guanina

CREB1: cAMP Responsive Element Binding Protein 1

CS: Conducta suicida

CSPG4: Chondroitin Sulfate Proteoglycan 4

CTLA4: Cytotoxic T-Lymphocyte Associated Protein 4

CTQ: Cuestionario de Trauma Infantil *(Childhood Trauma Questionnaire)*

CTQ-SF: Cuestionario de Trauma Infantil-Versión Corta *(Childhood Trauma Questionnaire-Short Form)*

CX3CL1: C-X3-C Motif Chemokine Ligand 1

CXCL1: C-X-C Motif Chemokine Ligand 1

DDR1: Discoidin Domain Receptor 1

DDR1-DT: DDR1 Divergent Transcript

DNasa I: Desoxirribonucleasa I

DNMT1: DNA Methyltransferase 1

DRD2: Dopamine Receptor D2

DRD3: Dopamine Receptor D3

DRD4: Dopamine Receptor D4

DSM: Manual Diagnóstico y Estadístico de los Trastornos Mentales *(Diagnostic and Statistical Manual of Mental Disorders)*

DTNBP1: Dystrobrevin Binding Protein 1

EDec: Método de deconvolución epigenómica *(Epigenomic deconvolution method)*

Eje HPA: Eje hipotálamo-pituitario-adrenal

EM: Esclerosis múltiple

ENCODE: Enciclopedia de Elementos del ADN *(Encyclopedia of DNA Elements)*

ENIGMA: Evidence-based Network for the Interpretation of Germline Mutant Alleles

ENIGMA-DTI: ENIGMA Diffusion Tensor Imaging Working Group

ERBB3: Erb-B2 Receptor Tyrosine Kinase 3

ESQ: Esquizofrenia

EWAS: Estudios de asociación de epigenoma completo *(epigenome-wide association studies)*

FKBP5: FKBP Prolyl Isomerase 5

FOX03A: Forkhead Box O3 A

FTs: Factores de transcripción

GABA: gamma-aminobutyric acid

GAD1: Glutamate Decarboxylase 1

GAD67: Glutamic acid decarboxylase 67

GALC: Galactosylceramidase

GDNF: Glial Cell Derived Neurotrophic Factor

GFAP: Glial Fibrillary Acidic Protein

GR: Glucocorticoid receptor

GSK3B: Glycogen Synthase Kinase 3 Beta

GWAS: Estudios de asociación de genoma completo *(genome-wide association studies)*

GWEIS: Estudios de interacción ambiental de genoma completo *(genome-wide environment interaction studies)*

GxE: interacción gen-ambiente *(gene–environment interaction)*

HDAC2: Histone Deacetylase 2

HTR1A: 5-Hydroxytryptamine Receptor 1A

HTR2A: 5-Hydroxytryptamine Receptor 2A

IL-1: Interleukin 1

ITGB1: Integrin Subunit Beta 1

KCNQ3: Potassium Voltage-Gated Channel Subfamily Q Member 3

KITLG: KIT Ligand

LINC00243: Long Intergenic Non-Protein Coding RNA 243

LINC02570: Long Intergenic Non-Protein Coding RNA 2570

LINGO3: Leucine Rich Repeat and Ig Domain Containing 3

lncRNA: ARN largo no codificante *(long non-coding RNA)*

LOC105374524: Gen de ARN clase lncRNA no caracterizado

mADN: Metilación del ADN

MAG: Myelin Associated Glycoprotein

MANCOVA: Análisis multivariante de covarianza

MAP2: Microtubule Associated Protein 2

MAPK1: Mitogen-Activated Protein Kinase 1

MAPT: Microtubule Associated Protein Tau

MB-COMT: Catechol O-Methyltransferase membrane-bound form

MBP: Myelin Basic Protein

MIR4640: MicroRNA 4640

miRNA: micro-ARN *(micro-RNA)*

MOG: Myelin Oligodendrocyte Glycoprotein

MPZL1: Myelin Protein Zero Like 1

ncRNA: ARN no codificante *(non-coding RNA)*

NeuN+: Núcleos neuronales

NLR: Índice neutrófilo/linfocito

NR3C1: Nuclear Receptor Subfamily 3 Group C Member 1

OLIG1: Oligodendrocyte Transcription Factor 1

OLIG2: Oligodendrocyte Transcription Factor 2

OLs: Oligodendrocitos

OMS: Organización Mundial de la Salud

OPCs: Células precursoras de oligodendrocitos

OPRM1: Opioid Receptor Mu 1

ORegAnno: Open Regulatory Annotation Database

OXTR: Oxytocin Receptor

PAX5: Paired box 5

PDGFRA: Platelet Derived Growth Factor Receptor Alpha

PI: Psicosis incipiente

PLLP: Plasmolipin

PLP1: Proteolipid Protein 1

PMI: Intervalo postmortem *(postmortem interval)*

PMP22: Peripheral Myelin Protein 22

POLR2A: RNA Polymerase II Subunit A

POU3F1: POU Class 3 Homeobox 1

PSS: Escala de Estrés Percibido *(Perceived Stress Scale)*

PVALB: Parvalbumin

RELN: Reelin

RIN: Número de integridad del ARN *(RNA Integrity Number)*

SIDA: Síndrome de inmunodeficiencia adquirida

SKA2: Spindle and Kinetochore Associated Complex Subunit 2

SLC1A4: Solute Carrier Family 1 Member 4

SLC6A3: Solute Carrier Family 6 Member 3

SLC6A4: Solute Carrier Family 6 Member 4

SNC: Sistema nervioso central

SNPs: Polimorfismos de nucleótido único *(single nucleotide polymorphisms)*

SNV: Variaciones de nucleótido único *(single nucleotide variant)*

SOX10: SRY-Box Transcription Factor 10

SPI1: Spi-1 Proto-Oncogene

SPSS: Paquete Estadístico para las Ciencias Sociales *(Statistical Package for the Social Sciences)*

TB: Trastorno bipolar

TBe: Trastorno bipolar en fase eutímica

TB-I: Trastorno bipolar tipo I

TB-II: Trastorno bipolar tipo II

TI: Trauma infantil

TNFalfa: Tumor Necrosis Factor

TPH1: Tryptophan Hydroxylase 1

TPH2: Tryptophan Hydroxylase 2

TRKB: Neurotrophic Receptor Tyrosine Kinase 2

VIH: Virus de la inmunodeficiencia humana

ZNF263: Zinc Finger Protein 263

RESUMEN DE LA TESIS DOCTORAL

Introducción: Los trastornos psiquiátricos son trastornos complejos multifactoriales con una alta heredabilidad. La predisposición genética se combina con factores ambientales que aumentan la susceptibilidad a padecerlos. En este sentido, la adversidad en la vida temprana, que incluye el trauma infantil por abuso y/o negligencia, se ha establecido como uno de los factores de riesgo ambientales más prevalentes y relevantes para desarrollar un amplio espectro de trastornos mentales a lo largo de la vida, asociándose con cambios en los mecanismos epigenéticos de genes implicados en la etiopatogenia de estos trastornos y con la conducta suicida. La metilación del ADN (mADN) es un mecanismo epigenético que regula la expresión génica y que es importante en la diferenciación de los oligodendrocitos y en el proceso de mielinización. Investigaciones recientes han demostrado anomalías en la estructura de la materia blanca, constituida principalmente por mielina, y cambios en la expresión de genes de oligodendrocitos en el cerebro de pacientes con esquizofrenia y trastorno bipolar. De forma similar, estudios comparativos han mostrado alteraciones muy cercanas en la microestructura de la materia blanca en ambos trastornos y un solapamiento en su arquitectura genética que no se da en otros diagnósticos psiquiátricos. El gen del receptor dominio discoidina 1 (*DDR1*) codifica un receptor de tirosina quinasa que se encuentra altamente expresado en oligodendrocitos en el sistema nervioso central, y que está implicado tanto en su función como en el proceso de mielinización. Sus isoformas coexpresan con genes de mielina y se han asociado con la esquizofrenia. Asimismo, también se han relacionado con alteraciones en la materia blanca cerebral y con una reducción de la velocidad del procesamiento cognitivo en estos pacientes.

Hipótesis y Objetivos: Con la hipótesis de que el estrés psicológico y la adversidad en la vida temprana, representada por el trauma infantil, pueden inducir alteraciones en el patrón de mADN de genes que codifican para proteínas relevantes para el proceso de mielinización como *DDR1*, se propusieron los siguientes objetivos que se llevaron a cabo en los tres artículos que conforman esta investigación:

Artículo 1

i. Estudiar los patrones de mADN de la región promotora de *DDR1* en leucocitos periféricos procedentes de una muestra de pacientes con un diagnóstico de psicosis incipiente y controles sanos.

ii. Replicar los resultados del objetivo (i) en tejido cerebral postmortem procedente de la corteza prefrontal dorsolateral en una muestra de pacientes con esquizofrenia y controles sanos.
iii. Estudiar si la mADN de *DDR1* influye en la expresión del gen y de sus isoformas en tejido cerebral postmortem procedente de la corteza prefrontal dorsolateral de pacientes con esquizofrenia y controles sanos.
iv. Analizar la asociación entre la mADN de la región promotora de *DDR1* en leucocitos periféricos y (a) el estrés psicológico percibido, acontecimientos vitales estresantes, y el trauma infantil; (b) el estrés fisiológico (cortisol en saliva); y (c) la inflamación en la muestra de pacientes con psicosis incipiente y controles sanos.

Artículo 2

i. Estudiar los patrones de mADN de *DDR1* en tejido cerebral postmortem procedente de la corteza occipital de una muestra de pacientes con diagnóstico de trastorno bipolar y controles sanos.
ii. Replicar los resultados del objetivo (i) en dos muestras independientes en tejido cerebral postmortem procedente de la corteza prefrontal dorsolateral y de núcleos aislados de células neuronales de la corteza frontal de pacientes con trastorno bipolar y controles sanos.
iii. Estudiar si la mADN de *DDR1* influye en la expresión del gen y de sus isoformas en tejido cerebral postmortem procedente de la corteza occipital de pacientes con trastorno bipolar y controles sanos.
iv. Estudiar la correlación entre los patrones de mADN de *DDR1* y los de un conjunto de genes de mielina y otros marcadores específicos de neuronas, astrocitos, y microglía en tejido cerebral postmortem procedente de la corteza occipital de pacientes con trastorno bipolar y controles sanos.

Artículo 3

i. Estudiar los patrones de mADN de la región promotora de *DDR1* en leucocitos periféricos procedentes de (a) una muestra de pacientes con trastorno bipolar en fase eutímica y controles sanos; y (b) el grupo de pacientes estratificados en base a la presencia/ausencia de conducta suicida.
ii. Analizar la asociación de la mADN de la región promotora de *DDR1* en leucocitos periféricos y la exposición al trauma infantil con el diagnóstico en la muestra de pacientes con trastorno bipolar en fase eutímica y controles sanos, y con la conducta suicida en el grupo de pacientes.

iii. Explorar los efectos de la mADN de *DDR1* que podrían estar mediando la asociación entre el trauma infantil y la conducta suicida.

Métodos: Se llevaron a cabo tres estudios con diseño transversal de caso-control. En el primer estudio se incluyeron pacientes con psicosis incipiente no afectiva y controles sanos de los que se recogieron niveles de cortisol salival, recuento de neutrófilos y linfocitos en sangre, ADN leucocitario, y un conjunto de variables clínicas y psicosociales de interés. Se compararon los patrones de mADN de *DDR1* entre casos y controles y se estudió su relación con el diagnóstico y las variables recogidas. A su vez, se realizó un análisis de mADN diferencial de *DDR1* en ADN procedente de tejido cerebral postmortem de la corteza prefrontal dorsolateral de pacientes con esquizofrenia y de controles sanos en el que se estudió la asociación entre la mADN del gen y su expresión. En el segundo estudio se llevó a cabo un análisis de perfiles de mADN del genoma completo en tejido cerebral postmortem procedente de la corteza occipital de pacientes con trastorno bipolar y controles sanos para investigar los patrones de mADN de *DDR1* en ambos grupos y su posible asociación con la expresión del gen. También se seleccionaron un conjunto de genes convencionales de mielina para estudiar su cometilación con *DDR1*. Además, se accedió a datos de metiloma completo y transcriptoma de la corteza prefrontal dorsolateral y de núcleos aislados de células neuronales de la corteza frontal de pacientes con trastorno bipolar y controles sanos para validar los resultados. En el tercer estudio se incluyeron pacientes diagnosticados con trastorno bipolar en fase eutímica y controles sanos y se determinaron los niveles de mADN de la región promotora de *DDR1* para compararlos entre casos y controles, así como entre pacientes en base a la presencia/ausencia de conducta suicida. Finalmente se estudió la asociación de la mADN y el trauma infantil con el diagnóstico de trastorno bipolar y la conducta suicida en estos pacientes.

Faltan los apartados de Resultados/Conclusiones del resumen de la tesis doctoral; contenido confidencial.

UNIVERSITAT ROVIRA I VIRGILI
RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
Beatriz García Ruiz

I. INTRODUCCIÓN

UNIVERSITAT ROVIRA I VIRGILI
RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
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1. La causa de los trastornos mentales

Una cuestión fundamental que ha preocupado a clínicos e investigadores durante más de un siglo ha sido la causa de los trastornos mentales. Con el objetivo de dar respuesta a esta pregunta, durante la última década se ha acumulado una enorme cantidad de datos provenientes de estudios genéticos. Los hallazgos que han surgido de estos estudios han establecido que la arquitectura genética de los trastornos psiquiátricos es altamente poligénica, con miles de alelos de riesgo que se distribuyen por todo el genoma y que muestran una amplia pleiotropía, es decir, variantes asociadas con múltiples rasgos y trastornos (Andreassen et al., 2023; Lee et al., 2021; Lu et al., 2021; Polushina et al., 2021). Sin embargo, los trastornos psiquiátricos son multifactoriales, y la predisposición genética se combina a lo largo de la vida con factores ambientales que aumentan la susceptibilidad a desarrollarlos (Andreassen et al., 2023; Assary et al., 2018; Uher & Zwicker, 2017).

En los últimos años, clarificar la naturaleza de la base genética compartida entre los trastornos psiquiátricos se ha convertido en un área de investigación importante (Andreassen et al., 2023). Investigar estas vías comunes puede arrojar luz sobre la comorbilidad generalizada y las características clínicas compartidas entre trastornos (**Figura 1**), y contribuiría a desentrañar la heterogeneidad dentro de las categorías diagnósticas, proporcionando un mayor conocimiento de la etiología de estos trastornos complejos y cambiando nuestro enfoque para el diagnóstico y desarrollo de tratamientos adaptados a la etiopatogenia única de cada paciente (Andreassen et al., 2023; Doherty & Owen, 2014).

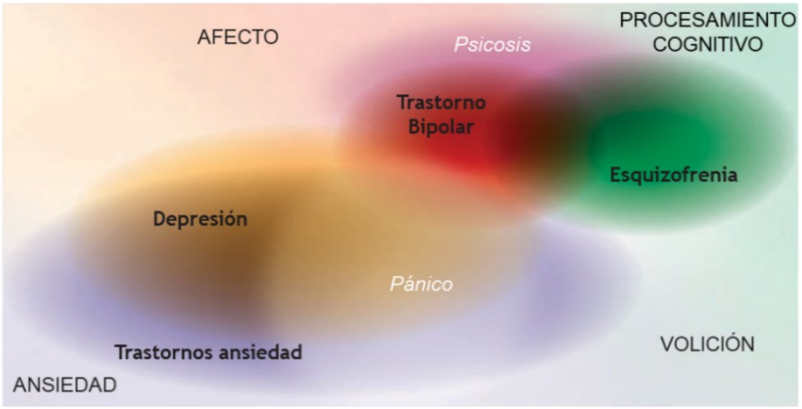

Figura 1. Superposición de los trastornos psiquiátricos

Los trastornos psiquiátricos se superponen y pueden ser extremos de los rasgos de personalidad. Las

vulnerabilidades genéticas para los trastornos psiquiátricos se muestran como emergentes del extremo de las variaciones de personalidad de la población normal, ilustradas como diferentes matices de fondo del estado de ánimo, la ansiedad, el procesamiento cognitivo y la volición. El término volición, que fue introducido por Kraepelin, combina la voluntad o el impulso de hacer algo con energía y nivel de actividad. Factores genéticos que afectan los niveles de estos rasgos subyacentes, en interacción con factores genéticos y ambientales adicionales, puede conducir a trastornos psiquiátricos (aquí se muestran el trastorno bipolar, la esquizofrenia, la depresión, y los trastornos de ansiedad), cuyos síntomas y factores de riesgo genéticos son en parte únicos y en parte superpuestos. La psicosis y el pánico son rasgos patológicos y no son una categoría diagnóstica formal, pero están asociados con varios diagnósticos psiquiátricos. Debido a que no todos los trastornos se pueden cubrir en dos dimensiones, existen interacciones y superposiciones en muchas más dimensiones de las que se pueden representar aquí (por ejemplo, la depresión y la ansiedad también están presentes en la esquizofrenia). Traducida y reproducida con el permiso de: Burmeister M, McInnis MG, Zöllner S. Psychiatric genetics: progress amid controversy. (2008). Nat Rev Genet, 9(7):527-40.

Esto supondría una ruptura paradigmática con los esquemas tradicionales de clasificación diagnóstica (American Psychiatric Association, 2013; World Health Organization, 2019) en los que los trastornos psiquiátricos se consideran categóricamente distintos unos de otros. Por lo tanto, se puede considerar que los hallazgos genéticos respaldan los esfuerzos para reconceptualizar la nosología psiquiátrica en un marco más dimensional (Smoller JW, Andreassen OA, Edenberg HJ, Faraone SV, Glatt SJ, 2019). Asimismo, el riesgo genético para los trastornos psiquiátricos también se superpone con la variación genética en los rasgos conductuales (Hindley et al., 2022), como los cinco grandes rasgos de personalidad (Lo et al., 2017), la inteligencia (Savage et al., 2018), el nivel educativo (Okbay et al., 2016a), el bienestar subjetivo (Okbay et al., 2016b), los patrones de sueño (Watanabe et al., 2022), y los síntomas psiquiátricos en individuos sanos (Roelfs et al., 2021), lo que indicaría que el riesgo de patología mental no es categóricamente diferente de la normalidad (Smoller et al., 2019). Para una revisión más extensa ver Andreassen et al., 2023.

1.1. Espectro de la esquizofrenia y otros trastornos psicóticos

Los trastornos psicóticos, especialmente la esquizofrenia (ESQ), suelen evolucionar a través de estadios premórbidos, prodrómicos, sindrómicos, progresivos, y crónicos (**Figura 2**). El curso del trastorno es impredecible, y la frecuencia, el número, y los tipos de síntomas psicóticos varían según el trastorno específico y pueden diferir entre pacientes con el mismo diagnóstico (Lieberman & First, 2018). La psicosis incipiente (PI) comprende las primeras etapas del trastorno, es decir, desde los primeros síntomas prodrómicos, hasta pasados 5 años tras el primer episodio psicótico. La fase prodrómica,

que se considera una forma atenuada de psicosis, marca el inicio de la sintomatología y precede a un primer episodio psicótico, aunque no siempre tiene que darse esta transición. Los primeros 2 a 5 años después de un primer episodio psicótico se consideran un período crítico que determina el pronóstico a largo plazo, de ahí la importancia del tratamiento en las primeras fases de estos trastornos. La intervención en estas primeras etapas debe centrarse no solo en los síntomas, sino también en los aspectos psicológicos y psicosociales (Sizer et al., 2022).

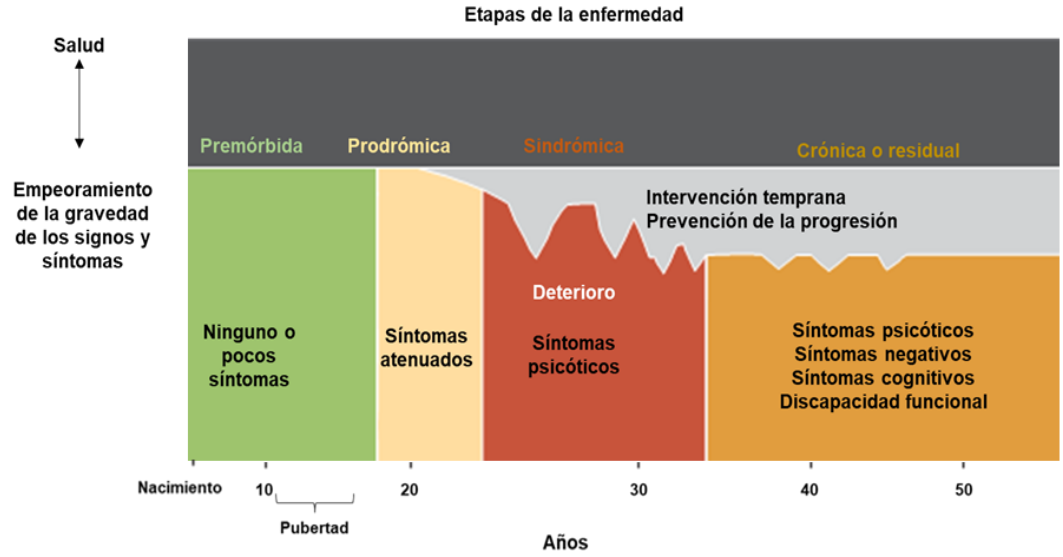

Figura 2. Historia natural de la esquizofrenia y prevención de la cronicidad

Se muestran las etapas de la enfermedad en la esquizofrenia, el trastorno psicótico prototípico. La detección y el tratamiento en las primeras etapas de la enfermedad, idealmente cerca del inicio del primer episodio de psicosis, acortan la duración de los episodios psicóticos, reducen las recurrencias, y limitan la disminución progresiva del funcionamiento (deterioro) que ocurre en la etapa sindrómica y que conduce a los efectos crónicos de la enfermedad. La etapa sindrómica comienza con el primer episodio de psicosis y continúa a través de la etapa progresiva. Traducida y reproducida con el permiso de: Lieberman JA, First MB. Psychotic Disorders. (2018). *N Engl J Med*, 19;379(3):270-280. Copyright Massachusetts Medical Society. New England.

La ESQ está considerada como uno de los trastornos mentales más graves. El estigma, el aislamiento social, la reducción de posibilidades de construir relaciones satisfactorias a lo largo de la vida, y una esperanza de vida reducida, son algunas de las consecuencias para las personas que la sufren. Generalmente se diagnostica entre los últimos años de la adolescencia y principios de los treinta. Se estima que su tasa de prevalencia global está entorno al 1% (McGrath et al., 2008), siendo moderadamente más frecuente en hombres (Jongsma et al., 2019). Alrededor del 5% de las personas con ESQ mueren por

suicidio, presentando mayor riesgo en las primeras etapas de la enfermedad (Hor & Taylor, 2010). Las características clínicas de la ESQ incluyen síntomas positivos, también conocidos como psicosis o síndrome psicótico, es decir, delirios, alucinaciones, y trastorno del pensamiento formal; síntomas negativos, que consisten en la afectación de la capacidad volitiva, reducción de la producción verbal, y aplanamiento del afecto; y síntomas cognitivos o de desorganización, aunque a partir de los resultados de estudios factoriales, actualmente esta distinción sintomatológica se puede segregar en tres grupos: distorsión de la realidad, desorganización, y síntomas negativos o el llamado "síndrome de pobreza clínica" (Jauhar et al., 2022). El diagnóstico se realiza evaluando los signos y síntomas específicos del paciente y se basa en los criterios diagnósticos de los sistemas de clasificación diagnóstica, el Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM, del inglés Diagnostic and Statistical Manual of Mental Disorders) y la Clasificación internacional de enfermedades (CIE). El tratamiento va dirigido a abordar los síntomas, prevenir las recaídas, y aumentar el funcionamiento adaptativo de la persona. Para ello, la estrategia farmacológica, basada fundamentalmente en el uso de fármacos antipsicóticos, la psicoterapia, y las intervenciones psicosociales son centrales para conseguir estos objetivos (Patel et al., 2014).

1.2. Trastorno bipolar

El trastorno bipolar (TB) es un trastorno psiquiátrico crónico que cursa con síntomas gravemente debilitantes. Se caracteriza principalmente por la presencia de episodios depresivos y maníacos o hipomaníacos recurrentes que fluctúan con el tiempo, causando profundos efectos adversos en el funcionamiento mental, físico, y psicosocial de las personas que lo padecen (McIntyre et al., 2020). El TB tipo I (TB-I) se define por la presencia de un episodio maníaco sindrómico, que puede estar precedido o seguido de un episodio hipomaníaco o un episodio depresivo mayor, a su vez, el TB tipo II (TB-II) se define por la presencia de un episodio hipomaníaco sindrómico y un episodio depresivo mayor (McIntyre et al., 2020). Ambos muestran una prevalencia global estimada del 0.6–1.0% y 0.4–1.1%, respectivamente (Merikangas et al., 2011). Los estudios de mortalidad indican que el TB es una condición psiquiátrica asociada a una de las mayores tasas de suicidio, entre el 15-20% (Miller & Black, 2020; Plans et al., 2019, Pompili et al, 2013), siendo una de las preocupaciones más importantes para los clínicos en el manejo del trastorno. Como en el caso de la ESQ, el diagnóstico de TB se realiza mediante una evaluación clínica integral basada en los criterios diagnósticos del DSM y/o CIE, y se complementa, cuando es posible, con información de terceros (p.ej., familiares).

Normalmente se necesita una evaluación longitudinal complementada con diarios de estado de ánimo e información corroborativa para llegar a un diagnóstico (McIntyre et al., 2020). El tratamiento comprende medidas farmacológicas, principalmente estabilizadores del estado del ánimo, como el litio, solos o en combinación con antidepresivos, antiepilépticos y/o antipsicóticos, psicoterapia, intervenciones psicosociales, terapias neuroestimuladoras, y estrategias de autocuidados para incidir en la prevención y tratamiento de los distintos episodios, la mejora y conservación de la función cognitiva, el tratamiento y prevención de la comorbilidad psiquiátrica y médica, y la reducción del suicidio (McIntyre et al., 2020).

2. Etiopatogenia de la esquizofrenia y el trastorno bipolar

2.1. Factores genéticos

La ESQ y el TB son trastornos altamente hereditarios y poligénicos. Estudios en gemelos y familias estiman una heredabilidad de aproximadamente el 60-80% para la ESQ (Sullivan et al., 2003), y del 60-85% para el TB (Mullins et al., 2021), lo que deja un promedio del 20-40% de variabilidad sin explicar atribuible a factores ambientales.

Los estudios de asociación de genoma completo (GWAS, del inglés genome-wide association studies) proporcionan nuevos conocimientos sobre la biología y la arquitectura genética de los trastornos psiquiátricos. Se han utilizado para evaluar diferentes tipos de variación del ADN relevantes para la psicopatología: variantes comunes como los polimorfismos de nucleótido único (SNPs, del inglés single nucleotide polymorphisms), o variantes estructurales raras, como las variantes de nucleótido único (SNV, del inglés single nucleotide variants) y las deleciones y duplicaciones de regiones genómicas conocidas como variantes del número de copias (CNVs, del inglés copy number variants) (Andreassen et al., 2023). Sin embargo, identificar las variantes genéticas implicadas en la aparición de un trastorno mental es una tarea compleja, ya que la evidencia científica recogida hasta la fecha indica que existen múltiples genes implicados.

Los últimos GWAS han revelado un total de 287 loci de riesgo genético para la ESQ (Trubetskoy et al., 2022) y 64 loci asociados con el TB (Mullins et al., 2021). No obstante, la proporción de la varianza explicada debida a variantes tipo SNP por la suma de todos los alelos de riesgo es de baja a moderada, y se estima en ~32% en la ESQ

(Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014) y ~20% en el TB (Stahl et al., 2019), lo que sugiere que otras variantes como SNVs y CNVs contribuyen al riesgo genético.

2.2. Base genética compartida entre la esquizofrenia y el trastorno bipolar

En 2019, los miembros del Cross-Disorder Group del Psychiatric Genomics Consortium (Lee et al., 2019) llevaron a cabo el GWAS y metaanálisis de trastornos neuropsiquiátricos más grande que se conoce hasta la fecha, y que contó con una muestra combinada de más de 725 000 casos y controles. En el estudio se analizaron datos de 6 786 993 de SNPs de todo el genoma humano para ocho trastornos psiquiátricos, entre ellos la ESQ y el TB, con el objetivo de identificar variantes que se asociaran a más de un trastorno. Los resultados derivados del análisis de correlaciones entre pares de trastornos mostraron que la correlación genética más alta se daba entre la ESQ y el TB (**Figura 3**). Estos resultados coinciden ampliamente con estimaciones previas (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2014; The Brainstorm Consortium, 2018), y hasta la fecha, ya se han identificado 114 loci que contribuyen a ambos trastornos (Ruderfer et al., 2018) poniendo de relieve la base genética que comparten.

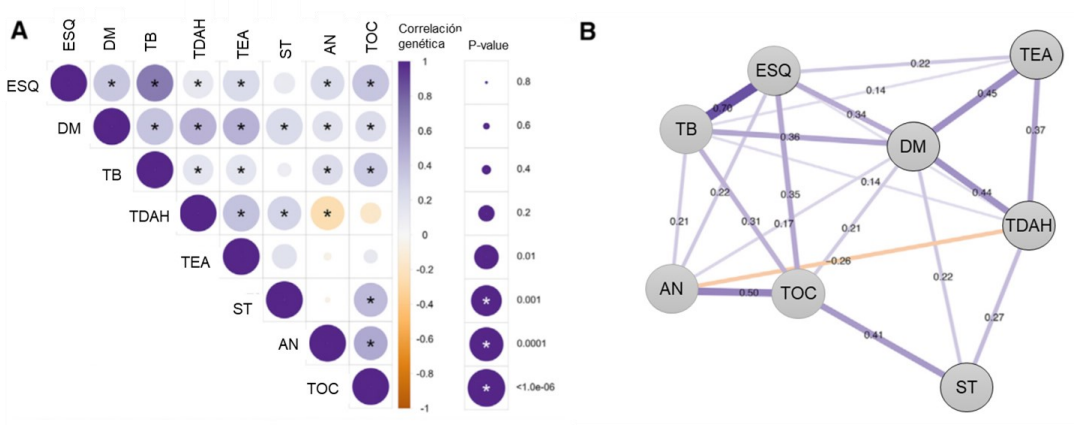

Figura 3. Relaciones genéticas entre trastornos neuropsiquiátricos

A. Se estiman correlaciones genéticas basadas en SNP (r_g) en todo el genoma para ocho trastornos neuropsiquiátricos combinando una muestra de 232 964 casos y 494 162 controles mediante LDSC. El tamaño de los círculos se escala con la importancia de los valores de *p*. Cuanto más oscuro es el color, mayor es la magnitud de r_g. El signo asterisco (∗) indica significación estadística después de la corrección de Bonferroni. **B.** Las correlaciones genéticas basadas en SNPs entre los ocho trastornos se

representan mediante un gráfico indirecto para revelar relaciones genéticas complejas. Solo se muestran correlaciones genéticas significativas después de la corrección de Bonferroni en (A). Cada nodo representa un trastorno, con bordes que indican la fuerza de las correlaciones por pares. El ancho de los bordes aumenta, mientras que la longitud disminuye, con los valores absolutos de r_g. Abreviaturas: AN: Anorexia nerviosa; DM: Depresión mayor; ESQ: Esquizofrenia; LDSC: Puntuaciones de desequilibrio de ligamiento; SNP: Polimorfismo de nucleótido único; ST: Síndrome de Tourette; TB: Trastorno bipolar; TDAH: Trastorno por déficit de atención e hiperactividad; TEA: Trastornos del espectro autista; TOC: Trastorno obsesivo compulsivo. Traducida y reproducida con el permiso de: Cross-Disorder Group of the Psychiatric Genomics Consortium. Genomic Relationships, Novel Loci, and Pleiotropic Mechanisms across Eight Psychiatric Disorders. (2019). *Cell*, 179(7):1469-1482.e11.

2.3. *Factores ambientales: la adversidad en la vida temprana*

Desde la década de 1960, los investigadores han identificado fuertes relaciones entre el entorno adverso y el desarrollo de patología mental. En la actualidad, gracias a estudios más amplios y representativos, se han identificado factores de riesgo ambientales diversos que aumentan la susceptibilidad a desarrollar un trastorno psiquiátrico, y que incluyen, entre otros, la exposición a infecciones virales y sustancias tóxicas durante la gestación, la deficiencia de vitamina D, crecer en un entorno urbano, la condición de minoría étnica, las desventajas socioeconómicas, el maltrato infantil, o la victimización por intimidación o bullying (Uher & Zwicker, 2017).

La exposición a la adversidad en la vida temprana (AVT), que incluye el trauma infantil (TI) por abuso y/o negligencia, es una forma severa de estrés que se ha establecido como uno de los factores de riesgo ambientales más prevalentes y relevantes para desarrollar un amplio espectro de trastornos mentales a lo largo de la vida (McKay et al., 2021; Popovic et al., 2019). A su vez, el TI puede interferir en la formación del cerebro en períodos sensibles del desarrollo, alterando procesos como, por ejemplo, la poda sináptica y la mielinización, lo que resulta en reducciones en el grosor cortical y la integridad de la materia blanca, que, a su vez, inician procesos psicopatológicos (Mclaughlin et al., 2017; Montalvo-Ortiz, 2017).

Los pacientes con ESQ expuestos a AVT, incluidos aquellos con un alto riesgo de desarrollar psicosis, muestran un deterioro de la memoria de trabajo, la función ejecutiva, el aprendizaje verbal, la atención, y la cognición social. En estos pacientes, los niveles más altos de TI se correlacionan con un aumento de síntomas positivos atenuados, síntomas generales, síntomas depresivos, deterioro del funcionamiento global, y con un

peor rendimiento cognitivo en memoria episódica visual y en las funciones ejecutivas (Popovic et al., 2019).

En los pacientes con TB, la exposición al TI se ha asociado con el deterioro de la función cognitiva, mostrando un peor desempeño en memoria de trabajo, funcionamiento ejecutivo, velocidad de procesamiento, atención, memoria e inteligencia verbal, así como en la cognición social. Estos pacientes muestran una expresión clínica más grave, inestable, y compleja del trastorno que se caracteriza por una edad de inicio más temprana, síntomas más graves de depresión, manía, y psicosis, ciclación rápida, y más comorbilidades con trastornos de ansiedad o consumo de sustancias, así como intentos de suicidio más frecuentes (Agnew-Blais & Danese, 2016; Grillault-Laroche et al., 2022).

2.4. Interacción gen-ambiente

Como se ha comentado previamente, la evidencia sugiere que los trastornos psiquiátricos resultan de una interacción compleja entre factores genéticos y ambientales (Andreassen, et al., 2023; Assary et al., 2018; Uher & Zwicker, 2017). Esto ha dado lugar a un gran número de estudios con el objetivo de identificar estos factores de riesgo ambientales y sus posibles interacciones con la carga genética del individuo. Comprender estas interacciones durante el desarrollo es de gran importancia, ya que permite la identificación de vías relacionadas con diferentes trastornos, que, a su vez, pueden ayudar a identificar individuos con mayor riesgo en presencia de ciertas exposiciones.

La mayor parte de la evidencia de la interacción gen-ambiente (GxE, del inglés gene–environment interaction) en el desarrollo de los trastornos psiquiátricos se basa en estudios de genes candidatos realizados desde una perspectiva de diátesis-estrés, en estudios de GWAS, y recientemente en estudios de interacción ambiental de genoma completo (GWEIS, del inglés genome-wide environment interaction studies) (Assary et al., 2018). Hasta la fecha, se han publicado varias interacciones GxE en ESQ y TB, aunque la mayoría de los estudios se han centrado en el efecto de la variación en genes candidatos. Por ejemplo, se han identificado variantes en el gen *NR3C1,* que codifica el receptor de glucocorticoides (GR), y en el gen *FKBP5,* que codifica una proteína que se une a GR y modula su función, que interaccionan con factores ambientales estresantes aumentando el riesgo de aparición de un trastorno psiquiátrico. Otros dos ejemplos son el gen *COMT,* que codifica una enzima clave en la síntesis de dopamina, *y BDNF,* que

codifica un factor neurotrófico, en los que también se ha hallado una interacción entre sus variantes y la exposición a la AVT (Misiak et al., 2018).

3. Conducta suicida

La conducta suicida (CS), que incluye la ideación suicida, los intentos de suicidio y el suicidio, es un importante problema de salud pública global. A nivel mundial, 703 000 personas mueren por suicidio cada año siendo una de las principales causas de muerte en todo el mundo, contabilizándose más muertes por suicidio que por malaria, VIH/SIDA, cáncer de mama, o guerras y homicidios. En 2019, más de una de cada 100 muertes (1.3 %) fue el resultado de un suicidio (World Health Organization, 2021). Para los objetivos de esta tesis doctoral el término "CS" se utilizará para referirse tanto a la ideación suicida como a las tentativas de suicidio, considerándose como una entidad única.

3.1. Etiopatogenia de la conducta suicida

Aunque la literatura sobre el comportamiento suicida ha ido en aumento, los múltiples fenotipos que pueden considerarse en el espectro del suicidio dificultan su integración e interpretación. Estos fenotipos incluyen la ideación suicida, que se define como pensamientos de acabar con la propia vida (ya sea activa (con un plan) o pasiva (se da sólo el deseo de morir, pero sin plan)), el intento de suicidio, y el suicidio consumado o muerte por suicidio (Turecki et al., 2019).

En la etiología de la CS intervienen diversos factores: (a) factores distales o predisponentes, como la predisposición familiar y genética, y la exposición a la AVT, que producen cambios epigenéticos en los genes alterando su expresión a largo plazo; (b) factores mediadores que aumentan el riesgo de suicidio a largo plazo al interactuar con los factores distales; y (c) factores proximales o precipitantes, que provocan alteraciones en los sistemas de neurotransmisores clave, cambios inflamatorios, y disfunción glial en el cerebro, y que sí están relacionados directamente con la precipitación de un evento suicida (Turecki et al., 2019). En la **Figura 4** se muestra una visión detallada de los factores involucrados en la etiología de la CS y de sus asociaciones y contribución al riesgo de suicidio.

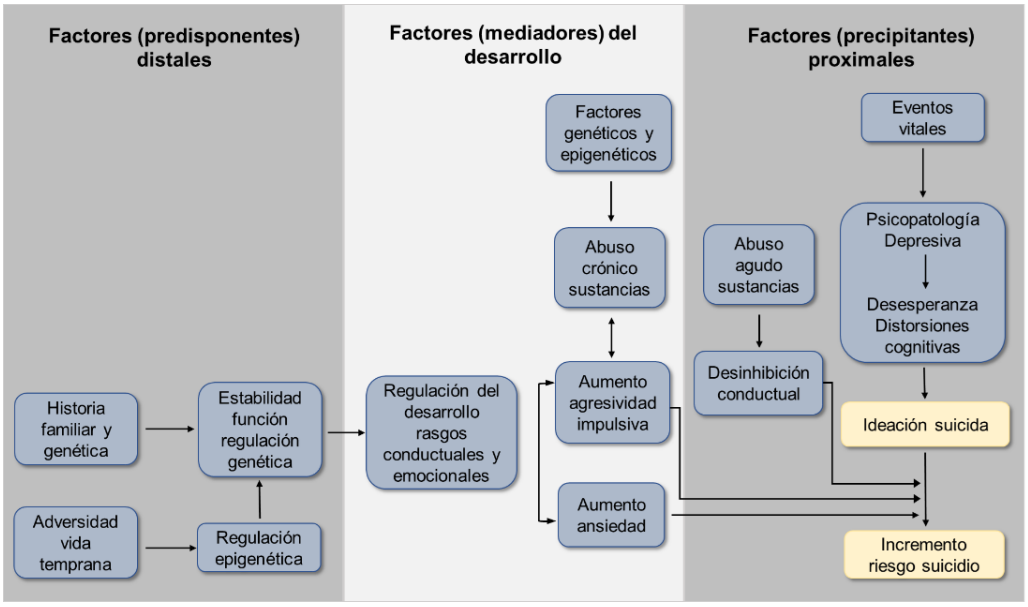

Figura 4. Esquema de los factores contribuyentes a la conducta suicida

El comportamiento suicida está regulado por varios factores diferentes que pueden clasificarse en términos generales como factores distales (predisponentes), de desarrollo (mediadores), o proximales (precipitantes). El modelo propuesto tiene en cuenta los factores de riesgo genéticos y psicosociales clásicos para el suicidio e integra hallazgos más recientes sobre cambios epigenéticos asociados con la tendencia suicida. Los factores predisponentes incluyen antecedentes familiares de suicidio y predisposición genética asociada, adversidad en la vida temprana y cambios epigenéticos asociados. En ambos casos, los factores predisponentes conducen a efectos a largo plazo sobre la expresión y regulación génica. Los factores predisponentes no desencadenan directamente eventos suicidas, pero están relacionados con un mayor riesgo de suicidio a través de los efectos de los factores mediadores. Los factores mediadores, que pueden resultar directamente de los cambios genéticos que ocurren como consecuencia de factores predisponentes, o que pueden estar asociados con otros factores como el abuso crónico de sustancias, aumentan el riesgo de suicidio al acentuar los rasgos relacionados con la tendencia suicida. Específicamente, la disposición familiar y los eventos traumáticos en la vida temprana pueden configurar rasgos conductuales y emocionales, como el comportamiento agresivo impulsivo y los rasgos de ansiedad, lo que aumenta el riesgo de actuar sobre la ideación suicida, que es una característica común de la psicopatología depresiva y la desesperanza. Los factores de riesgo proximales, como la psicopatología depresiva y el abuso agudo de sustancias, también pueden estar asociados con factores genéticos y epigenéticos y, a menudo, son desencadenados por eventos de la vida. Adaptada y reproducida con el permiso de: Turecki G, Brent DA, Gunnell D, O'Connor RC, Oquendo MA, Pirkis J, Stanley BH. (2019). Suicide and suicide risk. *Nat Rev Dis Primers* 24;5(1):74.

3.2. *Conducta suicida en la esquizofrenia y el trastorno bipolar*

La ESQ y el TB son las condiciones psiquiátricas asociadas con las mayores tasas de suicidio (Bai et al., 2021; Miller & Black, 2020).

La tasa de suicidio a lo largo de la vida en personas con ESQ es aproximadamente del 10% dándose el riesgo más alto en las primeras etapas del trastorno. Tener <35 años, ser hombre, no estar casado/a, vivir solo/a, el desempleo, un funcionamiento laboral deficiente, tener conciencia de los síntomas, la depresión comórbida, historia de AVT, los antecedentes personales y familiares de CS, o la falta de adherencia al tratamiento, entre otros, se asocian con un mayor riesgo de suicidio en la ESQ, siendo la provisión y cumplimiento de un tratamiento integral el único factor protector confiable para el suicidio en estos pacientes (Sher & Kahn, 2019).

El TB tiene una de las tasas más altas de suicidio, siendo aproximadamente de 20 a 30 veces mayor que en la población general (Miller & Black, 2020; Plans et al., 2019). Los factores de riesgo psicosociales para la CS en el TB incluyen: ser hombre, vivir solo/a, estar divorciado/a, no tener hijos, raza caucásica, tener < 35 años o edad avanzada (>75 años), desempleo, historia de AVT, antecedentes personales y familiares de intento de suicidio, y antecedentes familiares de suicidio consumado (Miller & Black, 2020). La CS en el TB se asocia a los subtipos depresivos o mixtos. El litio sigue siendo el tratamiento farmacológico de elección para prevenir la reincidencia de actos suicidas a pesar de que los resultados de los ensayos clínicos no son concluyentes acerca de su efecto protector frente a la CS y el suicidio consumado (Nabi et al., 2022).

También hay evidencia consistente del importante papel que desempeñan los factores genéticos en la CS. Así, por ejemplo, en estudios de genes candidatos se ha hallado un vínculo significativo entre la CS y los genes *ADRA2B* (receptor adrenérgico), *SLC6A3* (transportador de dopamina) (Lindholm-Carlström et al., 2012), y *SLC6A4* (transportador de serotonina) en la ESQ (Sher & Kahn, 2019). En el caso del TB los genes relacionados con la serotonina (transportadores y receptores) *5-HTT* y *5-HT1–7*, los genes de triptófano hidroxilasa *TPH1* y *TPH2*, y otros genes como *AKT1, ADRA2, BDNF, COMT, CREB1, GSK3B, FOX03A* y *MAPK1* se han asociado a la CS (Miller & Black, 2020; Plans et al., 2019). Más recientemente, varios estudios de GWAS han informado de la asociación entre la ESQ y el TB con las tendencias suicidas. En concreto, se identificó un locus significativo del cromosoma 4 en *LOC105374524*, un ARN no codificante, para el intento de suicidio asociado al TB (Mullins et al., 2019). En este mismo estudio se encontró que el intento de suicidio también se asoció con las puntuaciones de riesgo poligénico para la ESQ y el TB (Mullins et al., 2019). Finalmente, a pesar de que no se encontraron locus significativos para la muerte por suicidio asociados a ninguno de estos trastornos, si se halló una asociación entre esta y las puntuaciones de riesgo poligénico para la ESQ (Docherty et al., 2020; Li et al., 2023) y el TB (Li et al., 2023).

4. Oligodendrocitos y mielina en la esquizofrenia y el trastorno bipolar

Los oligodendrocitos (OLs) son células gliales del sistema nervioso central (SNC) que representan hasta el 40% de las células neurales en las regiones corticales en el cerebro humano (Pelvig et al., 2008). Los OLs son los responsables de la formación de las vainas de mielina que envuelven los axones de las neuronas proporcionándoles aislamiento para una rápida conducción de las señales eléctricas y soporte trófico. También se ha demostrado que poseen propiedades inmunomoduladoras, por lo que contribuyen activamente a la respuesta inmuno/inflamatoria en enfermedades neurológicas, como la esclerosis múltiple (EM) (Boccazzi et al., 2022; Harrington et al., 2020; Madeira et al., 2022). Esto es relevante para los trastornos neuropsiquiátricos dado que cada vez hay más evidencia de que la inflamación puede jugar un papel en su etiopatogenia (Yuan et al., 2019).

El linaje oligodendroglial se divide en cuatro estadios bien definidos: empieza por las células precursoras de OLs (OPCs, del inglés oligodendrocyte precursor cells), sigue con los pre-OLs (o OPCs tardías) y OLs inmaduros (o premielinizantes), y acaba con los OLs maduros (o mielinizantes) (Kuhn et al., 2019; Pruvost & Moyon, 2021). Durante su diferenciación los OLs van adquiriendo una morfología compleja (**Figura 5)** que se puede identificar por los biomarcadores implicados en cada una de ellas, y van perdiendo la capacidad de proliferar y migrar (Pruvost & Moyon, 2021).

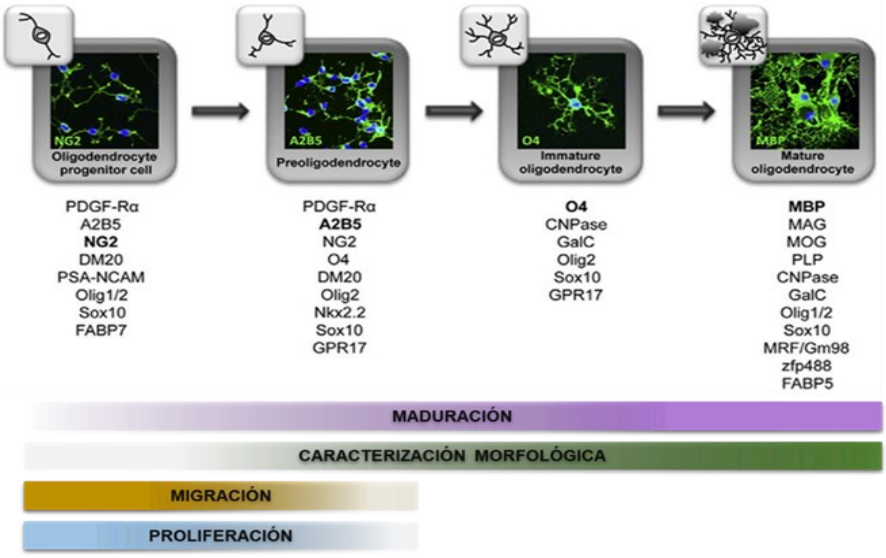

Figura 5. Fases de maduración de las células del linaje oligodendroglial

Células progenitoras de oligodendrocitos (OPCs), pre-oligodendrocitos, oligodendrocitos inmaduros y

oligodendrocitos maduros. Estos estadios son identificables según su morfología cada vez más compleja, el patrón de expresión de marcadores bien definidos, y su capacidad para proliferar, migrar y diferenciarse. CNPase, 2′,3′-nucleótido cíclico 3′-fosfodiesterasa; proteínas de unión a ácidos grasos (*FABP)*; galactocerebrósido C (*GalC*); glicoproteína asociada a mielina (*MAG*); proteína básica de mielina (*MBP*); glicoproteína de oligodendrocitos de mielina (*MOG*); factor regulador del gen de la mielina (*MRF*); factor de crecimiento derivado de plaquetas (PDGF-Rα); proteína proteolipídica (*PLP*); ácido polisiálico-molécula de adhesión celular neural (*PSA-NCAM*); proteínas zfp. Traducida y reproducida con el permiso de: Barateiro A, Fernandes A. Temporal oligodendrocyte lineage progression: in vitro models of proliferation, differentiation and myelination. (2014). *Biochim Biophys Acta*, 1843(9):1917-29.

La mielina producida por los OLs es una membrana lipídica que forma la materia blanca del cerebro. La evidencia reciente indica que la mielinización y remielinización son procesos prolongados y plásticos que continúan a lo largo de la edad adulta en el SNC (**Figura 6**). A su vez, la mielina es un modulador de las redes neuronales y un factor importante para el moldeamiento del aprendizaje y el comportamiento humanos (de Faria et al., 2021; Stadelmann et al., 2019). Las alteraciones en la mielina, la pérdida de mielina debido a una enfermedad, o la desmielinización en períodos críticos de la vida, pueden afectar la función cerebral y provocar una discapacidad grave según la extensión del daño y de las áreas de materia blanca que se vean afectadas. En este sentido, estudios recientes de neuroimagen han puesto de manifiesto alteraciones en la mielina en muchas enfermedades neurodegenerativas y trastornos psiquiátricos, entre ellos la ESQ y el TB (Koshiyama et al., 2020; Prins & Scheltens, 2015; Rizvi et al., 2021) Asimismo, estudios de transcriptoma (Mathys et al., 2019; Nagy et al., 2020) y GWAS (Zhao et al., 2021) también han evidenciado alteraciones en la expresión de genes codificantes de proteínas de mielina en estos trastornos.

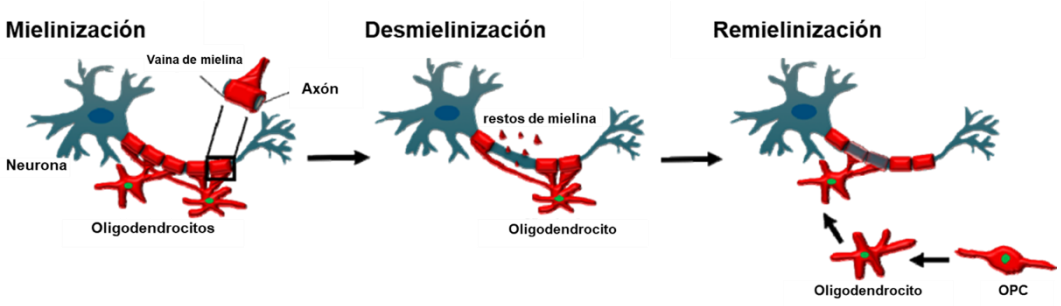

Figura 6. Oligodendrocitos en mielinización, desmielinización, y remielinizacion

Los OLs mielinizan axones de gran diámetro en el SNC y brindan apoyo trófico al axón subyacente. Los OLs son muy vulnerables y las agresiones como los traumatismos, los ataques inmunomediados o la isquemia pueden provocar su muerte y la desmielinización. Los OLs recién diferenciados derivados de un

grupo de OPCs adultas pueden reemplazar a los OLs perdidos, lo que puede restablecer la vaina de mielina alrededor de los axones desmielinizados (remielinización), aunque la mielina regenerada es más delgada que la vaina de mielina original. Traducida y reproducida con el permiso de: Kuhn S, Gritti L, Crooks D, Dombrowski Y. (2019). Oligodendrocytes in Development, Myelin Generation and Beyond. *Cells*, 12;8(11):1424.

4.1. Alteraciones en la expresión de genes de oligodendrocitos

Las fases de diferenciación y maduración de los OLs están reguladas por la expresión de factores de transcripción (FTs) que controlan la expresión de genes específicos del linaje oligodendroglial y de aquellos que codifican proteínas de la mielina (Pruvost & Moyon, 2021). También es muy relevante la regulación de la diferenciación y maduración de los OLs por mecanismos epigenéticos, y más concretamente por la metilación del ADN (mADN) (Arthur-Farraj & Moyon, 2020). En este sentido, una reducción en los perfiles de expresión tanto de genes relacionados con los OLs y la mielina como de varios FTs conocidos por coordinar la expresión de estos genes ha sido hallada tanto en la ESQ como en el TB. En concreto, se han encontrado niveles de expresión reducidos en *ERBB3, CNP, MBP, CLDN11, MAG, MPZL1, SOX10, PMP22, PLLP, PLP1, OLIG1* y *OLIG2*, en la ESQ (Dracheva et al., 2006; Iwamoto et al., 2005; Katsel et al., 2005; Tkachev et al., 2003), y en *GALC, MBP, MOG, OLIG2, PLP1,* y *SOX10* en el TB (Tkachev et al., 2003). En este último trabajo, Tkachev y colegas (Tkachev et al., 2003) demostraron que los cambios en la expresión en los genes analizados para ambos trastornos mostraron un alto grado de superposición.

4.2. Alteraciones en la microestructura de la materia blanca

La disfunción de los OLs y las alteraciones de la mielina en los trastornos psiquiátricos es congruente con los estudios neuroanatómicos de resonancia magnética que utilizan imágenes de tensor de difusión y que examinan la microarquitectura de la materia blanca del cerebro, formada mayoritariamente por los axones mielinizados. Los diferentes parámetros cuantificados en las imágenes por tensor de difusión, o sus combinaciones, se asocian con el grado de organización y mielinización de los tractos de fibras y con la integridad axonal. Los más importantes son la anisotropía fraccional, la difusividad media, la difusividad axial, y la difusividad radial (Pasternak et al., 2018).

Recientemente, dentro del consorcio internacional ENIGMA, el grupo de trabajo ENIGMA-DTI de ESQ realizó un metaanálisis a gran escala en 4 322 individuos, que reveló amplias

diferencias microestructurales de la materia blanca en pacientes con ESQ en comparación con controles sanos. Los autores encontraron reducciones generalizadas de anisotropía fraccional en 20 de 25 regiones, siendo debidas a anomalías periféricas de la sustancia blanca más que a alteraciones en regiones centrales específicas. La corona radiada anterior y el cuerpo calloso mostraron los mayores efectos. También se encontró un aumento generalizado en difusividad media y difusividad radial, sugiriendo que la reducción de anisotropía fraccional posiblemente se debiera a una mielinización aberrante en la mayoría de las regiones (Kelly et al., 2018).

Con respecto al TB, el mismo grupo llevó a cabo un metaanálisis en el que se incluyeron 3 033 individuos, donde se analizó la anisotropía fraccional media de 43 regiones de interés, y que reveló una anisotropía fraccional significativamente más baja en pacientes con TB en comparación con individuos sanos en 29 regiones, con los tamaños de efecto más altos observados dentro del cuerpo calloso y la circunvolución del cíngulo (Favre et al., 2019).

También hay evidencia de alteraciones de la materia blanca compartidas por ambos trastornos. En un reciente mega-análisis donde se comparó la microestructura de la materia blanca en 2 937 individuos en cuatro trastornos psiquiátricos graves, Koshiyama y colegas (Koshiyama et al., 2020) encontraron diferencias similares en la microestructura de la materia blanca en el cuerpo calloso y en el sistema límbico tanto en la ESQ como en el TB.

5. El gen del receptor dominio discoidina 1 (*DDR1*) y los trastornos mentales

El gen del receptor dominio discoidina 1 (*DDR1*) es un gen que codifica un receptor tirosina quinasa transmembrana cuyo ligando es el colágeno. Comprende 17 exones y abarca 12 kb de la secuencia genómica en la región p21.33 del cromosoma 6 (**Figura 7**). En el mismo locus se encuentran 4 genes de ARN. A –45.8 kb se encuentra el gen *LINC00243*, a –28.3 kb el gen *LINC02570,* ambos ARN largos no codificantes (lncRNA, del inglés long non-coding RNA). A –0.5 kb se encuentra el gen *DDR1-DT* (del inglés *DDR1* Divergent Transcript) cuyo producto de ARN hibrida con el intrón 9 de *DDR1.* Finalmente, solapado con el exón 4 se encuentra el gen *MIR4640* que pertenece a la clase de micro-ARN (miRNA, del inglés micro-RNA).

DDR1 se expresa en células epiteliales, particularmente en el riñón, pulmón, y tracto gastro intestinal, así como en el cerebro (Leitinger, 2014; Vilella et al., 2019). *DDR1*, también se encuentra altamente expresado en OLs en el SNC y su patrón de expresión muestra una alta correlación con la expresión de marcadores clásicos de mielina tanto en el cerebro humano (Muntané et al., 2021; Roig et al., 2012) como en el de ratón (Franco-Pons et al., 2006, 2009; Vilella, 2019). Además, varios estudios han demostrado la participación de *DDR1* en el inicio de la mielinización del cerebro (Vilella et al., 2019) y de los nervios periféricos (Corty et al., 2022).

Aunque hasta la fecha se han identificado más de 58 transcritos de *DDR1*, únicamente se han descrito cinco isoformas diferentes, *DDR1*a-e, de las cuales solo *DDR1*a, b y c tienen actividad tirosina quinasa (Alves et al., 2001) (**Figura 7**). La isoforma *DDR1*c es más abundante en el cerebro que en otros tejidos, y su expresión está fuertemente correlacionada con la expresión de genes de mielina como *MBP*, *MAG* o *OLIG2* (Roig et al., 2010; Roig et al., 2012). La isoforma *DDR1*b es la más abundante en el cerebro y en muchos tipos de células tumorales, la isoforma *DDR1*a es la más abundante en leucocitos circulantes (Kamohara et al., 2001), mientras que la isoforma *DDR1*e es la más abundante en linfocitos T activados (Hachehouche et al., 2010).

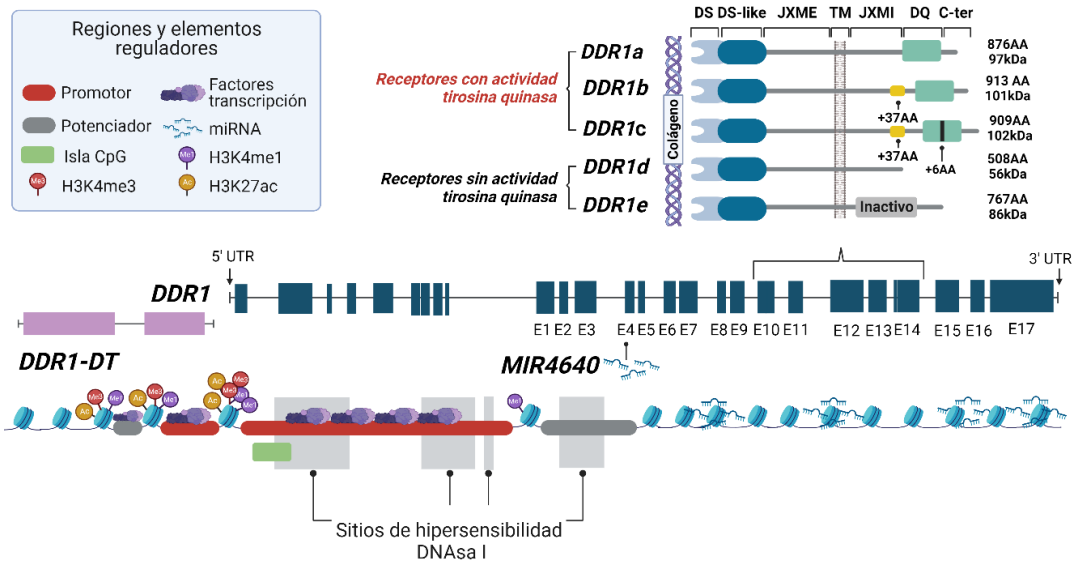

Figura 7. DDR1 humano e isoformas y regiones reguladoras

Representación genómica de *DDR1* humano y de sus regiones y elementos reguladores, y de los genes vecinos *DDR1-DT* y *MIR4640* según UCSC Genome Browser (Cromosoma 6. GRCh37. p12). *DDR1-DT* y *MIR4640* son genes que codifican ARN. Diagrama esquemático de las 5 isoformas

primarias de *DDR1* (a-e) generadas por el proceso de splicing alternativo del exón 10 al exón 14. Abreviaturas: AA: Aminoácido; C-ter: fragmento C-terminal; DQ: Dominio quinasa; DS: Dominio discoidina; DS-like: Dominio similar a la discoidina; JXME: Juxtamembrana extracelular; JXMI: Juxtamembrana intracelular; TM: Transmembrana. Creada con BioRender.com.

DDR1 ha sido ampliamente estudiado en cáncer (Tian et al., 2023) y en otras patologías, como la enfermedad dermatológica conocida como vitíligo (Almasi-Nasrabadi et al., 2019), o diversas afecciones fibróticas como la fibrosis hepática, renal, o pulmonar (Moll et al., 2019). También se han encontrado mutaciones recurrentes de *DDR1* en células de Schwann (análogas a los OLs en el sistema nervioso periférico) de tumores de pacientes con schwannomas (Agnihotri et al., 2016).

Con respecto a la asociación de *DDR1* con los trastornos psiquiátricos, previamente nuestro grupo encontró una asociación genética entre las variantes de *DDR1* y la ESQ en diferentes muestras españolas (Gas et al., 2019; Roig et al., 2007). Más recientemente, también se ha encontrado que las variantes de *DDR1* pueden conferir un riesgo de ESQ y disfunción cognitiva a través de alteraciones en la microestructura de la materia blanca del cerebro. En concreto, un estudio llevado a cabo por nuestro grupo encontró que los pacientes con ESQ portadores del genotipo de *DDR1* rs1264323AA mostraban una reducción de la anisotropía fraccional en algunas regiones de la materia blanca junto con una disminución de la velocidad de procesamiento cognitivo (Gas et al., 2019). Posteriormente, en un estudio con una muestra de pacientes con PI y un seguimiento de 10 años se observó que una combinación alélica de *DDR1* asociada al riesgo de ESQ se relacionó con una mejor velocidad de procesamiento en pacientes, pero no en controles (Gas et al., 2022). Estos resultados contradictorios reflejan la complejidad del impacto de las variantes genéticas en las manifestaciones fenotípicas. En relación a la expresión de *DDR1* en tejido cerebral postmortem de pacientes con ESQ nuestro grupo observó un aumento de la expresión de la isoforma *DDR1*c en comparación con individuos sanos (Roig et al., 2007). Sin embargo, el papel específico de cada isoforma en el SNC es desconocido.

A pesar de estos hallazgos, hacen falta más estudios, genéticos y epigenéticos, para avanzar en el conocimiento del papel de *DDR1* en la ESQ y en otros trastornos psiquiátricos, como el TB.

6. Epigenética

El término epigenética fue acuñado por primera vez por el biólogo Conrad H. Waddington en 1942 (Waddington, 2012), pero no sería hasta las décadas de 1990 y 2000 cuando el campo de la epigenética tendría su gran auge gracias a la aparición de técnicas bioquímicas y de clonación que permitieron la identificación de enzimas que podían añadir o borrar marcas epigenéticas en la cadena de ADN. De hecho, la identificación de de estas enzimas permitió la realización de experimentos genéticos y bioquímicos que aportaron conocimiento sobre el significado biológico de estas modificaciones (Peixoto et al., 2020).

A diferencia de la variación genómica que afecta la secuencia de ADN, los procesos epigenéticos consisten en cambios bioquímicos en el ADN o en sus proteínas y/o ARN asociados, que no cambian la secuencia de ADN en sí, pero permiten un sistema de control dinámico y de múltiples niveles que afecta a todas las etapas de la expresión génica (Gibney & Nolan, 2010). La mADN, la modificación de histonas, y el ARN no codificante (ncRNA, del inglés non-coding RNA), comprenden tres de los principales mecanismos de la maquinaria epigenética (**Figura 8**). La contribución de estos mecanismos epigenéticos a los fenotipos heredados entre generaciones ha sido controvertida durante muchos años. A pesar de ello, trabajos recientes han arrojado luz sobre las señales que subyacen a estas epimutaciones y los mecanismos por los cuales podrían transmitirse de generación en generación a nivel molecular (Fitz-James & Cavalli, 2022).

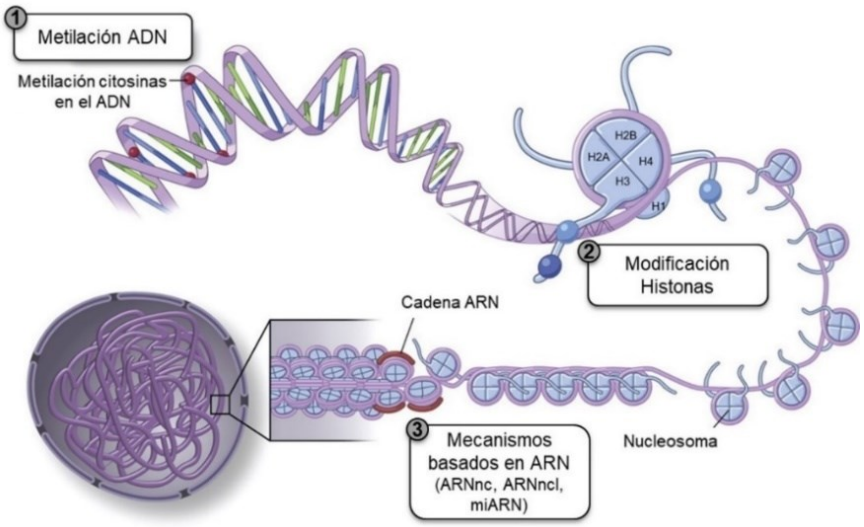

Figura 8. Mecanismos epigenéticos de regulación génica

Los mecanismos epigenéticos regulatorios de la expresión génica están conformados por tres mecanismos

distintos, aunque altamente interrelacionados. 1) La metilación del ADN se refiere a la adición de un grupo metilo a la posición 5 de la citosina en el contexto de los dinucleótidos CG para definir la "quinta base del ADN". 2) La unidad repetitiva fundamental de la cromatina es el nucleosoma compuesto por un octámero central de proteínas histonas. Las modificaciones posteriores a la traducción de las colas amino-terminales de las proteínas histonas (bolas azul claro y oscuro) y la densidad de estas proteínas por unidad de longitud de ADN pueden afectar de manera importante la estructura de la cromatina y constituir un supuesto "código de histonas". 3) Los mecanismos basados en ARN tienen un impacto en la estructura de orden superior de la cromatina. Se está estudiando cómo el ARN mensajero (ARNm), y específicamente el ARN no codificante (ARNnc), el ARN largo no codificante (ARNlnc), y el micro ARN (ARNmi), regulan la expresión génica. Traducida y reproducida con el permiso de: Yan MS, Matouk CC, Marsden PA. Epigenetics of the vascular endothelium. (2010). *J Appl Physiol*, 109(3):916-26.

Los cambios epigenéticos ocurren como una función del desarrollo normal (p.ej., en la diferenciación celular) pero también pueden darse en respuesta a una variedad de factores ambientales que incluyen: la dieta, la salud física, el estrés, y el trauma psicológico, entre otros, lo que genera cambios adaptativos a largo plazo en la expresión de los genes (Feil & Fraga, 2012).

6.1. Metilación del ADN (mADN)

La mADN es la modificación epigenética mejor estudiada, y se caracteriza por la adición de un grupo metilo (CH_3) al carbono 5' de un anillo de citosina (**Figura 9**), lo que da como resultado 5-metilcitosina (5mC). Esto ocurre principalmente en los llamados dinucleótidos citosina-fosfato-guanina (CpG), que son citosinas que preceden a las guaninas en la secuencia de ADN a lo largo de su dirección 5' → 3' (**Figura 9**). Los sitios CpG tienden a concentrarse en regiones cortas de ADN llamadas islas CpG ubicadas en las regiones promotoras de aproximadamente el 60% de los genes humanos (Moore et al., 2013).

La mADN en mamíferos es dinámica, cambia a lo largo de la vida, y desempeña un papel fundamental en la regulación del desarrollo, el silenciamiento de elementos retrovirales, la regulación de la expresión génica, la impronta genómica, la inactivación del cromosoma X (Moore et al., 2013), y en el funcionamiento y la supervivencia de las neuronas (Feng et al., 2007; Wheater et al., 2020). Por lo general, la mADN en la región promotora de un gen se correlaciona con el silenciamiento transcripcional, mientras que la desmetilación del ADN del promotor se correlaciona con el aumento correspondiente de la expresión del gen (Suzuki & Bird, 2008).

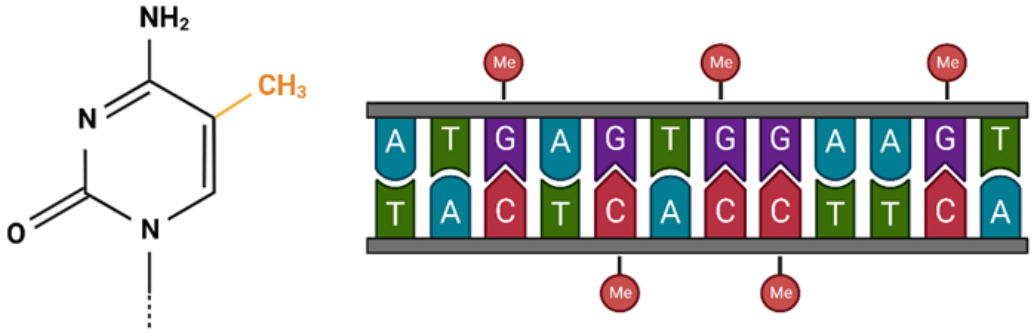

Figura 9. Metilación del ADN

La adición de un grupo metilo al carbono 5 de la citosina en los sitios CpG y otras secuencias de nucleótidos inhibe la unión de los factores de transcripción a los promotores. Abreviaturas: A: Adenina; C: Citosina; CH3: Grupo metilo; G: Guanina; CpG: Citosina-fosfato-guanina; Me: Metilación; T: Timina. Creada con BioRender.com.

6.2. Alteraciones en la mADN relacionadas con el estrés

El estrés produce cambios epigenéticos duraderos en la expresión génica en varias estructuras cerebrales que pueden conferir riesgos para el desarrollo de diferentes patologías del SNC, incluyendo los trastornos psiquiátricos (Stankiewicz et al., 2013).

En este sentido, estudios basados en modelos animales (Dion et al., 2022) y en humanos (Mourtzi et al., 2021) apuntan a una desregulación epigenética persistente causada por los cambios ambientales estresantes. Por ejemplo, en modelos murinos experimentales se ha demostrado que la negligencia en el cuidado a la progenie proporcionado por las madres se traduce en cambios en la mADN de genes de proteínas del eje hipotálamo-pituitario-adrenal (HPA) causando una desregulación de la respuesta al estrés (Dion et al., 2022). Asimismo, la mADN de los genes relacionados con la respuesta al estrés también se ha visto alterada en respuesta a la deprivación socioeconómica (Morris et al., 2019), al estrés perinatal (Szyf, 2019), la exposición a conflictos bélicos (Raza et al., 2023), y a experiencias traumáticas como el Holocausto (Bierer et al., 2020; Yehuda et al., 2016) o los ataques terroristas del World Trade Center de Nueva York (Kuan et al., 2021).

Como se ha comentado en la sección 2.3, la AVT puede suponer una forma severa de estrés y un factor de riesgo importante asociado a problemas graves de salud mental a lo largo de la vida (Kessler et al., 2010; McKay et al., 2021; Palmier-Claus et al., 2016;

Popovic et al., 2019). El mecanismo subyacente podría ser debido a los cambios en la mADN de genes implicados en los diversos trastornos psiquiátricos (Dunn et al., 2019; Fachim et al., 2021; Løkhammer et al., 2022; Lutz et al., 2017; Palmier-Claus et al., 2016; Parade et al., 2021; Turecki & Meaney, 2016).

El eje HPA es uno de los principales sistemas de respuesta al estrés y uno de los más estudiados en personas con antecedentes de AVT. Su activación conduce a la liberación de cortisol que es secretado en respuesta al estrés y que promueve la excitación y la atención, entre otros cambios fisiológicos. El cortisol también inhibe la estimulación adicional del eje HPA en un bucle de retroalimentación negativa. Las personas con historia de TI muestran una hiperactivación del eje HPA, y en consecuencia, un aumento en los niveles de cortisol (Turecki et al., 2019; Turecki & Meaney, 2016) que se ha relacionado con diversos trastornos mentales (Fachim et al., 2021; Klengel et al., 2013; McGowan et al., 2009; McIntyre et al., 2020; Miller & Black, 2020) y alteraciones en otros sistemas, como el sistema inmunitario y la respuesta inflamatoria (Chrousos, 2000; Igarashi et al., 2005).

En la última década los estudios epigenéticos han destacado el papel significativo de los cambios en la mADN en las secuelas de la exposición a la AVT. Los genes candidatos más estudiados han sido *NR3C1*, *FKBP5,* genes de señalización de la serotonina, entre ellos *SLC6A4*, que codifica el receptor transportador de la serotonina (5-HTT), *HTR2A,* que codifica el receptor de la serotonina subtipo 5-HT2A, y *OXTR,* el gen del receptor de la hormona pituitaria oxitocina (Parade et al., 2021). Pero a pesar de la asociación significativa entre la AVT y los cambios en la mADN, existe una variabilidad considerable en los hallazgos de estos estudios, mostrando un incremento de la mADN en aquellos individuos expuestos a AVT en unos casos, o una disminución de la mADN o ausencia de asociación con la AVT en otros. (Parade et al., 2021).

Por otro lado, a partir de estudios de asociación de epigenoma completo (EWAS, del inglés epigenome-wide association studies) se han identificado algunos genes que muestran consistencia con los hallados en estudios previos de genes candidatos. Concretamente, genes del desarrollo de células neurales (*BDNF, KITLG* y *POU3F1*), señalización y apoptosis (*LINGO3* y *2NPFF2*), trastornos del movimiento (*ALS2*), neuroinflamación (*ITGB1*), y alguna evidencia de marcadores inmunitarios (*CXCL1*) (Parade et al., 2021). En la **Figura 10** se puede ver un esquema más completo de los genes y sistemas implicados en la vía epigenética de la AVT en la salud física y mental.

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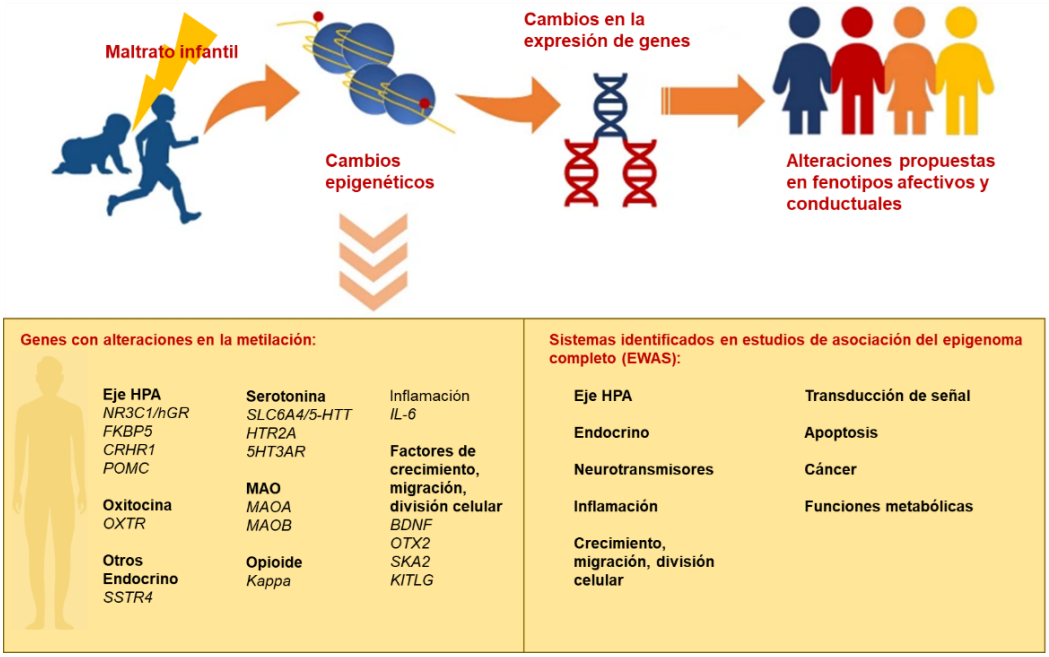

Figura 10. Alteraciones en la mADN relacionadas con la exposición a la AVT

Genes con alteraciones en la mADN a consecuencia de la exposición a la AVT y disfunción de sistemas implicados en la salud física y mental. Abreviaturas: AVT: Adversidad en la vida temprana; Eje HPA: eje hipotálamo-pituitario-adrenal; mADN: Metilación del ADN; MAO: Monoamino oxidasas. Traducida y reproducida con el permiso de: Parade SH, Huffhines L, Daniels TE, Stroud LR, Nugent NR, Tyrka AR. (2021). A systematic review of childhood maltreatment and DNA methylation: candidate gene and epigenome-wide approaches. *Transl Psychiatry*, 19;11(1):134.

6.3. *Alteraciones en la mADN en la esquizofrenia y el trastorno bipolar*

Los procesos epigenéticos no solo pueden mediar los efectos del riesgo ambiental en el desarrollo de los trastornos psiquiátricos, sino que también pueden interactuar con el riesgo genómico asociado con estos trastornos (Kumar et al., 2015; Montano et al., 2016).

Los primeros estudios con respecto a cambios en los patrones de mADN y su asociación con la alteración de la expresión génica en trastornos psiquiátricos, se llevaron a cabo desde un enfoque de gen candidato. Algunos de esos trabajos pusieron de relieve que la reducción de la transcripción de la proteína de matriz extracelular reelina (*RELN*) en el cerebro de las personas con ESQ (Grayson et al., 2005) y TB (Grayson et al., 2005; Guidotti et al., 2000; Tamura et al., 2007) podría deberse a la hipermetilación de su región promotora. A partir de ahí, se encontró que muchos otros genes estaban diferencialmente metilados (algunos hiper- y otros hypometilados) en tejido cerebral y periférico, incluidos genes implicados en funciones glutamatérgicas (*DTNBP1*, *GAD1*, *RELN*, GABAérgicas),

funciones dopaminérgicas (*DRD2*, *DRD3*, *DRD4, MB-COMT*, *COMT*, *RELN*, *DTNBP1*), funciones serotoninérgicas (*5-HTT*, *HTR1A*, *HTR2A*, *SLC6A4*), función inmunitaria (*FKBP5*, *CTLA4*), y el factor neurotrófico derivado del cerebro (*BDNF*) tanto en la ESQ (Magwai et al., 2021; Richetto & Meyer, 2021; Smigielski et al., 2020) como en el TB (Fries et al., 2016; Legrand et al., 2021; Ludwig & Dwivedi, 2016). Aquellos diferencialmente metilados en la ESQ, como el factor de transcripción de oligodendrocitos *SOX10* (Iwamoto et al., 2005; Magwai et al., 2021; Richetto & Meyer, 2021; Smigielski et al., 2020) y el gen que codifica el receptor de oxitocina *OXTR* (Bang et al., 2019; Magwai et al., 2021). Y finalmente, los genes *KCNQ3* (Fries et al., 2016) y *CACNA1C* (Starnawska et al., 2016) de los canales de potasio y calcio respectivamente, en el TB.

Por otro lado, los estudios del perfil de mADN de genoma completo han detectado numerosos sitios diferencialmente metilados entre pacientes con ESQ y TB y sus respectivos controles. Específicamente, se identificaron 2 104 sitios CpG diferencialmente metilados en la corteza prefrontal (CPF) de pacientes con ESQ en comparación con los sujetos del grupo control (Jaffe et al., 2015). Estos sitios CpG correlacionaban con cambios relacionados con la transición prenatal-postnatal y mostraron un enriquecimiento para genes relevantes para el desarrollo embrionario, el compromiso de destino celular, la diferenciación del sistema nervioso, y la plasticidad sináptica. También con loci de riesgo para la ESQ identificados en estudios de GWAS. Sin embargo, no se correspondieron con los sitios CpG que cambian los patrones de mADN en la adolescencia y la vida adulta, sugiriendo que el componente epigenético de las etapas tempranas del neurodesarrollo es más relevante en la ESQ. Algunos de los hallazgos basados en perfiles de mADN de genoma completo se superponen con los encontrados en los estudios de genes candidatos, es decir, genes como *RELN*, *COMT*, *DTNBP1,* y *SOX10* se han encontrado diferencialmente metilados en la ESQ (Richetto & Meyer, 2021).

En un estudio reciente se encontraron 39 039 sitios CpG diferencialmente metilados en pacientes con TB. Tras un análisis de enriquecimiento ontológico-funcional, los genes identificados sugirieron una desregulación glutamatérgica, y un mayor impacto en la sinaptogénesis y la plasticidad sináptica (Veldic et al., 2021). En otro trabajo que estudió perfiles de mADN de genoma completo en promotores de células neuronales y no-neuronales en la CPF de pacientes con TB, Bundo y colegas (Bundo et al., 2021) encontraron 987 regiones diferencialmente metiladas correspondientes a 664 genes, 90 de ellas hipermetiladas en células neuronales, y 1 296 regiones, 72 de ellas hipermetiladas, correspondientes a 948 genes en células no-neuronales. También observaron que un total de 63 regiones diferencialmente metiladas se superponían con

los loci de riesgo informados en el último GWAS realizado en TB (Mullins et al., 2021). Un análisis ontológico-funcional de los genes asociados a las regiones diferencialmente metiladas reveló un enriquecimiento de genes relacionados con funciones motoras en neuronas, genes relacionados con canales iónicos y transportadores en células no-neuronales, y quimiocinas en ambos tipos de células (Bundo et al., 2021).

Los cambios epigenéticos primarios también se han investigado en el TB mediante la evaluación de *DNMT1*, una enzima clave que mantiene el patrón de mADN en las divisiones celulares. Se ha descrito que la unión de *DNMT1* a los promotores de los genes *GAD67*, *RELN*, y *BDNF* aumenta en pacientes con TB en comparación con controles sanos independientemente del estado de metilación, lo que sugiere un posible vínculo entre las vías GABAérgicas y los cambios primarios de la mADN (Legrand et al., 2021).

También ha habido un incremento considerable de estos estudios en tejidos periféricos, como la sangre y la saliva, con el objetivo de descubrir biomarcadores para la ESQ y el TB en grandes cohortes. Sin embargo, el perfil epigenético periférico no necesariamente captura los cambios epigenéticos asociados a los trastornos que ocurren en el SNC. En este sentido, se ha evidenciado una baja superposición entre los hallazgos obtenidos en tejido cerebral y los hallados en tejidos periféricos (Richetto & Meyer, 2021). Por lo tanto, parece que las firmas epigenéticas periféricas no reflejan en gran medida las del SNC y viceversa, aunque siguen siendo válidas para la identificación de biomarcadores moleculares (Richetto & Meyer, 2021).

6.4. Alteraciones en la mADN en la conducta suicida

La mayor parte de estudios epigenéticos que investigan la CS se han centrado en marcas epigenéticas presumiblemente estables, como la mADN, que se cree actúan distalmente (**Figura 11**). Asimismo, como los cambios en la mADN se asocian con las respuestas genómicas a los estímulos ambientales, y debido a que la CS está fuertemente asociada con la exposición al TI (Sahle et al., 2022), gran parte del esfuerzo inicial para investigar los factores epigenéticos asociados con la CS se ha centrado en individuos con historia de TI (Turecki & Meaney, 2016; Turecki et al., 2019). En este sentido, los estudios de genes candidatos para la CS se han focalizado predominantemente en los sistemas de monoaminas, incluidos los sistemas serotoninérgicos (*TPH2*, *SLC6A4*, 5-*HT*2A) (Cheung et al., 2020; Turecki et al., 2019), el eje HPA (*FKBP5*, *NR3C1*, *SKA2*) (Cheung et al.,

2021; Clive et al., 2016, Kaminsky et al., 2015; Mirza et al., 2022; Shade et al., 2016; Turecki, 2019), genes implicados en funciones glutamatérgicas (*DTNBP1*, *GAD1*, *RELN*, genes relacionados con el GABA) (Turecki et al., 2019), genes implicados en el funcionamiento neurotrófico/neuroplástico (*BDNF, GDNF)* (Mirza et al., 2022; Turecki et al., 2019), y en la respuesta inmunitaria/inflamatoria (*TNFalfa*, *IL-1*) (Turecki et al., 2019), observándose alteraciones de la mAND muy diversas.

Por otro lado, los estudios de EWAS aportan resultados contradictorios, ya sea que no informan de diferencias significativas en la metilación de genes entre casos de suicidio y controles, o lo hacen de diferentes cambios incluyendo hiper e hipometilación (Cheung et al., 2020; Mirza et al., 2022), siendo necesarios más estudios para replicar los resultados y arrojar luz sobre la importancia biológica de estas asociaciones epigenéticas que sigue sin estar clara.

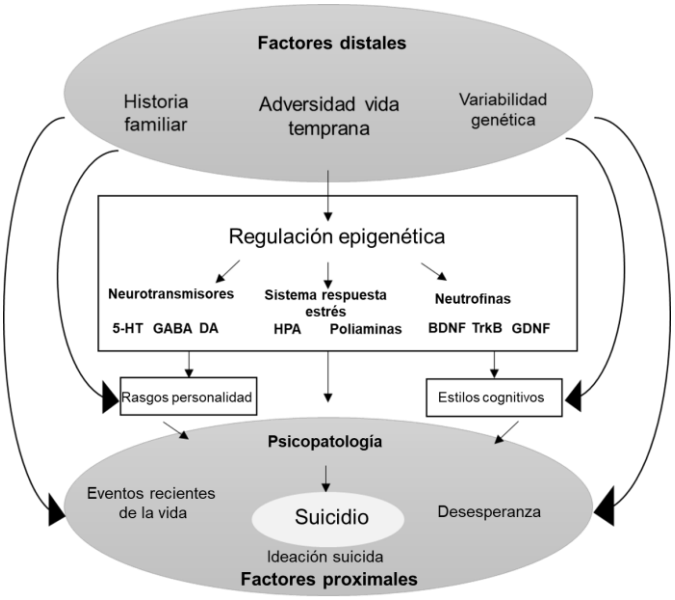

Figura 11. Factores epigenéticos distales en el suicidio y la conducta suicida

BDNF: Factor neurotrófico derivado del cerebro; DA: Dopamina; GABA: ácido γ-aminobutírico; GDNF: Factor neurotrófico derivado de células gliales; HPA: Eje hipotálamo-hipófisis-suprarrenal; HT: Hidroxitriptamina; TrkB: Tirosina quinasa B. Traducida y reproducida con el permiso de: Turecki G. (2014). Epigenetics and suicidal behavior research pathways. *Am J Prev Med*, 47(3 Suppl 2):S144-51

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Beatriz García Ruiz

II. HIPÓTESIS Y OBJETIVOS

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Hipótesis general

El estrés psicológico y la exposición a la AVT, representada por el TI, pueden inducir alteraciones en el patrón de mADN de genes que codifican para proteínas relevantes para el proceso de mielinización como *DDR1*.

Los patrones de mADN de *DDR1* en sangre y en cerebro serán diferentes en pacientes con diagnóstico de trastornos del espectro de la esquizofrenia y otras psicosis o trastorno bipolar comparado con sus respectivos controles.

En particular, se propusieron **siete hipótesis específicas** para abordar nuestra hipótesis general:

(i) Los patrones de mADN de *DDR1* en sangre en pacientes con PI y TB en fase eutímica (TBe) se encontrarán alterados al ser comparados con controles sanos.

(ii) Los patrones de mADN de *DDR1* en el cerebro de pacientes con ESQ y TB se encontrarán alterados al ser comparados con controles sanos.

(iii) *DDR1* cometilará con genes de marcadores convencionales de mielina.

(iv) La mADN de *DDR1* se asociará con la expresión del gen y de sus isoformas en el tejido cerebral de pacientes con ESQ y TB.

(v) El estrés psicológico y fisiológico, y el TI se asociarán con la mADN de *DDR1* en sangre en pacientes con PI.

(vi) El TI se asociará con la mADN de *DDR1* en sangre en pacientes con TBe y con la CS.

(vii) Los sitios CpG de *DDR1* diferencialmente metilados en la PI, la ESQ y el TB se encontrarán en secuencias de unión de factores de transcripción relevantes para la expresión de *DDR1* en el tejido de estudio.

Objetivos específicos

Para abordar estas siete hipótesis específicas, se desarrollaron los siguientes objetivos llevados a cabo en los tres artículos que conforman esta tesis doctoral:

Artículo 1

Objetivo 1. Estudiar los patrones de mADN de la región promotora de *DDR1* en leucocitos periféricos procedentes de una muestra de pacientes con un diagnóstico de PI (<3 años de evolución) y controles sanos.

Objetivo 2. Replicar los resultados del objetivo 1 en tejido cerebral postmortem procedente de la corteza prefrontal dorsolateral (CPFDL) en una muestra de pacientes con ESQ y controles sanos.

Objetivo 3. Estudiar si la mADN de *DDR1* influye en la expresión del gen y de sus isoformas en tejido cerebral postmortem CPFDL de pacientes con ESQ y controles sanos.

Objetivo 4. Analizar la asociación entre la mADN de la región promotora de *DDR1* en leucocitos periféricos y (a) estrés psicológico percibido, acontecimientos vitales estresantes, y TI; (b) estrés fisiológico (niveles de cortisol en saliva); y (c) la inflamación (NLR, índice neutrófilo/linfocito) en la muestra de pacientes con PI y controles sanos.

Artículo 2

Objetivo 1. Estudiar los patrones de mADN de *DDR1* en tejido cerebral postmortem procedente de la corteza occipital (CO) de una muestra de pacientes con diagnóstico de TB y controles sanos.

Objetivo 2. Replicar los resultados del objetivo 1 en dos muestras independientes de tejido cerebral postmortem procedente de la CPFDL y de núcleos aislados de células neuronales (NeuN+) de la corteza frontal (CF) de pacientes con TB y controles sanos.

Objetivo 3. Estudiar si la mADN de *DDR1* influye en la expresión del gen y de sus isoformas en tejido cerebral postmortem procedente de la CO de pacientes con TB y controles sanos.

Objetivo 4. Estudiar la correlación entre los patrones de mADN del gen *DDR1* y los de un conjunto de genes de mielina (*CNP, CSPG4, GALC, MAG, MBP, OLIG1, OLIG2, PDGFRA,* y *SOX10*) y otros marcadores específicos de neuronas, astrocitos, y microglía en tejido cerebral postmortem procedente de la CO de pacientes con TB y controles sanos.

Artículo 3

Objetivo 1. Estudiar los patrones de mADN de la región promotora de *DDR1* en leucocitos periféricos procedentes de (a) una muestra de pacientes con TBe y controles sanos; y (b) el grupo de pacientes estratificados en base a la presencia/ausencia de CS.

Objetivo 2. Analizar la asociación de la mADN de la región promotora de *DDR1* en leucocitos periféricos y el TI con el diagnóstico en la muestra de pacientes con TBe y controles sanos, y con la CS en el grupo de pacientes.

Objetivo 3. Explorar los efectos de la mADN de *DDR1* que podrían estar mediando la relación entre el TI y la CS.

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III. RESUMEN GLOBAL DE RESULTADOS

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ARTÍCULO 1

Garcia-Ruiz B, Moreno L, Muntané G, Sánchez-Gistau V, Gutiérrez-Zotes A, Martorell L, Labad J, Vilella E. Leukocyte and brain *DDR1* hypermethylation is altered in psychosis and is correlated with stress and inflammatory markers**.** *Epigenomics*. 2020;12(3):251-265.

OBJETIVOS

1. Comparar los niveles de mADN de *DDR1* en leucocitos periféricos entre pacientes con PI y controles sanos.
2. Validar este resultado en tejido cerebral de la CPFDL de pacientes con ESQ y sus respectivos controles.
3. Probar si los niveles de mADN de *DDR1* influyen en la expresión del gen y de sus isoformas en el tejido cerebral de pacientes con ESQ.
4. Explorar si el estrés (psicológico y fisiológico), y la inflamación están relacionados con la mADN de *DDR1* en la PI.

METODOLOGÍA

Se llevó a cabo un diseño transversal de caso-control. La muestra de sangre incluyó 60 pacientes con diagnóstico de PI y 40 controles sanos. Todos los participantes fueron entrevistados y se recogieron los siguientes datos: confirmación del diagnóstico DSM-IV; datos sociodemográficos, clínicos, medicación psiquiátrica y uso de sustancias, sintomatología psicótica, remisión de síntomas psicóticos, síntomas depresivos, exposición a la AVT (TI), acontecimientos vitales estresantes, y estrés psicológico percibido. Se accedió a una muestra de saliva para determinar los niveles de cortisol, y a una muestra de sangre y a ADN leucocitario para la cuantificación de los niveles de mADN en 43 sitios CpG de *DDR1* mediante la tecnología EpiTYPER MassARRAY. De la muestra para hemograma se obtuvo el recuento de neutrófilos y linfocitos para calcular el NLR como biomarcador de inflamación. Una segunda muestra consistente en tejido cerebral de la CPFDL incluyó a 35 pacientes con ESQ y 34 controles sanos de la que se disponía de datos sociodemográficos, edad de inicio y duración de la enfermedad, historia de uso de antipsicóticos y sustancias, estatus de suicidio, intervalo postmortem (PMI), pH cerebral, número de integridad del ARN (RIN), concentraciones de ARNm de *DDR1*a, b y c, datos de genotipado de SNPs de *DDR1* (rs1264323, rs2267641, rs2844654) determinados por ensayos de expresión génica TaqMan, y niveles de mADN en 43 sitios CpG de *DDR1* cuantificados mediante la tecnología EpiTYPER MassARRAY.

Análisis estadístico

El análisis de datos y la preparación de gráficos y figuras se llevó a cabo mediante los programas estadísticos SPSS, R, y GraphPad Prism. El nivel de significación se fijó en $p < 0.05$ para todos los análisis. Los métodos de ajuste Benjamini & Hochberg (BH) y Bonferroni se utilizaron para controlar las comparaciones múltiples en los análisis de mADN diferencial y asociación, respectivamente. Para comparar variables entre grupos se realizaron pruebas T, Mann-Whitney, y $\chi 2$. El análisis de mADN diferencial entre pacientes y controles se llevó a cabo mediante la prueba de Mann-Whitney. Se comprobó la correlación de variables en un análisis bivariado mediante correlaciones de Spearman, y el análisis de asociación para determinar las variables asociadas con la mADN de *DDR1* se llevó a cabo mediante modelos de regresión lineal. Se obtuvieron los datos de secuencias reguladoras en el locus *DDR1* de la Enciclopedia de Elementos del ADN (ENCODE) y de la base de datos Open Regulatory Annotation (ORegAnno).

RESULTADOS

Hipermetilación de DDR1 en sangre en pacientes con PI y en tejido cerebral en pacientes con ESQ

La exploración de los patrones de mADN de *DDR1* reveló que en comparación con los participantes del grupo control, los pacientes con PI mostraban un aumento de los niveles de mADN en leucocitos periféricos en dos sitios CpG (cg19215110 y cg23953820) de la región promotora del gen que se encuentran en secuencias de unión de factores de transcripción importantes para la transcripción, la diferenciación celular, y la regulación del estrés y el sistema inmunitario. Este resultado se replicó en uno de los sitios CpG (cg23953820) en una muestra de tejido cerebral postmortem procedente de la CPFDL de pacientes con ESQ cuando fueron comparados con controles.

Asociación de la mADN de DDR1 con su expresión en tejido cerebral en la ESQ

El estudio de la CPFDL de pacientes con ESQ mostró una relación inversa entre los niveles de mADN de *DDR1* en un sitio CpG de la región promotora (cg14279856) y la expresión de la isoforma *DDR1*c, así como una relación directa entre la expresión de la isoforma *DDR1*b y la mADN en un sito CpG (CpG 1_3) del promotor del gen *DDR1-DT.*

Asociación de la mADN de DDR1 en sangre con el estrés y la inflamación en la PI

El estudio de la muestra de pacientes con PI y controles reveló que un sitio CpG (cg19215110) se asoció con el estrés psicológico y psicosocial que reportan los pacientes

con PI. Por otro lado, el cortisol salival se correlacionó negativamente con los niveles de metilación en un sitio CpG (cg24727290) en el grupo de pacientes. Además, el NLR se asoció positivamente con la mADN de los sitios cg19215110 y cg23953820 en pacientes. Asimismo, los pacientes con un NLR más alto presentaron un aumento de los niveles de mADN en comparación con los controles. Finalmente, la mADN de *DDR1* en su región promotora se asoció con el diagnóstico de PI y de ESQ.

ARTÍCULO 2

Garcia-Ruiz B, de Moura MC, Muntané G, Martorell L, Bosch E, Esteller M, J Canales-Rodríguez E, Pomarol-Clotet E, Jiménez E, Vieta E, Vilella E. *DDR1* methylation is associated with bipolar disorder and the isoform expression and methylation of myelin genes. *Epigenomics*. 2021;13(11):845-858.

OBJETIVOS

1. Comparar los niveles de mADN de *DDR1* en tejido cerebral entre pacientes con TB y controles sanos en diferentes conjuntos de datos.
2. Probar si los niveles mADN de *DDR1* alteran la expresión del gen y de sus isoformas en el cerebro de pacientes con TB.
3. Evaluar la cometilación de *DDR1* con un conjunto seleccionado de genes de mielina en el cerebro humano adulto para respaldar el papel de *DDR1* en el proceso de mielinización.

METODOLOGÍA

Se llevó a cabo un diseño transversal de caso-control. La muestra fue conformada por tejido cerebral de la CO de 15 pacientes con diagnóstico de TB y 15 controles sanos de los que se disponía de datos sociodemográficos, edad de inicio y duración de la enfermedad, historia de uso de antipsicóticos y sustancias, estatus de suicidio, PMI, pH cerebral, RIN, concentraciones de ARNm de *DDR1*a, b y c, y datos de genotipado de SNPs de *DDR1* (rs1264323, rs2267641, rs2844654) determinados por ensayos de expresión génica TaqMan. Se determinaron los perfiles de mADN de genoma completo mediante la plataforma Illumina Infinium Methylation EPIC BeadChip 850k. Se incluyeron dos grupos de datos de metiloma y transcriptoma para validación de resultados conformados por tejido cerebral de la CPFDL de 4 pacientes con TB y 4 controles sanos, y núcleos neuronales aislados de la CF de 26 pacientes con TB y 27 controles sanos.

Análisis estadístico

El análisis de datos y la preparación de gráficos y figuras se llevaron a cabo mediante los programas estadísticos SPSS y R. El nivel de significación para los análisis de correlación, mADN diferencial, y asociación se fijó en $p < 0.05$ y el método de ajuste de BH se utilizó para controlar las comparaciones múltiples. El preprocesamiento de los datos de mADN se llevó a cabo mediante el paquete "minfi" de R/Bioconductor. Se utilizó el Método *in silico* de Deconvolución Epigenómica (EDec) para obtener la proporción de los tipos de células del tejido cerebral. Se llevaron a cabo correlaciones de Spearman para el análisis bivariado y de cometilación. El análisis de mADN diferencial entre pacientes y controles y los análisis de asociación se realizaron mediante modelos de regresión lineal. Se obtuvieron los datos de secuencias reguladoras en el locus *DDR1* de ENCODE y de la base de datos ORegAnno.

RESULTADOS

Alteración de patrones de mADN de DDR1 en tejido cerebral en pacientes con TB

El análisis de mADN diferencial de *DDR1* controlado por la proporción de células gliales mostró un aumento de los niveles de mADN en dos sitios CpG (cg01936707 y cg22485298) en pacientes cuando se compararon con controles, uno de ellos (cg22485298) en la misma región promotora descrita en el artículo 1. En las muestras de replicación, no se encontraron diferencias significativas en la mADN entre grupos ni en tejido de la CPFDL, ni en NeuN+, aunque se observó una tendencia a la hipermetilación y a la hipometilación, respectivamente, en el grupo de pacientes.

Asociación de la mADN de DDR1 con su expresión en pacientes con TB

Los pacientes con diagnóstico de TB presentaron una disminución de los niveles de expresión de la isoforma *DDR1*b, que, a su vez, se asoció positivamente con la mADN del gen en un sitio CpG (cg25943433) y negativamente con el genotipo AC del SNP rs2267641. La expresión del ARNm total de *DDR1* y de sus isoformas *DDR1*a, -c, -d y -e se asoció inversamente con la mADN del gen en diferentes sitios CpG, pero en ningún caso se observó mADN diferencial en el grupo de pacientes. En las muestras de replicación, de las que sólo se disponía de la expresión total de *DDR1*, se encontró que el ARNm total se asoció directamente con el sitio CpG cg01598675 y mostró una relación inversa con el diagnóstico de TB. En las muestras de tejido de la CPFDL no se encontró asociación entre la mADN de *DDR1* y su expresión. Finalmente, todos los sitios CpG de *DDR1* que presentaron resultados significativos relevantes en el estudio se encontraron

en secuencias de unión de DNasa I, *POLR2A*, y sitios de unión de acetilasas y metilasas de histonas. Todo ello indica que estos sitios CpG están implicados en la regulación de la transcripción. Además, también se superponen con regiones de unión de factores de transcripción importantes para la expresión del gen.

Cometilación de DDR1 con genes de mielina

La comparación de los patrones de mADN de *DDR1* con los de los genes de mielina demostró que *DDR1* cometila con OLIG1 y SOX10, factores de transcripción de OLs, y con *CNP*, *MAG*, *MBP*, y *PDGFRA*, que codifican proteínas relevantes de OLs y componentes importantes para la síntesis y el mantenimiento de la mielina. El patrón de cometilación en la muestra de pacientes con TB resultó ligeramente diferente al de los controles sanos.

Falta el resumen de resultados del Artículo 3; contenido confidencial.

UNIVERSITAT ROVIRA I VIRGILI
RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
Beatriz García Ruiz

IV. PUBLICACIONES

UNIVERSITAT ROVIRA I VIRGILI
RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
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Leukocyte and brain DDR1 hypermethylation is altered in psychosis and is correlated with stress and inflammatory markers.

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UNIVERSITAT ROVIRA I VIRGILI
RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
Beatriz García Ruiz

Research Article

Epigenomics

Leukocyte and brain *DDR1* hypermethylation is altered in psychosis and is correlated with stress and inflammatory markers

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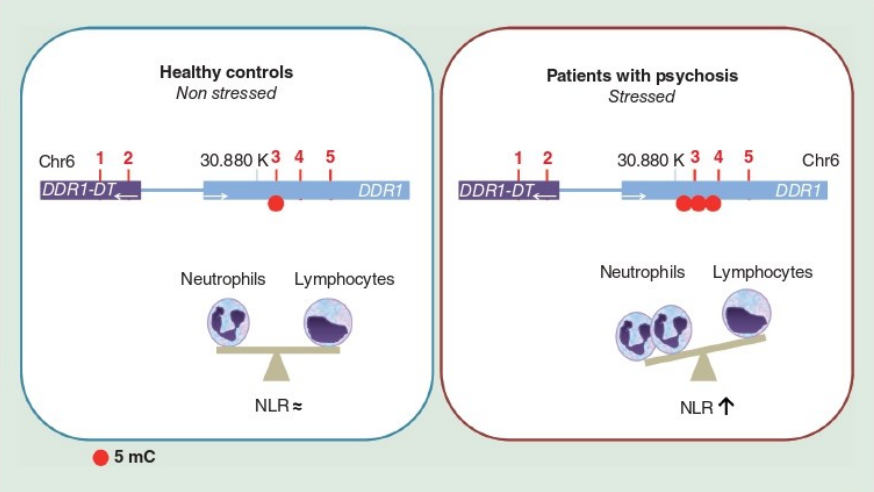
Aim: To investigate *DDR1* methylation in blood and brain DNA in psychosis and its relationship with stress markers. **Materials & methods:** Saliva cortisol, blood neutrophil and lymphocyte counts, leukocyte DNA and psychological variables were collected from 60 patients with nonaffective psychosis and 40 healthy controls (HC). Brain dorsolateral prefrontal cortex DNA from 35 patients with schizophrenia and 34 HC was studied. *DDR1* methylation at 43 CpG sites was measured using the MassARRAY EpiTYPER platform. **Results:** We describe leukocyte DDR1 hypermethylation in patients with psychosis compared with HC; this hypermethylation is associated with psychological stress, neutrophil-to-lymphocyte ratios, and, in the dorsolateral prefrontal cortex, *DDR1* methylation correlated with *DDR1* isoform expression. **Conclusion:** We confirmed a relationship between stress and blood and brain *DDR1* methylation in psychosis.

Graphical abstract:



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Keywords: cortisol • *DDR1* • early psychosis • methylation • NLR • psychological stress • schizophrenia

Future Medicine

DDR1 is a tyrosine kinase membrane receptor expressed in epithelial cells, particularly in the kidney, lung and GI tract, and in endothelial cells in the brain [1,2]. *DDR1* is highly expressed in CNS oligodendrocytes, and its expression parallels that of many myelin proteins [1,3]. Moreover, recurrent mutations in *DDR1* have been found in the Schwann cells (the PNS counterparts of oligodendrocytes) of tumors from patients with schwannomas [4]. We previously found a genetic association between *DDR1* variants and schizophrenia in two Spanish samples [5,6]. Although more than 30 *DDR1* transcripts have been identified to date only five different isoforms are described, DDR1a–e, of which only DDR1a, b and c have kinase activity [7]. The *DDR1*c isoform is more abundant in the brain than in other tissues, and its expression is strongly correlated with that of myelin genes [3,8]. The *DDR1*b isoform is the most abundant in the brain and many tumor cell types, and isoform a is the most abundant in circulating leukocytes [9], whereas isoform e is the most abundant in activated T lymphocytes [10]. We have described the increased expression of the *DDR1*c isoform in brain samples from schizophrenic patients compared with controls [11]. However, the specific role of each isoform has not been deciphered.

Schizophrenia is a severe psychiatric disorder caused by genetic and environmental factors. Child maltreatment and stressful life events are among the environmental factors most frequently associated with psychiatric illnesses and specifically with psychosis [12,13]. Interestingly, experiencing environmental stress has been related to changes in genome-wide methylation patterns in brain tissue [14], including changes in the methylation of the well-studied glucocorticoid receptor gene [15]. Notably, the natural regulation of myelination is in part exerted by changes in methylation at myelin protein-coding genes [16,17]. Therefore, environmental factors can influence the methylation of myelin genes and, as a consequence, the myelination process. Psychosis has recently been associated with an increase in blood and brain stress and inflammation biomarkers [18,19]. However, whether this increase is a cause or consequence of the psychiatric illness remains unknown. Additionally, whether there is a net effect of DNA methylation on this phenomenon remains elusive. One hypothesis is that psychological stress leads to hypothalamic–pituitary–adrenal (HPA) axis dysregulation, partially by DNA methylation and triggering an increase in stress and inflammatory biomarkers. Such a mechanism would be especially important in subjects with a high number of environmental stressors and/or high genetic vulnerability to environmental stress. Notably, *DDR1* methylation at CpG cg08469255 was found in a biosignature of stress state, which, in turn, was correlated with inflammatory biomarkers in several cohorts of patients at risk for depression and suicide [20]. Unfortunately, data on *DDR1* methylation in psychiatric disorders are scarce.

The primary objective of the present study was to compare the levels of leukocyte DNA methylation as 5-methyl cytosine (5-mC) at the *DDR1* locus between patients with early psychosis and healthy controls (HC) and to explore whether psychological and physiological stress and inflammation biomarkers are related to *DDR1* methylation. The second objective was to validate the findings observed in leukocytes in brain by comparing the levels of *DDR1* 5-mC in the dorsolateral prefrontal cortex (DLPFC) between patients with a diagnosis of schizophrenia and HC. A third objective was to test whether levels of *DDR1* 5-mC influence isoform gene expression in brain tissue; finally, we compared whether the *DDR1* methylation pattern in peripheral blood leukocytes compares to the pattern in brain tissue.

Materials & methods

Subjects

Blood sample set

The sample consisted of 60 outpatient subjects attending our Early Psychosis Intervention Program at the Hospital Universitari Institut Pere Mata (Reus, Spain) and 40 HC recruited between 2012 and 2014 [21]. All participants were Caucasian and aged between 18 and 37 years (Table 1). The patients had diagnoses of recent onset psychosis (<3 years) and fulfilled the diagnostic and statistical manual of mental disorders (DSM)-IV criteria for psychotic disorder not otherwise specified (78.3%), schizophreniform disorder (11.7%), paranoid schizophrenia (6.7%) and simple schizophrenia (3.3%). Patients with a diagnosis of affective psychosis were excluded. HC were matched by age and sex and were recruited from the community using advertisements. A trained psychiatrist screened these individuals to rule out past or current history of psychiatric disorders (by direct interviewing using Structured Clinical Interview for DSM-IV).

The exclusion criteria for all participants were pregnancy or puerperium, language difficulties, visual and hearing impairment, intellectual disability, severe head injury or medical disease, treatment with corticoids or contraceptive

Table 1. Blood sample set description.

Characteristic	Patients	Controls	p-value
Sociodemographic data			
N	60	40	
Female gender, N (%)	30 (50)	20 (50)	NS
Age (years), means ± SD	24.3 ± 4.6	24.8 ± 5.4	NS
Substance use (at least 1 × per week), N (%)			
Tobacco	43 (71.7)	11 (27.5)	1.3×10^{-5}
Coffee	33 (55.0)	27 (67.5)	NS
Cannabis	14 (23.3)	3 (7.5)	4.0×10^{-2}
Alcohol	22 (36.7)	15 (37.5)	NS
Cocaine	3 (5.0)	0 (0)	NS
Ecstasy	1 (1.7)	0 (0)	NS
Clinical features			
PANNS total score, mean ± SD	57.6 ± 17.9	–	NA
Remission, N (%)†	24 (40.0)	–	NA
CDSS score, mean ± SD	2.2 ± 3.7	–	NA
Antipsychotic dose (mg/day), mean ± SD†	256.6 ± 434.9	–	NA
Benzodiazepine dose (mg/day), mean ± SD†	1.3 ± 4.3	–	NA
Biperidene dose (mg/day), mean ± SD†	0.3 ± 1.0	–	NA
Psychological stress			
CTQ dimensions, mean ± SD;			
– Emotional abuse	11.0 ± 5.6	7.0 ± 2.7	5.0×10^{-5}
– Physical abuse	6.9 ± 3.2	5.4 ± 1.5	9.0×10^{-3}
– Sexual abuse	5.7 ± 1.8	5.1 ± 0.6	6.0×10^{-2}
– Emotional neglect	11.2 ± 5.0	7.7 ± 3.2	1.0×10^{-4}
– Physical neglect	7.6 ± 3.0	5.6 ± 1.1	1.0×10^{-4}
CTQ total score, mean ± SD	42.4 ± 14.2	30.8 ± 6.8	5.0×10^{-6}
HR-SRRS score, mean ± SD	154.9 ± 104.6	113.9 ± 102.8	NS
PSS, mean ± SD	23.9 ± 10.1	18.6 ± 7.7	6.0×10^{-3}
Stress and inflammation biomarkers			
Saliva cortisol (nmol/l), mean ± SD	23.6 ± 11.1	25.5 ± 10.4	NS
NLR, mean ± SD	1.9 ± 0.9	1.4 ± 0.6	2.0×10^{-2}

†See Materials and methods section.
CTQ: Childhood trauma questionnaire; CDSS: Calgary depression scale for schizophrenia; HR-SRRS: Holmes–Rahe's Social Readjustment Rating Scale; NA: Not applicable; NLR: Neutrophil-to-lymphocyte ratio; NS: Not significant; PANNS: Positive and negative syndrome scale; PSS: Perceived stress scale; SD: Standard deviation.

pill use in the previous 3 months, Type 1 diabetes mellitus and a diagnostic of substance dependence (other than tobacco or cannabis) according to DSM-IV.

All procedures were in accordance with the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee (CEIm IISPV, www.iispv.cat). All subjects consented to participate in the study and signed an informed consent form after a complete explanation of all procedures.

Clinical assessment

Sociodemographic and clinical variables were assessed by semistructured interview as described elsewhere [21]. All patients were interviewed by a trained psychiatrist with the Spanish adaptation of the Schedules for Clinical Assessment in Neuropsychiatry [22]. The operational criteria checklist (OPCRIT) version 4.0 was used to arrive at DSM-IV diagnoses. To assess the severity of psychotic symptoms, we used the Spanish adaptation of the Positive and Negative Syndrome Scale (PANSS) [23]. Clinical remission from psychotic symptoms was calculated as previously suggested [24], and patients were categorized with or without remission. The Calgary Depression Scale for Schizophrenia (CDSS) [25] was used to assess depressive symptoms. Doses of antipsychotic drugs were converted to chlorpromazine equivalents (in mg/day) [26], doses of benzodiazepine drugs were converted to diazepam equivalents (in mg/day) according to the Drug and Alcohol Services of the Government of South Australia (2014), and doses

of anticholinergic drug were reported as biperidene in milligram per day. Substance use was also assessed by semistructured interviews. Current substance use was defined as at least weekly.

Stress assessment

Childhood trauma was assessed with the Childhood Trauma Questionnaire (CTQ) [27]. This questionnaire is a 28-item selfreport inventory that provides a retrospective assessment of five subdimensions of childhood maltreatment: emotional, physical and sexual abuse, and emotional and physical neglect, as well as an overall measure of childhood trauma during childhood and adolescence. The Spanish adaptation of the Holmes–Rahe's Social Readjustment Rating Scale (HR-SRRS) [28] was used as a measure of psychosocial stress. This scale has 43 items of the life events of the past 6 months, and its advent is either indicative of or requires a significant change in the ongoing life pattern of an individual [29]. The Perceived Stress Scale (PSS) [30] was used to assess the psychological perception of stress. This instrument is a 14-item selfreport questionnaire designed to measure the degree to which the situations in one's life are appraised as stressful. Subjects indicate how often they have found their lives unpredictable, uncontrollable and overloaded in the last month.

Blood & saliva procedures & analyses

The participants were instructed to collect saliva samples using Salivette® tubes (Sarstedt AG & Co., Nümbrecht, Germany) immediately before a blood withdrawal (between 9:00 and 12:00 h). Then, a fasting blood sample was obtained by antecubital needle venipuncture and collected in appropriated vacuum tubes containing anticoagulant. A fresh blood tube was transported to the biochemistry laboratory to carry out a hemogram (Beckman Coulter Diagnostics, Barcelona, Spain), which provided blood cell counts, including neutrophil and lymphocyte counts. From these values, we calculated the neutrophil-to-lymphocyte ratio (NLR), a biomarker for inflammation accepted for psychiatric conditions and other diseases [31]. EDTA-containing blood tubes and Salivette tubes were transported to the IISPV Biobank in less than 2 h for processing, and sample aliquots were stored. One EDTA-containing tube was centrifuged to separate leukocytes to isolate DNA using the Puregene Blood Kit (QIAGEN Iberia SL, L'Hospitalet de Llobregat, Spain). Isolated DNA was stored at 4°C until needed. The Salivette tubes were centrifuged at 3000 rpm for 5 min, the saliva was aliquoted and frozen at -20°C until salivary cortisol was tested using a high-sensitivity commercial chemiluminescence immunoassay (IBL, Hamburg, Germany). The intra-assay and interassay coefficients of variation were under 8%. The sensitivity of the assay was 0.08 nmol/l.

Brain sample set

DLPFC (Broadmann Area 46) samples from the Stanley Array Collection were kindly provided by Stanley Medical Research Institute (MD, USA). A total of 35 brain DNA samples from subjects with schizophrenia diagnosis and 35 HC were included (Table 2). Details on DNA, mRNA isolation and clinical variables collected were published elsewhere [3,32]. *DDR1*a, b and c mRNA concentrations measured by quantitative reverse transcription (RT-qPCR) were available from previous studies [3,8]. *DDR1* (rs1264323, rs2267641) and DDR1-DT (rs2844654) SNPs previously shown to influence *DDR1* expression [3,8] and determined by TaqMann assays were also available from previous studies and included as covariables into the analyses.

DNA methylation analysis

Putative CpGs to be methylated at the *DDR1* locus were identified from the literature [20,33–35] and by screening for CpG islands at the promoter region of the gene (-1000 bp from the transcription start site, including the locus of the *DDR1-DT* gene whose RNA product hybridizes with *DDR1* at intron 9). Five CpG-rich regions (arbitrarily named 1, 2, 3, 4 and 5) with a total of 45 CpG sites were identified (for detailed information, see Figure 1A and Supplementary Table 1) and analyzed. Additional information about the regulatory elements present at this locus was obtained from the ENCODE project and shown in Figure 1 [36]. Methylated (5-mC) and nonmethylated cytosines in blood and brain DNA samples with the SEQUENOM EpiTYPER® kit in a MassARRAY Analyzer (Agena Bioscience, Inc., CA, USA) following the manufacturer's instructions. The relative methylation levels were calculated by comparing the signal intensity for the mass signals from methylated and nonmethylated template DNA and expressed as percentage of 5-mC. Intra-assay variation was calculated with 5% of the samples performed in duplicate and resulted in a coefficient of variation <10%. The analyses were performed blinded to the phenotypes. From all five regions, two pairs out of the 45 CpGs showed identical values; therefore, only one of the two sites

Table 2. Brain sample description.

Characteristic	Patients with schizophrenia	Healthy controls	p†
Sociodemographic data			
N	35	35	NA
Male/female ratio	26/9	26/9	NS
Age (years), mean ± SD	42.6 ± 8.5	44.2 ± 7.6	NS
Clinical features			
Age at onset (years), mean ± SD	21.3 ± 1.2	–	NA
Suicide, N (%)	7.0 (20.0)	0 (0.0)	0.011
Duration of illness (years), mean ± SD	21.3 ± 1.7	–	NA
Time in hospital (years), mean ± SD	1.2 ± 0.38	–	NA
Lifetime antipsychotic exposure (mg)‡, mean ± SD	85,004 ± 16,959		
Lifetime alcohol use§, mean ± SD	2.3 ± 2.0	0.8 ± 1.1	0.0004
Lifetime drug use§, mean ± SD	1.8 ± 2.0	0.2 ± 0.6	0.00001
Smoking at time of death, N	23/27	9/18	0.014
Tissue features			
PMI	31.4 ± 15.5	29.4 ± 12.9	NS
Brain pH	6.5 ± 0.24	6.6 ± 0.20	0.03
RIN	8.5 ± 0.65	8.3 ± 0.68	NS
DDR1 mRNA¶			
DDR1a (relative units)	1.10 ± 0.42	1.06 ± 0.37	NS
DDR1b (relative units)	1.06 ± 0.41	1.07 ± 0.45	NS
DDR1c (relative units)	1.29 ± 0.59	1.19 ± 0.76	0.048

†t-test and χ^2 tests, more details in Materials and methods section.
‡Total lifetime antipsychotic medication in fluphenazine mg equivalents according to Torrey *et al.* [33].
§Quantitative ratings (1–5 scale) according to Torrey *et al.* [33].
¶According to Roig *et al.* [11].
NA: Not applicable; NS: Not significant; PMI: Postmortem interval; RIN: RNA integrity number; SD: Standard deviation.

is shown. Finally, 43 CpGs (referred to as consecutive numbers and grouped in the five regions studied hereafter; i.e., CpG 1_1, CpG 1_2, etc.) were included in the present analysis (Supplementary Table 1).

To test whether leukocyte DNA methylation was similar to brain DNA methylation at the *DDR1* locus, *DDR1* methylation levels from HC individuals were compared between the two tissues. The rationale was to find similar methylation islands in both tissues to use leukocyte methylation as a proxy of brain methylation. Data from the BECon web application [37] containing five 5-mC levels in blood and brain samples from the same subjects [38] were used to compare the results we obtained from brain and blood samples from different HC.

Statistical analyses

The normal distribution of quantitative variables was tested with a one-sample Kolmogorov–Smirnov test. The 5-mC CpG levels were log transformed.

Univariate & bivariate analyses

Associations between variables were assessed prior to the regression analysis. To assess the correlations between continuous variables, Spearman's coefficients were calculated. Correlations between 5-mC DDR1 CpG levels and sociodemographic, clinical and biochemical variables in blood and brain sample sets are shown in Supplementary Table 2. T-tests for normally distributed variables and Mann–Whitney tests for nonnormally distributed variables were used to compare continuous variables between groups and results shown in Supplementary Table 2. A χ^2 test was used to compare the frequencies between groups. All tests were two-tailed. The false discovery rate according to the Benjamini–Hochberg procedure was run to correct for multiple testing when comparing 5-mC levels between patients and HC.

Figure 1. CpG-enriched regions at the *DDR1* locus and levels of 5-methyl cytosine in hypermethylated CpGs in patients and healthy control. (A) Schematic drawing of the *DDR1* locus in chromosome 6. GRCh38, chr6: 30,865,000–30,901,000 containing three genes: *DDR1*, *MIR4640* and *DDR1-DT*. *DDR1-DT* transcript and *DDR1*b, *DDR1*a and *DDR1*c isoforms transcripts are displayed. *DDR1*b and *DDR1*a can result from other transcripts not shown for clarity. *DDR1-DT* encodes a nontranslated reverse transcript that hybridizes with *DDR1* intron 9 and has a possible regulatory function. Clusters of DNase I hypersensitivity. Regulatory regions tend to be DNase-sensitive. The darkness is proportional to the maximum signal strength observed in any cell lines. H3K27Ac Marks. Levels of enrichment of the H3K27Ac histone mark, which is the acetylation of lysine 27 of the H3 histone protein and it is thought to enhance transcription. 3a corresponds to the GM12878 lymphoblastoid cell line and 3b to the K562 granulocyte cell line. **(B)** Yellow rectangles point to the location of each of the 5 CpG regions analyzed and arbitrarily named 1, 2, 3, 4 and 5. **(C)** Graph plot representing % 5-mC at CpGs that were increased in patient subjects compared with healthy control in the regression analysis controlling for covariates (regression model details in the Materials and methods section) in the blood dataset and replicated in the brain dataset. **(D)** Identification of regions of transcription factor binding included in the CpGs 3_3 and 3_4. A signal intensity of 1 corresponds to the maximum signal strength observed in any cell type contributing to the cluster. Data from the ENCODE project. †Transcription factor (gene name) that bind to the GpG sequence. ‡Signal intensity observed. §Information adapted from gene cards.
5-mC: 5-methyl cytosine; CNS: Central nervous system; DLPFC: Dorsolateral prefrontal cortex.

Regression analyses

To test which variables were associated with 5-mC levels at all CpG sites in blood samples, we conducted a linear regression analysis using log-transformed 5-mC CpG levels as dependent variables and three models to evaluate different scenarios. In the first model, all participants were included, and the independent variables were sex, diagnostic group, psychosocial stress scores (CTQ, HR-SRRS, PSS), physiological stress (saliva cortisol) and the inflammatory marker (NLR) and the variables associated with the CpG according to the bivariate analysis. In the second model, only patients were included, and the independent variables were sex, remission from psychotic symptoms status, depression status (CDSS), psychosocial and physiological stress and NLR. Variables such as

antipsychotic, benzodiazepine and biperidene doses, coffee, alcohol and cannabis consumption and age – among others, were also included according to the bivariate analysis. Finally, a third model included only control subjects and used sex, psychosocial and physiological stress and NLR as independent variables. Here, other variables were also included in the equation according to the bivariate analysis. In all regression models, the 'enter' method was used, and the standardized residuals (ZR) were calculated. Subjects with ZR lying outside ±1.96 were excluded, and the regression analysis was performed again.The number of subjects excluded, if any, is indicated in the corresponding table footnote. Finally, we applied a Bonferroni correction ($p = 0.05/43 = 0.001$) for the p-values to minimize false positive results due to multiple testing.

In the brain sample set, a single linear regression analysis was performed with those CpGs found hypermethylated in blood from patients as the dependent variables and sex, postmortem interval, smoking and suicide status included as independent variables according to the bivariate analysis.

IBM SPSS Statistics for Windows version 20.0 (IBM Corp., NY, USA) was used to perform statistical analyses. R software (R Foundation for Statistical Computing, Vienna, Austria) [39] was used to prepare correlation plots, and GraphPad Prism 5 (GraphPad Software, LLC, CA, USA) was used to prepare all other figures.

Results

Blood & brain sample sets description

The blood sample set description for the patient and HC subjects is shown in Table 1. Tobacco and cannabis use was higher in patients (Table 1). Patients had a mean total PANSS score of approximately 60, and 40% of patients were in remission upon study assessment. The CDSS scores were low (2.2 ± 5.4); consequently, on average, patients were not depressed. Psychological stress was higher in patients than in controls (Table 1) and statistically significant for CTQ (42.4 ± 14.2 vs 30.8 ± 6.8, $p = 5 \times 10^{-6}$) and PSS (23.9 ± 10.1 vs 18.6 ± 7.7, $p = 0.006$). The HR-SRRS, number of life-stressing events, was higher in patients than in controls (154.9 ± 104.6 vs 113.9 ± 102.8) but did not reach statistical significance. Saliva cortisol levels were similar in both groups, but the NLR was higher in patients than in controls (1.9 ± 0.9 vs 1.4 ± 0.6, $p = 0.02$). The brain sample set participant characteristics are shown in Table 2. Briefly, patients and HC had an average of 43 years and the same proportion of males to females (3/1). Patients had higher lifetime alcohol and drug use and higher rates of smoking and suicide (Table 2).

Blood *DDR1* methylation in patients & HC

All 5 *DDR1* CpG-rich regions (regions 1, 2, 3, 4 and 5; Figure 1A) analyzed were methylated. The percentage of 5-mC varied among the five regions (mean range for each region = 0.70–0.96, 0.90–0.97, 0.73–0.84, 0.54–0.85 and 0.01–0.15, respectively). Region 1 showed 3 differentially methylated CpGs between patients and HC, and all patients presented lower values (Mann–Whitney test, Supplementary Figure 1). In region 2, three CpGs were different between patients and controls, and of these sites, two presented higher methylation levels in patients than in HC. Similarly, region 3, with four differentially methylated CpGs, showed the highest values in the patient group except CpG 3_1, with lower 5-mC values in patients. In region 4, the three CpGs were hypermethylated in patients. One CpG in region 5 presented statistically higher values in patients, while another CpG showed higher values in HC (Supplementary Figure 1).

Bivariate correlations between *DDR1* leukocyte 5-mC levels and stress and inflammatory biomarkers showed a characteristic region 3 pattern in HC, with CpG 3_4 presenting a high-positive association with neutrophil counts and NLR and conversely a negative association with lymphocyte counts (Figure 2). This pattern is lost in the patient group, where neutrophil and lymphocyte counts are equally associated and without statistical significance with 5-mC levels at CpGs 3_3, 3_4 and 3_5. Notably, in the patient group, saliva cortisol concentration was significantly correlated with CpGs 3_4 and 4_3 in this region (Figure 2).

The main hypothesis of this study was tested by linear regression analysis using 5-mC levels at each CpG as dependent variables and diagnostic group, sex, psychosocial stress, saliva cortisol and NLR as independent variables. Other variables such as age, education, coffee, tobacco, alcohol and cannabis consumption that showed statistical correlation in the bivariate analysis for some CpGs were included in the regression models. Table 3 shows the linear regression analysis results for all CpGs with a statistically significant model. In CpGs 3_2, 3_3 and 3_5, H-SRRS, PSS or NLR scores were significantly associated with 5-mC levels. For CpGs 3_4, only diagnostic group and NLR contributed significantly to the model. Interestingly, PSS scores, which measure perceived stress, showed an inverse (negative) association with 5-mC levels ($r = -0.202$, $p = 0.038$ and $r = -0.258$, $p = 0.036$ for CpG 3_3 and 3_5, respectively), while NLR, which is a well-established inflammatory biomarker, showed a direct (positive)

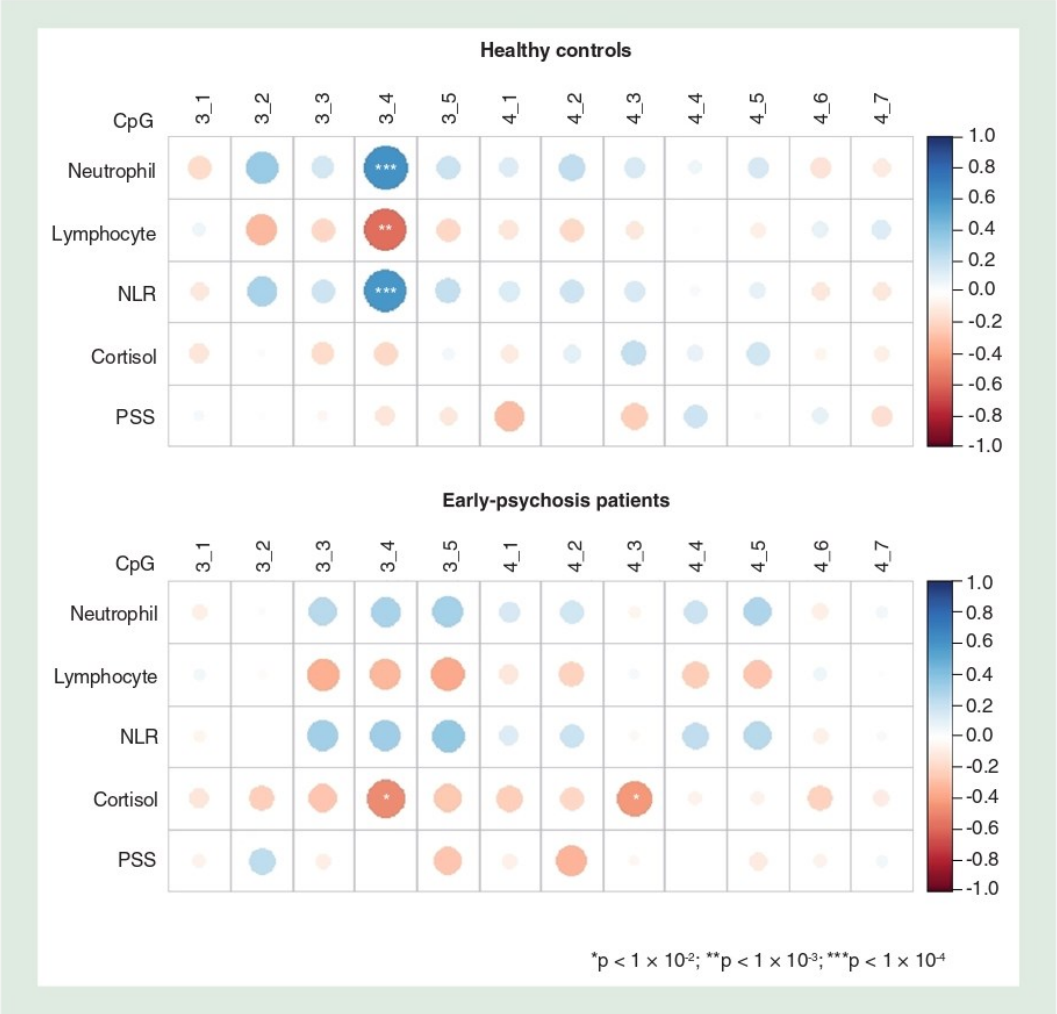

Figure 2. Correlation between percentage 5-methyl cytosine at CpG regions 3 and 4 and inflammatory and stress variables in early psychosis patients and healthy control.
NLR: Neutrophil-to-lymphocyte ratio; PSS: Perceived stress scale.

relationship (r = 0.327, p = 0.002; r = 0.479, p = 3×10^{-5}; and r = 0.314, p = 0.013 for CpGs 3_3, 3_4 and 3_5, respectively), and these two variables (PSS and NLR) showed no correlation (r = 0.14, p = 0.23). CpG 3_3 methylation as a dependent variable reached the highest statistical significance (p = 1.2×10^{-7}) in the model and the highest adjusted R^2 (adj R^2 = 0.479). PSS had a higher impact on CpG 3_5 (p = 0.036), but NLR showed a higher association with CpG 3_4 (p = 3×10^{-5}). Notably, after Bonferroni correction for multiple testing only CpGs 3_3 and 3_4 resulted statistically hypermethylated in patients compared with HC (Table 3 & Figure 1C).

We then assessed which variables influence the *DDR1* 5-mC levels in patients by a second regression analysis (Supplementary Table 3). Here, the 5-mC level at each CpG was used as the dependent variable, and sex, clinical psychotic symptom remission, presence of depression (CDSS), psychological stress (CTQ, HR-SRRS, PSS), saliva cortisol and NLR for all CpGs and other variables (i.e., age, education, medication and toxic consumption) for some CpGs according to the bivariate analysis. In CpG 3_1, a positive association with 5-mC levels was observed for women (β = 0.333, p = 0.034) and having a remission status (β = 0.795, p = 0.0001), concomitant with a negative association with cortisol (β = -0.499, p = 0.010) and NLR (β = -0.533, p = 0.003), with an adj R^2 = 0.425 (p = 0.007). In the HC group, we tested which variables explain the variability in 5-mC with all CpGs (Supplementary

Table 3. Linear regression analysis using methylation of DDR1 CpG islands as dependent variables and sex, diagnostic group, psychological stress test scores, stress, and plasma inflammatory biomarkers as independent variables in the blood sample set.

DDR1 CpG†	Variable‡	Variable statistics		Model		
		β	p-value	Adjusted R^2	p-value	Adjusted p-value§
1_5¶	Coffee	0.334	0.007	0.128	0.036	NS
3_1#	Diagnosis	0.282	0.047	0.148	0.029	NS
	Education	-0.351	0.016			
3_2††	Diagnosis	0.415	0.006	0.152	0.027	NS
	HR-SRRS	0.251	0.043			
3_3‡‡	Diagnosis	0.420	3×10^{-4}	0.479	1.2×10^{-7}	
	PSS	-0.202	0.038			<0.001
	NLR	0.327	0.002			
3_4	Diagnosis	0.233	0.048	0.357	1.1×10^{-5}	<0.001
	NLR	0.479	3×10^{-5}			
3_5§§	Diagnosis	0.261	0.050	0.206	0.004	NS
	PSS	-0.258	0.036			
	NLR	0.314	0.013			
4_2¶¶	Diagnosis	0.462	4×10^{-4}	0.281	0.001	NS
4_3	Sex	0.417	0.001	0.109	0.047	NS
4_5##	Diagnosis	0.331	0.021	0.180	0.009	NS
5_4†††	Diagnosis	-0.280	0.050	0.173	0.016	NS
	Age	0.280	0.043			

†Log-transformed variables.
‡The independent variables included in the equation were sex, diagnostic group, childhood trauma questionnaire total score, HR-SRRS total score, PSS total score, saliva cortisol and NLR. Only variables (dependent and independent) showing statistical significance in the equation are shown. Two subjects, one from the healthy control and one from the patients group, were excluded because their standardized residuals was >±1.96.
§Adjusted p-value after Bonferroni correction (p = 0.05/43 = 0.001).
¶According to the bivariate analysis (Supplementary Table 2), coffee consumption was also included into the equation.
#According to the bivariate analysis (Supplementary Table 2), education and alcohol consumption were also included into the equation.
††According to the bivariate analysis (Supplementary Table 2), education and tobacco consumption were also included into the equation.
‡‡According to the bivariate analysis (Supplementary Table 2), education was also included into the equation.
§§According to the bivariate analysis (Supplementary Table 2), age was also included into the equation.
¶¶According to the bivariate analysis (Supplementary Table 2), education and tobacco consumption were also included into the equation.
##According to the bivariate analysis (Supplementary Table 2), tobacco consumption was also included into the equation.
†††According to the bivariate analysis (Supplementary Table 2), education and age were also included into the equation.
HR-SRRS: Holmes–Rahe's Social Readjustment Rating Scale; NLR: Neutrophil-to-lymphocyte ratio; NS: Not significant; PSS: Perceived stress scale.

Table 3) also by linear regression analysis with psychological stress (CTQ, HR-SRRS, PSS), saliva cortisol and NLR and other variables (i.e., age, education and toxic consumption) as independent variables. Coffee and cannabis consumption were associated with 5-mC levels at CpG 1_5 (adj R^2 = 0.335, p = 0.011). Cortisol showed a positive association with 5-mC levels at CpG 2_7 and 5_10 (β = 0.310, p = 0.047 and β = 0.315, p = 0.05, respectively). NLR showed association with 5-mC levels at CpG 2_7, 3_3 and 3_4, being strongest at CpG 3_4 (β = 0.613, p = 1.3×10^{-4}, adj R^2 = 0.369, p = 0.003). Sex was inversely associated with 5-mC at CpG 5_6 and 5_10 (β = -0.450, p = 0.007 and β = -0.382, p = 0.018, respectively). Females having lower 5-mC levels than males.

Brain *DDR1* hypermethylation in patients with schizophrenia diagnosis

In brain DLPFC tissue, all five *DDR1* CpG regions were methylated; however, only CpG 3_3 was statistically higher in patients than in HC following a bivariate analysis (Supplementary Figure 1) and in the linear regression analysis (Figure 1C).

*DDR1*a, b and c mRNA levels were available from a previous study and were used to test whether *DDR1* methylation influences gene expression. The linear regression analysis (Table 4) showed that CpG 1_3 significantly associates with *DDR1*b expression (β = 0.243, p = 0.028), whereas CpG 3_5 and diagnostic associate with *DDR1*c expression (Table 4). *DDR1*c levels were higher in patients (diagnosis β = 0.224, p = 0.018), lower in both rs2267641_C carriers and rs2844654_T allele carriers (β = -0.551, p = 3.0×10^{-7} and β = -0.238, p = 0.015,

Table 4. Linear regression analysis using DDR1 isoform mRNA as the dependent variable and DDR1 methylation CpG, biometric variables, diagnostic group, tissue quality and DDR1 SNP genotype as independent variables in the DLPFC brain sample set.

DDR1 isoform	Variable†	Variable statistics		Model	
		β	p-value	Adj R^2	p-value
DDR1b‡	rs2267641_AA	0.501	1.9×10^{-5}	0.368	4.9×10^{-7}
	CpG 1_3	0.243	2.8×10^{-2}		
DDR1c‡	rs2267641_AA	-0.551	3.0×10^{-7}	0.484	1.4×10^{-8}
	CpG 3_5	-0.257	7.0×10^{-3}		
	rs2844654_CC	-0.238	1.5×10^{-2}		
	Diagnosis	0.224	1.8×10^{-2}		

†The independent variables included in the equation were sex, age, diagnostic group, postmortem interval, RNA integrity number, rs2844654, rs1264323 and rs2267641 for all isoforms; CpGs 1_3, 2_5 and 4_5 for DDR1b; and CpGs 2_5, 3_5 and 5_8 for DDR1c. Selection of independent variables is explained in the 'Materials and methods' section. Only variables (dependent and independent) showing statistical significance in the final equation are shown.
‡Log-transformed variables.

respectively) and inversely correlated with 5-mC levels at CpG 3_5 ($\beta = -0.257$, $p = 7.0 \times 10^{-3}$). *DDR1*a expression did not show any relationship with *DDR1* 5-mC levels.

Blood–brain *DDR1* methylation concordance

We aimed to compare *DDR1* blood methylation levels to those in the brain. The mean percentage of 5-mC at each region in blood was R-1 = 0.93%, R-2 = 0.88%, R-3 = 0.78%, R-4 = 0.71% and R-5 = 0.09% compared with 0.91, 0.50, 0.53, 0.51 and 0.07% in brain, respectively. Although we had blood DNA from HC, we did not have access to the brain DNA in these same subjects and vice versa. Therefore, no statistical comparisons were carried out. In contrast, we could use *DDR1* methylation data in the blood and brain tissue from the same individual from a free-access dataset (BECon) [38]. The BECon samples were determined with the Illumina Methylation Array, and 13 *DDR1* CpGs coincide with CpGs measured in our samples.The blood–brain data concordance (Supplementary Figure 2) obtained from our samples, although from different subjects, is very similar to the BECon data (from the same subjects, data available at BECon web application [37]). In summary, the percentage of 5-mC at regions 1 and 5 were similar in blood and brain but regions 2, 3 and 4 were much higher methylated in blood (0.71–0.88%) than in brain (0.50–0.53%).

Discussion

The present study showed that in 2 *DDR1* CpGs (3_3 and 3_4), leukocyte methylation was associated with the diagnostic group and inflammation (NLR), and CpG 3_3 also showed association with psychological stress. Compared with HC, patients with an early psychosis diagnosis showed hypermethylation in both CpGs. Interestingly, PSS scores were inversely associated and NLR was directly associated with 5-mC levels. However, the effect of NLR was stronger than that of PSS (higher β and p-values), and patients with higher NLR had higher 5-mC levels than did the controls. Thus, the effect of inflammation was apparently more important than that of stress to explain the 5-mC levels at these *DDR1* CpGs. Moreover, although we can explain 16–46% of the 5-mC variance in these CpGs, there is still approximately 50% to be explained by other no studied variables. Regarding variables such as age, tobacco and toxic use, which were highlighted in the literature as variables influencing DNA methylation [40,41], we found several statistically significant associations with 5-mC levels in the bivariate analysis, but only a few remained in the linear regression models and none of these survived after Bonferroni correction. Similarly, clinical variables, such as PANSS, antipsychotic benzodiazepine and biperidene drug doses, showed relevant associations in the bivariate analyses of the patient subgroup but did not in the regression model. To consider other variables that could influence DNA methylation, we have to bear in mind that this study has a cross-section design, and therefore, extensive retrospective and prospective information was not available. Additionally, we cannot rule out that some genetic factors could determine, in part, the levels of methylation, and patients can harbor more genetic variants predisposing to altered methylation patterns than HC do, as previously reported [42]. Interestingly, we could replicate the blood finding in a surrogate brain sample, were *DDR1* CpGs 3_3 was also hypermethylated in patients with a schizophrenia diagnosis compared with HC. To our knowledge, this is the first report showing differential brain *DDR1* methylation in a psychiatric disorder.

The methylation of *DDR1* has been explored for regions 3 and 4 in previous studies on nonpsychiatric disorders [20,33–35], but this study is the first to also determine the methylation levels of region 5 and the regions at the neighboring upstream gene *DDR1-DT* (regions 1 and 2). The 5′UTR region of *DDR1* (CpGs at regions 3, 4 and 5; Figures 1A & B) studied here are located in a region with high density of DNase I sensitivity clusters (Figure 1A) and also with high levels of enrichment of the H3K27Ac Mark for lymphoblastoid and granulocytic cell lines which strongly suggests that represents the promoter region of the gene (GTEx project platform [43] and ENCODE project data [36]). The hypermethylation of *DDR1* region 3 (cg13329862; CpG 3_2) in Sertoli cells in patients with idiopathic nonobstructive azoospermia was associated with a 1.8-fold decrease in gene expression [33]. Similarly, higher methylation in the promoter region of *DDR1* was associated with lower mRNA and protein expression in endothelial ovarian cancer cells [44]. Conversely, an 8.9-fold decrease in *DDR1* region 4 methylation in non-small-cell lung cancer was observed when *DDR1* was overexpressed [34]. Additionally, higher *DDR1* expression with lower *DDR1* methylation was observed in endometrial cells [35]. In agreement with these data, in brain DLPFC tissue, we found an inverse relationship between methylation levels at *DDR1* CpG 3_5 and DDR1c isoform expression. Together, these studies show that *DDR1* promoter methylation regulates gene expression and that the relationship is inverse; higher expression of the gene is associated with lower methylation at these CpG sites. However, in the brain, we found a direct relationship between methylation levels at CpG 1_3 (*DDR1-DT*) and the *DDR1*b isoform. These results need to be confirmed in larger samples but suggest that *DDR1-DT*, which is expressed in some tissues, including the brain (Expression Atlas, www.ebi.ac.uk/gxa/), and whose RNA is complementary to intron 9 in *DDR1* may also differentially regulate *DDR1* isoform expression.

We found higher leukocyte *DDR1* methylation (region 3) in patients than in HC but did not have data on *DDR1* expression. The increased expression of the *DDR1a* isoform has been described in activated neutrophils [9], suggesting that *DDR1* methylation may play a role in leukocyte differentiation/activation.

In the present study, patients with psychosis (nonaffective) at early disease stages showed higher NLRs due to a higher number of neutrophils concomitant with a lower number of lymphocytes (data not shown). Interestingly, the 5-mC levels at CpG 3_4 (cg23953820) showed a strong positive correlation with neutrophil counts and a strong negative correlation with lymphocyte counts in HC, but this correlation was lower in early psychosis patients. CpG 3_4 hits a binding site for the transcription factor PAX5 (Figure 1D) involved in B-cell linage differentiation which suggest that CpG 3_4 hypermethylation prevents PAX5 binding to the *DDR1* regulatory region and that this mechanism may be involved in lymphocyte proliferation. Such hypothesis deserves to be fully investigated. Our results of *DDR1*-altered methylation in patients' blood leukocytes and its strong correlation with NLR, are in agreement with the hypothesis that schizophrenia presents with systemic inflammation [45].

Moreover, in patients with early psychosis, the 5-mC levels in regions 3 and 4 were also significantly correlated with saliva cortisol levels. PSS scores showed an inverse correlation with 5-mC levels at CpGs 3_3 and 3_5. Cortisol correlated with 5-mC levels at CpGs 3_1 in the patient group (inversely) and with CpGs 2_7 and 5_10 in HC (directly). HR-SRRS scores correlated with CpG 3_2 in the whole sample and CTQ scores with CpG 4_4 in HC. CpG 3_3 and 3_4 hit a binding site for the glucocorticoid receptor (Figure 1D). This result suggests that the hormonal stress axis is involved in *DDR1* gene expression at least in blood leukocytes. Clive *et al.* [20] found altered methylation related to suicidal ideation in several genes, including *DDR1* and specifically with the probe cg08469255 (CpG 3_4 according to our nomenclature). They hypothesized that the results were consistent with a model whereby suicide-associated HPA axis dysregulation causes an overproduction of circulating cortisol, which causes DNA methylation changes in various tissues, including the brain, resulting in behavioral changes. Notably, we found a statistically significant association between brain CpG 3_5 methylation and suicidal status in the bivariate analysis. In the present study, CTQ scores, although higher in the patient group, were not consistently associated with the 5-mC levels at *DDR1* CpGs, probably because of the limited sample size. Studies on the impact of adverse events in DNA methylation in rodents are abundant, but subsequent studies in humans are still scarce [15]. One of the most studied genes regarding stress is the *NR3C1*, and its hypermethylation has been associated with several forms of stress [15,46]. More recently, methylation at the *KITLG* has been associated with saliva cortisol levels under stress [47], and *SPDEF* methylation has been associated with stressful life events [48].

Regarding the comparison between the pattern of methylation of *DDR1* in blood leukocytes and brain tissue, our results indicate that region 1 had similar 5-mC levels in both tissues. The 5-mC levels in this region in blood DNA did not show differences between patients and controls. However, in the brain, CpG 1_3 was associated with *DDR1*b expression. *DDR1* is expressed in several tissues; therefore, we cannot rule out that stress alters the

normal pattern of *DDR1* methylation in all of these tissues, resulting in a pleiotropic effect, for instance, in blood leukocytes and in the brain, as shown here. Future studies are needed to address this issue.

Some limitations in the present study need to be mentioned. First, the limited sample size did not allow us to stratify the sample by sex when examining the association of 5-mC levels with cortisol, which would be interesting given the adult sexual dimorphism of HPA axis activity. Second, the retrospective nature of the CTQ and HR-SRRS tests that we used to measure the impact of life-stressing factors on *DDR1* methylation, although the CTQ measures were confirmed to be stable before and after patient treatment [49]. We believe that our results are based on rather small but very well-selected and exhaustively phenotyped samples (patients and controls were matched for age and gender in both the brain and the blood datasets). Third, we used only one inflammatory marker (NLR), what limits data interpretation. Fourth, oligodendrocyte counts and distribution have been found altered in schizophrenia [50] which could alter the relative amounts of *DDR1* mRNAs and 5-mC levels and we did not had such information to correct for. Regarding this limitation, future studies could be addressed in isolated cell-type specimens. Finally, in the blood sample cohort, RNA was not available to measure *DDR1* mRNA expression.

In summary, in patients with schizophrenia and related psychosis, we found an increase in *DDR1* 5-mC levels in 2 CpG sites which associated with inflammatory and stress biomarkers, and one of these sites was also hypermethylated in DLPFC from patients with the same diagnosis. These changes, if confirmed, could be used as biomarkers in the future to improve patient stratification.

Future perspective

Identifying biomarkers in psychiatry is challenging. This is the first study reporting *DDR1* CpG methylation associated to NLR, psychological stress and psychosis diagnosis. Future efforts will focus on assessing whether these associations are also present in other psychiatric disorders such as bipolar disorder, personality disorder and major depression. In order to decipher whether increased *DDR1* methylation acts as an inflammatory mechanism, we will measure *DDR1* methylation in blood samples from patients with a chronic inflammatory disorders such as rheumatoid arthritis at different stages of disease activity (from high activity to disease remission). Also, we will study brain *DDR1* methylation in larger samples of patients with psychiatric diagnostics. We believe that in the near future biomarkers based on blood measurements of DNA methylation at certain genes such as *DDR1*, reflecting in part brain methylation, will be useful in stratifying and staging psychiatric patients.

Summary points

- We found increased leukocyte 5-mC levels at 2 *DDR1* CpG sites in patients with a diagnosis of early psychosis compared with healthy controls (HC).
- Leukocyte *DDR1* 5-mC levels at CpGs 3_3 and 3_4 were associated with neutrophil to lymphcyte counts, psychological stress and the presence of a psychosis diagnosis.
- The strong correlation between 5-mC levels at CpGs 3_4 and neutrophil-to-lymphocyte ratio observed in HC is lost in patients with a diagnosis of early psychosis.
- We found an increase in brain dorsolateral prefrontal cortex tissue *DDR1* 5-mC levels at CpGs 3_3 in patients with a diagnosis of schizophrenia compared with HC.
- We found that 5-mC levels at CpG 3_5 in brain DLPFC tissue associated to *DDR1*c isoform expression which was higher in patients with schizophrenia than in HC.
- We found that brain dorsolateral prefrontal cortex tissue 5-mC levels at CpG 1_3 site located at *DDR1-DT* gene were associated to DDR1b isoform expression.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.future-science.com/doi/suppl/10.2217/epi-2019-0191

Author contributions

B Garcia-Ruiz, G Muntané and L Martorell participated in the design, analysis and interpretation of data; drafting and critically revising the manuscript content and approved the final version of the manuscript. L Moreno, V Sánchez-Gistau, A Gutiérrez-Zotes, J Labad and E Vilella participated in the design, acquisition, analysis and interpretation of data; drafting and critically revising the manuscript content and approved the final version of the manuscript.

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

All procedures were in accordance with the Declaration of Helsinki. Ethical approval was obtained from the local ethics committee (CEIm IISPV, www.iispv.cat). All subjects consented to participate in the study and signed an informed consent form after a complete explanation of all procedures.

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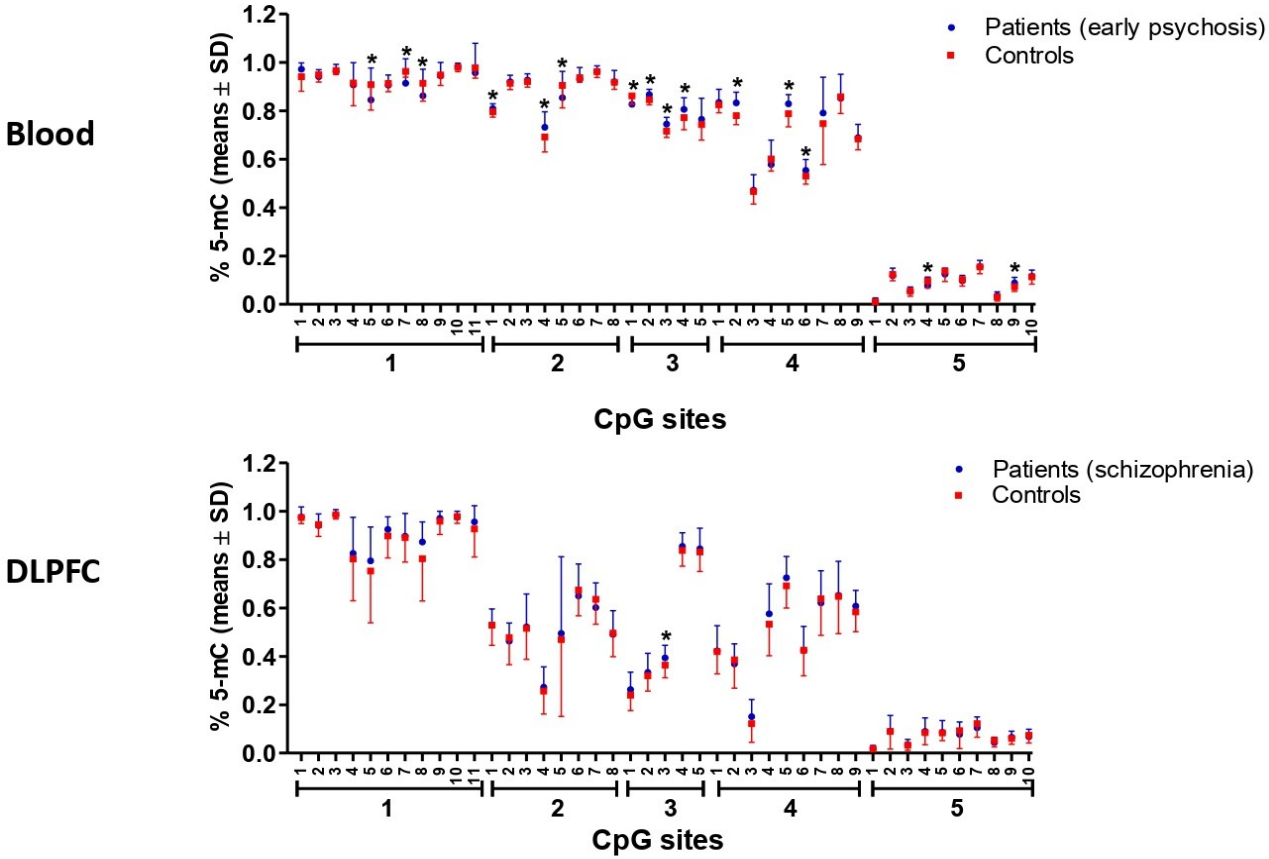
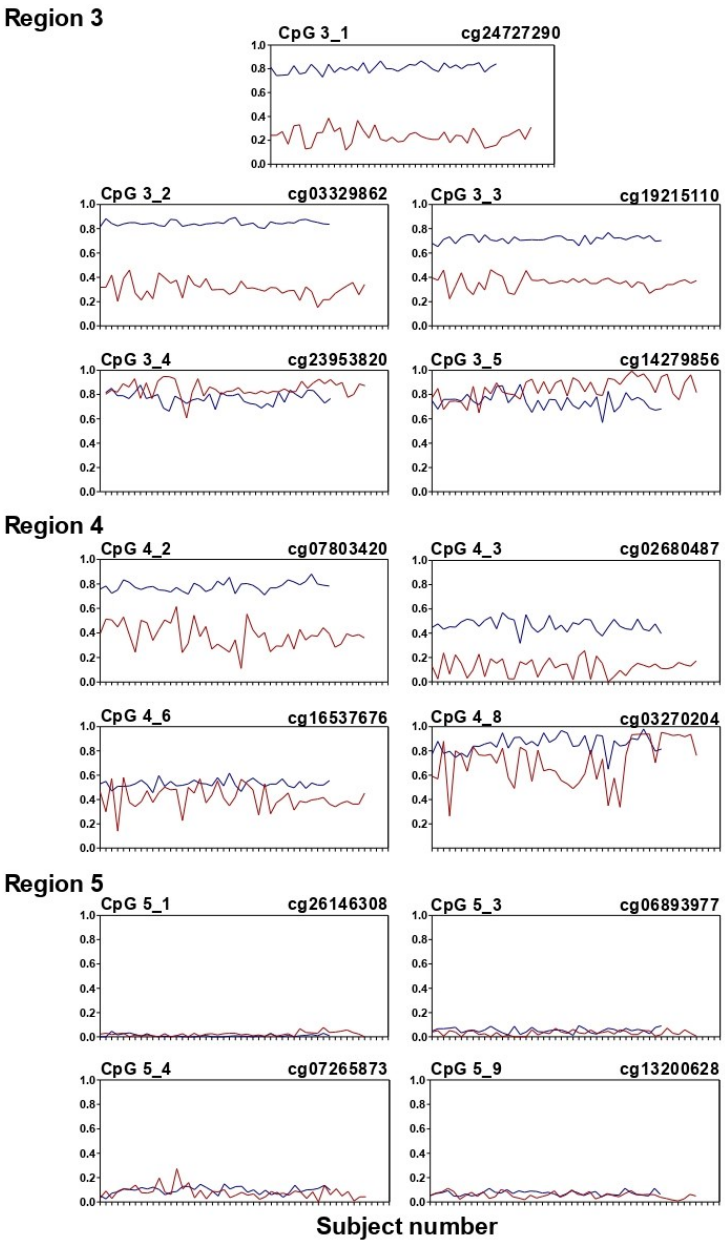
Supplementary material Article 1

Supplementary Figure S1. Percentage of 5-mC at all 43 DDR1 CpGs analyzed in DNA from blood leukocytes in patients with early psychosis and healthy controls and brain dorsolateral prefrontal cortex (DLPFC) from patients with schizophrenia and healthy controls.



Mann Whitney Test comparing pacient vs control subjects. *Statistically significant using the Benjamini-Hochberg FDR procedure, FDR < 5%.

Figure S2. Percentage of 5-mC at *DDR1* CpGs with data available from BECon and analyzed in the present study in blood DNA and brain DNA from healthy control subjects



DNA from blood (blue line) collected from subjects free of any psychiatric diagnosis (n=40) and DNA isolated from the dorsolateral prefrontal cortex (red line) of healthy controls (N=35) from the Stanley Medical Research Institute collection (Array Collection) were analyzed to determine 5-mC at *DDR1* CpGs using the EpiTyper MassARRAY System (Agena Bioscience, San Diego, CA, USA). Similar patterns of concordance of *DDR1* methylation in blood and brain are published in the Blood–Brain Epigenetic Concordance (BECon; https://redgar598.shinyapps.io/BECon/) data base.

Table S1. *DDR1* and *DDR1-DT* regions and CpG sites analyzed

Primers, adaptors and sequences[a]	CG	Illumina probes[b]	CpG ID Present
DDR1_AS_5F: aggaagagagTAAGAATTGGTTAGGTGAGGTTAGG DDR1_AS_5R: cagtaatacgactcactatagggagaaggctCCCCTTTCCTATAACAAAATTACAA CAAGAATTGGCCAGGTGAGGCCAGGCG[1]CCCTGGCTCACACCTGTAATCCCAGCACTCTGGGAGGGCG[2]AGGTGGGCG[3]GATCACG[4]GGGT CAGGAGATCG[5]AGACCATCCTGGCTAACACG[6]GTGAAACCTCG[7]TCTCTACTAAAAATACAAAAAAACG[8]AGCCG[9]GGCG[10]TGGTGGCG[11]GGC CCCTGTAGTCCCAGCTACTCAGGAGGCTGAAGCG[12]GCAGGATGGCG[13]TGAACCG[14]GGGAGGCG[15]GAGCTTGCAGTGAGCCAAGACCG[16]C ACCACTGCACTCCAGCCTGGGCG[17]ACAGAGCAAGACTCCATCTCAAAAAAAAAAAAAAAGGCCAGGTGAGGTGGCG[18]CACG[19]GCTGTAAT CCTGTTACAGGAAAGGGGTCTCAATCCAGACCCCAAGAGAGGGTTGTTGGATTTCGCAC	1	na	1_1
	2	na	1_2
	3	na	1_3
	4	na	1_4
	6	na	1_5
	7	na	1_6
	14	na	1_7
	16	na	1_8
	17	na	1_9
	18	na	1_10
	19	na	1_11
DDR1_AS_4F: aggaagagagGGGGTTTGTTATTTTATGTTAGGAAA DDR1_AS_4R: cagtaatacgactcactatagggagaaggctTCCCTTCTCTATCAACCACAAATAC AGTTGTCTGGGGTAAATACCCGGGGTTTGCCATCCCATGCCAGGAAAATGTAGGACACG[1]GACACACG[2]CG[3]AGGAGTCG[4]CG[5]AGGAGTTTA AGAGGGAAGGTTTAATAGGCAAAAGAAAGAGAAAGGAAAACAGCTCTCTCTCTAGTGAGAGAGGGGACTTCCG[6]AGAGAAAAGGGGCAGCT GGAGGCAGATGAGCCG[7]AATTTATAGTCCAGCTTGAGGAGGCG[8]GCG[9]TCTGATTTACTTAGGACTCACAGATTGGTTTGATCAGGTGTTTGT TTACATAGCTGGGAAGGCTGGCCG[10]CCCCACCCTAAGCTTATTATGCAAATGAACTCTCTCG[11]GAGGGTGCCATTTTGTCG[12]GCTCCTTACT GCACCTGTGGCTGACAGAGAAGGGATGATGGGGCCGCCATTTTGAACACGATTGG	2	na	2_1
	4	na	2_2
	6	na	2_3
	7	na	2_4
	8	na	2_5
	10	na	2_6
	11	na	2_7
	12	na	2_8
DDR1_1F: aggaagagagATTTTGGGGTTGTTTGTTAGTAGGT DDR1_1R: cagtaatacgactcactatagggagaaggctAATACTTTTTCCCCACTCAACACTA AGGAAGGCGGGAAGAAGCTGCTCTTCGAGTGACCCTGGGGCTGTCTGTTAGCAGGTCCCTCAGCCG[1]TTGGAA**CG**[2*]TCCTTGGGCTTCTGA ACTAGTGCCCATGTGTGCCTCG[3]GCCTTTCCCAAGGGCCAGCTTCTTCCTGGTAGTGCTTTTGTGTACTTGTCTGGTTGGGACTTCG[4]TGTTT CTTTCTTGGGATTGTTGTCTGGGACTGCAAGCAGGGTATGTTTTTATCTACTGTGAGGTTCCTGGGGCG[5‡]GAGATGTGCAGTGGAGCG[6]AGA ACTTCCTGTGACCG[7]TGACATTGTCTAGGTGGTGAGCAGGTGTGGGGGTGTGGAGAGAGGTGAGGGGCTGAGGTAGTGCTGAGTGGGGAA AAAGCACCTCCCACCACAAGCTGTTCTGTC	1	cg19215110 cg17604312 **cg24727290** cg13329862	3_1
	2	cg19215110 cg17604312 **cg13329862**	3_2
	3	**cg19215110**	3_3
	5	cg08469255 **cg23953820**	3_4
	7	cg23953820 **cg14279856**	3_5

4	3088356930 883988	DDR1_2F: aggaagagagTGTTTTGAGGATTTTTGAGTTTTTT DDR1_2R: cagtaatacgactcactatagggagaaggctAACCAAACCCCAAACTACTCTTCT AGCTGGCTGGGCCTGAGGGAGGCTTGCCCTGAGGACTCCTGAGTCCCCCTCCCACTCCACTCCG[1]TTGGGAGCCCAGGGGAATCA GGGCCTGGGCG[2]TCTGGACCCCCG[3]§GGTCCCTTAGAACG[4]CCCTTCAGAGAGAGGAACTGAGAGGAGAAGGAGAAGAGAGTGGGC CCG[5]CCTTCAGGGTCTGGGGCCTTCCAGGTTGGGTCG[6]TAGGGGCG[7]GGAGCG[8]¥CACAGGCTGCG[9]AGAGAGGAGCAAAGGTTGGT GGAGGGAGAAGAGCAGTCTGGGGCCTGGCTGGACAGGTGAGCCCTGAGACCTGAGCTCTGCT	1	na	4_1
			2	**cg07803420**	4_2
			3	cg07803420 **cg02680487**	4_3
			4	na	4_4
			5	na	4_5
			6	cg16707952 cg03270204 **cg16537676**	4_6
			7	na	4_7
			8	**cg03270204**	4_8
			9	na	4_9
5	3088391930 884478	DDR1_3F: aggaagagagTGTGTTTTGGGGTTGTTTTTTT DDR1_3R: cagtaatacgactcactatagggagaaggctCCAATAATCCCAATAACTCCCAC TGGCTGGACAGGTGAGCCCTGAGACCTGAGCTCTGCTCCCTTCTCTGGGCTAACTCCCGCAGCTGGGCTGGGCCGAGCCTGTGG GAACCTGCTTCTTCCTCTGTGCCCTGGGGCTGCTCCCCTTTGCCTCTCCCACCAGGAACCG[1]ATCCCAGAAGTAGGAGGGGCG[2]TCT TCCCCTCG[3]TGGGCCCTGAGCG[4]GGACTGCAGCCAGCCCCCTGGGGCG[5]CCAGCTTTGGAGGTTCTCG[6]TTTGGGGAAGCG[7]GGGG TGGGCTGCG[8]AGTGGGTGGAGGGGGCTGGGCG[9]CG[10]GAGCCG[11]GCCG[12]GAGGCAGCG[13]GCG[14]CG[15]GGCG[16]GCTGGGCG[17]GCCT GGGAGCG[18]CCCAGGCG[19]GGCTTGGCG[20]GGCG[21]GGTTACCTGGGGGAGGCCG[22]GGCCG[23]GGCG[24]CTAGCG[25]CG[26]CG[27]GGGTGG GCG[28]TGGCG[29]GGCG[30]CG[31]GGGCCTGGAGCTCG[32]GCG[33]CCG[34]GGCG[35]TGGGAGCCACTGGGACTACTGGGTCCGGGAGGGGGA AGGGAGGGCTGCGAGCCCGAACGCGCGGCGAGAAGGCCGAGGGGAGGGAGGGGAGCGAGGAGCGGGAGGAGGAAGGGAGGG AGCCGAGGCG	4	**cg26146308** cg06893977	5_1
			5	na	5_2
			6	cg26146308 **cg06893977**	5_3
			7	**cg07265873**	5_4
			9	na	5_5
			11	na	5_6
			18	na	5_7
			19	na	5_8
			22	cg10470808 **cg13200628**	5_9
			32	na	5_10

[a] Underlined text indicates the primer sequence. Red text indicates undetectable 5-mC at CpG. Green text indicates readable 5-mC at CpG. Magenta text indicates readable CpG but with values identical to the preceding CpG.
[b]Bold type text denotes cg probes in the Illumina 450K array used in the BECon project.
*According to Ramasamy, 2014 (Ramasamy et al., 2014): cg13329862 (CpG 3_2)
‡According to Clive, 2017 (Clive et al., 2016)
§According to Nelson, 2012 (Nelson et al., 2012): cg02680487 (CpG 4_6)
¥According to Houshdaran, 2014 (Houshdaran et al., 2014): cg03270204 (CpG 4_8)

Table S2. Linear regression analysis using methylation CpG sites as dependent variable and sex, clinical variables, psychological stress test scores, stress biomarker and plasma inflammatory biomarker as independent variables in patient subjects and in healthy controls in the Blood-sample.

DDR1 CpG[a]	Variables[b, c]	Variable statistics		Model	
		β	P	Adj R^2	P
Patients					
1_4	Sex	0.418	0.014	0.354	0.027
	Antipsychotic	0.362	0.040		
3_1	Sex	0.346	0.031	0.409	0.013
	Cortisol	-0.514	0.009		
	NLR	-0.542	0.003		
	Remission	0.793	2.8×10^{-4}		
Healthy controls					
2_7	Cortisol	0.310	0.047	0.265	0.018
	NLR	0.327	0.037		
3_4	NLR	0.613	1.3×10^{-4}	0.369	0.003
5_10	Sex	0.382	0.020	0.204	0.045
	Cortisol	-0.397	0.016		

[a]Log-transformed variables
[b]Patient group, independent variables included in the equation: sex, CDSS score, remission from psychotic symptoms, antipsychotic and diazepam equivalent dose, CTQ total score, HR-SRRS total score, PSS total score, saliva cortisol and NLR. Only variables showing statistical significance in the equation are shown.
[c]Healthy control group, independent variables included in the equation: sex, CDSS score, CTQ total score, HR-SRRS total score, PSS total score, saliva cortisol and NLR. Only variables showing statistical significance in the model are shown.
Abbreviations: CDSS: Calgary Depression Scale for Schizophrenia; CTQ: Childhood Trauma Questionnaire; HR-SRRS: Holmes and Rahe's Social Readjustment Rating Scale: NLR: Neutrophil-to-lymphocyte ratio; PSS: Perceived Stress Scale

Table S3. Blood-brain DDR1 CpG concordance in DNA from healthy subjects

pG	Blood[a] N=40	Brain[b] N=34	P[c]	P FDR
_1	**0.964 ± 0.060**	**0.974 ± 0.026**	**0.355**	**0.047**
1_2	**0.949 ± 0.030**	**0.944 ± 0.049**	**0.909**	**0.050**
1_3	0.967 ± 0.017	0.985 ± 0.018	3.8×10^{-6}	0.024
1_4	0.915 ± 0.094	0.803 ± 0.173	0.006	0.041
1_5	0.908 ± 0.105	0.753 ± 0.214	0.001	0.033
1_6	**0.913 ± 0.035**	**0.898 ± 0.091**	**0.629**	**0.049**
1_7	0.963 ± 0.025	0.891 ± 0.101	0.001	0.034
1_8	0.914 ± 0.074	0.803 ± 0.175	0.002	0.036
1_9	0.947 ± 0.043	0.958 ± 0.055	0.019	0.044
1_10	**0.980 ± 0.018**	**0.977 ± 0.028**	**0.547**	**0.048**
1_11	0.978 ± 0.043	0.926 ± 0.116	0.003	0.038
2_1	0.796 ± 0.022	0.528 ± 0.083	1.6×10^{-13}	0.002
2_2	0.913 ± 0.026	0.478 ± 0.112	1.6×10^{-13}	0.007
2_3	0.921 ± 0.023	0.515 ± 0.128	1.6×10^{-13}	0.006
2_4	0.692 ± 0.062	0.257 ± 0.095	1.6×10^{-13}	0.014
2_5	0.905 ± 0.093	0.470 ± 0.318	3.2×10^{-11}	0.016
2_6	0.937 ± 0.020	0.674 ± 0.106	5.1×10^{-13}	0.015
2_7	0.962 ± 0.020	0.636 ± 0.103	1.6×10^{-13}	0.005
2_8	0.918 ± 0.030	0.496 ± 0.098	1.6×10^{-13}	0.003
3_1	0.806 ± 0.036	0.240 ± 0.064	1.6×10^{-13}	0.013
3_2	0.845 ± 0.021	0.320 ± 0.064	1.6×10^{-13}	0.001
3_3	0.715 ± 0.026	0.363 ± 0.056	1.6×10^{-13}	0.008
3_4	0.772 ± 0.050	0.838 ± 0.065	1.0×10^{-6}	0.022
3_5	0.743 ± 0.064	0.832 ± 0.082	6.1×10^{-6}	0.027
4_1	0.824 ± 0.033	0.420 ± 0.092	1.6×10^{-13}	0.010
4_2	0.779 ± 0.038	0.385 ± 0.116	1.6×10^{-13}	0.009
4_3	0.466 ± 0.052	0.122 ± 0.077	1.6×10^{-13}	0.012
4_4	0.600 ± 0.049	0.533 ± 0.131	0.017	0.042
4_5	0.788 ± 0.054	0.692 ± 0.093	6.2×10^{-6}	0.028
4_6	0.530 ± 0.033	0.425 ± 0.106	2.5×10^{-6}	0.023
4_7	0.747 ± 0.170	0.638 ± 0.151	2.5×10^{-5}	0.029
4_8	0.857 ± 0.069	0.647 ± 0.154	6.7×10^{-10}	0.017
4_9	0.683 ± 0.045	0.584 ± 0.082	5.2×10^{-8}	0.020
5_1	0.011 ± 0.011	0.017 ± 0.010	0.003	0.040
5_2	0.124 ± 0.026	0.090 ± 0.073	2.1×10^{-7}	0.021
5_3	0.054 ± 0.021	0.032 ± 0.021	9.9×10^{-5}	0.030
5_4	0.097 ± 0.029	0.085 ± 0.050	0.018	0.043
5_5	0.138 ± 0.044	0.083 ± 0.032	5.7×10^{-9}	0.019
5_6	0.103 ± 0.027	0.092 ± 0.074	0.003	0.037
5_7	0.155 ± 0.029	0.121 ± 0.055	0.001	0.035
5_8	0.031 ± 0.017	0.053 ± 0.028	1.1×10^{-4}	0.031
5_9	0.073 ± 0.019	0.061 ± 0.025	0.020	0.045
5_10	0.114 ± 0.030	0.074 ± 0.032	5.9×10^{-6}	0.026

In bold type CpGs with FDR<0.05.
[a]Blood leukocyte DNA from Spanish healthy controls
[b]Brain tissue DNA from North American healthy controls (Stanley Medical Research Institute)
[c]Mann-Whitney Test

UNIVERSITAT ROVIRA I VIRGILI
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DDR1 methylation is associated with bipolar disorder and the isoform expression and methylation of myelin genes

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Research Article

Epigenomics

DDR1 methylation is associated with bipolar disorder and the isoform expression and methylation of myelin genes

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Aim: To investigate *DDR1* methylation in the brains of bipolar disorder (BD) patients and its association with *DDR1* mRNA levels and comethylation with myelin genes. **Materials & methods:** Genome-wide profiling of DNA methylation (Infinium MethylationEPIC BeadChip) corrected for glial composition and *DDR1* gene expression analysis in the occipital cortices of individuals with BD (n = 15) and healthy controls (n = 15) were conducted. **Results:** *DDR1* 5-methylcytosine levels were increased and directly associated with *DDR1*b mRNA expression in the brains of BD patients. We also observed that *DDR1* was comethylated with a group of myelin genes. **Conclusion:** *DDR1* is hypermethylated in BD brain tissue and is associated with isoform expression. Additionally, *DDR1* comethylation with myelin genes supports the role of this receptor in myelination.

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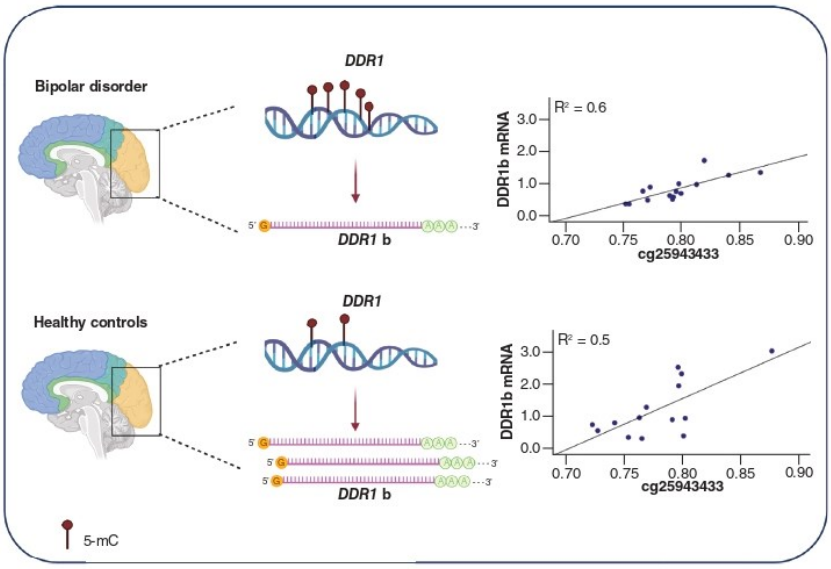
Keywords: bipolar disorder • discoidin domain receptor 1 • gene expression • human brain • methylation • myelin genes

Future Medicine

Graphical abstract:



Recent studies based upon neuroimaging, gene expression or both have demonstrated that abnormalities in white matter structure [1–3] and changes in oligodendrocyte gene expression [4] are present in the brains of patients with bipolar disorder (BD). Likewise, other studies have shown similar results in schizophrenia (SZ) [5–10]. Interestingly, comparative studies showed that the white matter abnormalities were closer between BD and SZ than with major depression [11,12]. Moreover, the genetic correlation between BD and SZ due to common genetic variants is the highest compared with that between other pairs of psychiatric diagnoses [13].

The principal constituent of white matter is myelin, the lipid-rich membrane belonging to oligodendrocytes that wraps axons. Myelination is a complex process that begins perinatally and ends in adulthood. The control of developmental myelination, myelin maintenance and remyelination after myelin injury is also complex and modulated in part by DNA methylation modification of key genes [14].

DDR1 is involved in the myelination process [15], and *DDR1* gene variants have been found to be associated with SZ [15]. Several transcripts of the *DDR1* gene have been described, and at least five correspond to protein isoforms (DDR1a to DDR1e). DDR1c, which has the highest expression in brain tissue, shows a high correlation with the expression of myelin genes such as *MBP*, *MAG* or *OLIG2* [15].

Our recent paper showed that patients with SZ had hypermethylated DNA at the promoter region of *DDR1* in blood leukocytes and in the brain dorsolateral prefrontal cortex (DLPFC), and interestingly, hypermethylation correlated with stress markers [16]. Additionally, we observed that *DDR1* methylation was associated with *DDR1* isoform expression in the DLPFC. However, to date, no studies have been conducted to assess whether *DDR1* is differentially methylated and involved in its expression in brain tissue from patients with BD. Furthermore, methylome studies on brain tissue in BD are scarce and based upon a reduced number of samples [17–19].

The main objective of this study was to compare the *DDR1* 5-mC levels between patients with BD and healthy controls (HCs) in different data sets. A second objective was to test whether *DDR1* 5-mC levels alter total *DDR1* and *DDR1* isoform expression in the human brains of BD patients and HCs. Finally, we evaluated the comethylation of *DDR1* with a selected set of myelin genes in the adult human brain to support that *DDR1* is involved in myelination.

Materials & methods

Brain sample

In this study, we analyzed genome-wide DNA methylome and gene expression data from the postmortem human brain. Occipital cortex (OC) tissue from the Neuropathology Consortium collection was kindly provided by the Stanley Medical Research Institute (MD, USA), and here, we used samples from 15 BD (diagnosis based on

DSM-IV) patients and 15 HCs. Tissue and clinical descriptions are provided in Supplementary Table 1. DNA and RNA were isolated as previously described [20,21]. *DDR1* SNP (rs2267641, rs1264323 and rs2844654) genotypes associated with gene expression were determined, and *DDR1* isoform expression was quantified as published [15,21]. To use these samples, the research project was submitted to the local ethics committee for approval, which assured that the samples were collected after signed informed consent was obtained [22].

For validation purposes, data (methylome and transcriptome) from the DLPFC from four BD patients and four HCs were accessed from the Gene Expression Omnibus (accession no.: GSE120341 and GSE120340) [17]. Finally, data from frontal cortex (FC) neuronal nuclei (isolated as NeuN+) from 26 patients with BD and 27 HCs were accessed from Gene Expression Omnibus (accession no.: GSE112179; GSE112523) [19]. Demographic and quality control (QC) tissue information as well as methods used to obtain genome-wide methylation and gene expression profiling in each sample set are provided in Supplementary Table 1.

Genome-wide methylation measurements & data pre-processing

In OC tissues, we measured genome-wide methylation after assessment of DNA purity by 260/280 and 260/230 ratio measurements with a NanoDrop spectrophotometer (Thermo Scientific, MA, USA). Then, 600 ng of DNA was bisulfite treated in one batch using the EZ-96 DNA Methylation Kit (Zymo Research Corp., CA, USA) following the manufacturer's recommendations. Bisulfite-converted DNA was then hybridized on the 850 K Infinium Methylation EPIC BeadChip (EPIC) (Illumina, Inc., CA, USA) according to the manufacturer's instructions. Both methylation analysis by EPIC array and data pre-processing were carried out at the Josep Carreras Leukemia Research Institute (Barcelona, Spain). The raw intensity data (IDAT) files from both the red and green color channels for each of the samples generated from the microarrays were preprocessed with the *minfi* package in R/Bioconductor [23]. The initial methylation data contained 866,091 probes. Filtering and QC of the data were applied to minimize errors and remove poor probe signals. First, we generated a detection p-value for every CpG in every sample, which is indicative of the quality of the signal. This method compares the total signal (methylated [M] + unmethylated [U]) for each probe to the background signal level, which was estimated from the negative control probes. Very small p-values are indicative of a reliable signal, while large p-values >0.01 generally indicate a poor-quality signal. Probes with a detection p-value > 0.01 in at least one sample were excluded. Next, to avoid confounding differential 5-mC levels with real polymorphisms in the DNA sequence, we removed probes containing a SNP at the CpG site and at the single nucleotide extension site for any minor allele frequency and probes with a SNP at the probe body for a minor allele frequency >5% within 10 bp of the single base extension site. Cross-reactive probes previously identified [24] were also removed to avoid generating inaccurate methylation measurements that could lead to the detection of artefactual differentially methylated sites. We also ruled out probes from the X and Y chromosomes. Normalization was performed through the ssNoob algorithm (single-sample normal-exponential out-of-band) for methylation arrays to reduce technical variation. Then, β-values were calculated based on M and U signals (M/M + U) for each individual at each CpG site using the methylation module available in GenomeStudio (v2011.1) software. The results are presented as % of methylated CpG. After QC procedures and normalizing the data, 29 samples (15 patients with BP and 14 HCs) and 718,197 probes were available for analysis.

β-values were transformed into M-values (logit2 of the β-values) since M-values are more statistically applicable for performing most statistical analysis methods as they satisfy the homoscedastic and normality assumptions. In contrast, β-values are much more biologically interpretable. Therefore, M-values were used for the statistical analyses, and β-values were used to report the results as recommended [25]. Subsequent analyses were performed using the *DDR1* average methylation (*DDR1* avg 5-mC) as well as the individual 5-mC levels of each of the 90 *DDR1* CpG sites analyzed. In the present study, we selected CpGs at *DDR1* and conventional marker genes for myelination-oligodendrocytes (*CNP, CSPG4, GALC, MAG, MBP, OLIG1, OLIG2, PDGFRA* and *SOX10*), astrocytes (*GFAP*), microglia (*CX3CL1*) and neurons (*MAP2, MAPT* and *PVALB*) (Supplementary Table 2). Ninety *DDR1* CpG sites from the whole-methylome data were identified with EPIC.

Cell type deconvolution analysis

Brain cellular heterogeneity in bulk tissue is an important limitation in DNA methylation analysis, affecting the findings of epigenetic studies [26]. To infer underlying cell type proportions in our sample, we used the *in silico* epigenomic deconvolution technique, which can accurately estimate the cell type composition [27]. *DDR1* is expressed in the brain, mainly in oligodendrocytes but also in astrocytes, microglia and vascular endothelial cells [15]. However, whole-methylome data were available from only glial cells, neurons and human brain microvascular

endothelial cells (HBMVECs). For this, we first performed an analysis throughout the 'estimate_stability' function of epigenomic deconvolution technique to choose the most appropriate number of cell types to introduce in our model, allowing for a more stable estimation of methylation profiles and cell proportions. We selected the best 500 informative marker loci from 38 reference methylation profiles accessed from GEO and derived from cells similar to those that make up our sample, glia (16) and neurons (16) from OC brain tissue (accession no.: GSE66351) [28] and HBMVECs (6) (accession no.: GSE138115) [29]; we performed deconvolution analysis, which was computed estimating the average methylation profiles and proportions of constituent cell types in our samples (Supplementary Figure 1 & Supplementary Tables 3–5). The average cell type composition in our OC tissue sample was 28.0% glial cells, 37.1% neurons and 34.9% HBMVECs. The same procedure was carried out in the DLPFC sample set. In this case, we used 52 reference methylation profiles that were also accessed from GEO, glia (23) and neurons (23) from FC brain tissue (accession no.: GSE418269) [30] and the same HBMVEC (6) profiles used above. With the rationale that *DDR1* is mainly expressed in oligodendrocytes, the percentage of glial cells in each sample was used as a covariate in the statistical analyses, and the data sets are referred to as glia-OC and glia-DLPFC hereafter.

Differential methylation analysis

Prior to implementing a linear regression model (LRM), tissue (brain pH, post-mortem interval [PMI] and proportion of glial cells [%glia]), biometric (age and sex) and clinical variables (history of psychosis, cause of death, lifetime antipsychotic exposure, current and past alcohol/drug abuse or dependence) were tested for association with CpG 5-mC levels by performing Spearman's correlations. Only variables showing a statistically significant association were included in the LRM to test for differentially methylated sites associated with BD. The 5-mC values for each CpG were regressed against the case–control status, with covariates for sex, age, PMI, brain pH and %glia and with a Benjamini–Hochberg (BH) post hoc test (false discovery rate [FDR] of 5%) for multiple testing correction [31].

Association analysis of the *DDR1* 5-mC levels & mRNA

Prior to the linear regression analyses, Spearman's correlations between *DDR1* CpG 5-mC levels (each *DDR1* CpG site and avg 5-mC *DDR1*) and mRNA levels (total *DDR1* and each *DDR1* isoform) were computed. Only those CpGs showing a statistically significant association with *DDR1* mRNA after correction for multiple testing by the BH procedure and with an FDR <5% were included in the subsequent LRM. After this, we carried out exploratory linear regression analyses (following the 'stepwise' method) using the whole transcript and isoform mRNA levels as the dependent variables and the *DDR1* 5-mC levels (avg 5-mC and individual CpG sites), SNP genotypes (rs2267641, rs2844654, rs1264323 alleles associated with gene expression according to [15]), sex, age, PMI, brain pH, % of glial cells and diagnosis as the independent variables. Finally, a final LRM was designed for each dependent variable using the 'enter' method that included only variables that showed a significant association with *DDR1* mRNA in the previous analysis.

DNA comethylation analysis

With the rationale that myelination is in part modulated by DNA methylation of key genes, we performed a comethylation analysis of *DDR1* with conventional myelin marker genes and nonmyelin control marker genes of astrocytes, microglia and neurons (Supplementary Table 2) to explore whether *DDR1* is methylated in a similar manner as myelin genes. The comethylation analysis based on Spearman correlations was carried out in two different ways. The first analysis was conducted using the mean methylation level of each gene (avg 5-mC). The second analysis was performed using individual CpG methylation levels in each gene to obtain more detailed information. Both correlation analyses were carried out in the whole sample sets and separately for patients and HCs. Only correlations with a coefficient >0.75 and adjusted (BH) p-value < 0.01 are shown.

Statistical software

DNA methylation data analyses, Spearman correlation tests, multiple testing corrections by the BH method, deconvolution analysis and figure generation were performed using the R environment for statistical computing (version 3.6.2). IBM SPSS Statistics 20.0 (IBM Corp., NY, USA) was used to perform the LRMs.

Table 1. *DDR1* CpG sites differentially methylated in glia-occipital cortex tissues between patients with bipolar disorder and healthy controls.

CpG	HC	BD	% Increase	p-value†	Adj p-value‡
	Mean ± SD	Mean ± SD			
DDR1 avg 5-mC	0.306 ± 0.029	0.322 ± 0.040	5.41	0.009	0.090
cg05703744	0.512 ± 0.102	0.575 ± 0.108	12.24	0.008	0.090
cg08951271	0.453 ± 0.078	0.474 ± 0.061	4.59	0.019	0.090
cg08684361	0.111 ± 0.034	0.124 ± 0.031	11.87	0.028	0.104
cg09965419	0.264 ± 0.024	0.290 ± 0.049	9.84	0.021	0.090
cg15656686	0.303 ± 0.052	0.339 ± 0.070	11.97	0.019	0.090
cg16537676	0.415 ± 0.037	0.442 ± 0.047	6.41	0.047	0.128
cg17604312	0.492 ± 0.035	0.515 ± 0.041	4.53	0.016	0.090
cg20955507	0.223 ± 0.027	0.246 ± 0.040	10.42	0.019	0.090
cg22485298*	0.153 ± 0.033	0.222 ± 0.066	44.85	0.001	0.045*
cg25607383	0.244 ± 0.024	0.265 ± 0.036	8.39	0.018	0.090
cg01598675	0.715 ± 0.037	0.740 ± 0.051	3.47	0.019	0.090
cg01936707*	0.699 ± 0.059	0.737 ± 0.059	5.42	0.001	0.045*
cg06200824	0.582 ± 0.054	0.615 ± 0.048	5.67	0.018	0.090
cg07908039	0.572 ± 0.085	0.632 ± 0.116	10.40	0.037	0.115
cg07912416	0.652 ± 0.068	0.692 ± 0.069	6.26	0.004	0.090
cg07979747	0.717 ± 0.080	0.770 ± 0.079	7.47	0.003	0.090
cg08673763	0.641 ± 0.046	0.673 ± 0.065	5.01	0.020	0.090
cg09810078	0.909 ± 0.032	0.926 ± 0.034	1.85	0.029	0.104
cg09822812	0.414 ± 0.062	0.462 ± 0.127	11.63	0.044	0.124
cg11530564	0.470 ± 0.137	0.539 ± 0.152	14.52	0.041	0.122
cg12669395	0.413 ± 0.047	0.449 ± 0.071	8.77	0.013	0.090
cg13351860	0.391 ± 0.079	0.430 ± 0.092	9.98	0.024	0.098
cg14790552	0.699 ± 0.056	0.731 ± 0.062	4.48	0.033	0.109
cg16111190	0.557 ± 0.039	0.588 ± 0.053	5.53	0.007	0.090
cg16993957	0.824 ± 0.025	0.846 ± 0.027	2.67	0.010	0.090
cg17176005	0.788 ± 0.051	0.818 ± 0.057	3.89	0.016	0.090
cg19148201	0.637 ± 0.076	0.674 ± 0.078	5.82	0.029	0.104
cg21677258	0.607 ± 0.100	0.672 ± 0.124	10.73	0.019	0.090
cg24517175	0.896 ± 0.013	0.908 ± 0.017	1.33	0.042	0.122
cg27237814	0.573 ± 0.070	0.597 ± 0.069	4.11	0.032	0.109
cg15720085	0.655 ± 0.052	0.684 ± 0.038	4.34	0.034	0.109
cg16797094	0.456 ± 0.106	0.529 ± 0.137	15.95	0.017	0.090
cg25613385	0.452 ± 0.030	0.477 ± 0.042	5.70	0.020	0.090

†F-test LRM comparing 5-mC levels (M-values) between cases and controls using sex, age, brain pH, PMI and %glia as covariables.
‡*Post hoc* Benjamini & Hochberg method for multiple testing correction.
*Highlight significant comparisons after multiple testing correction.
%glia: Proportion of glial cells; Avg: Average; BD: Bipolar disorder; HC: Healthy control; LRM: Linear regression model; OC: Occipital cortex; PMI: Postmortem interval.

Identification of gene regulatory sequences

We used large-scale data from the ENCODE project (ENCODE https://www.encodeproject.org), GeneHancer [32], and the Open Regulatory Annotation database (ORegAnno) [33] to map the regulatory elements that overlap with the hypermethylated *DDR1* CpG sites found in patients with BD or associated with *DDR1* mRNA expression.

Results

DDR1 CpGs in the brain tissues of patients with BD are differentially methylated compared with those in HC tissues

Table 1 shows the comparison analysis of brain *DDR1* 5-mC levels between individuals with BD and HCs in glia-OC. A total of 31 *DDR1* CpGs were differentially hypermethylated in patients with BD compared with HCs,

Table 2. Association between *DDR1* isoform expression and the 5-methylcytosine level in occipital cortex tissues.

DDR1 expression (isoforms a–e)†	Variable	Variable statistics				Model			Adj p-value‡
		B	SE B	β	p-value	AdjR^2	F	p-value	
DDR1 total	cg18093866	-1.679	0.655	-0.442	0.016	0.196	6.563	0.016	0.020
Isoform a	cg24282845	-0.738	0.345	-0.359	0.042	0.214	4.813	0.017	0.020
	brain_pH	-0.700	0.322	-0.365	0.039				
Isoform b	cg25943433	1.057	0.181	0.601	5.0×10^{-6}	0.719	18.943	3.8×10^{-7}	5.3×10^{-6}
	Diagnosis	-0.567	0.143	-0.485	0.001				
	rs2267641_AC	-1.071	0.206	-0.849	2.5×10^{-5}				
	Diagnosis*rs2267641_AC	0.945	0.264	0.656	0.001				
Isoform c	cg25943433	-1.020	0.310	-0.499	0.003	0.361	8.899	0.001	0.002
	rs2267641_AC	0.513	0.222	0.350	0.029				
Isoform d	cg16111190	-1.313	0.334	-0.536	0.001	0.535	17.095	1.8×10^{-5}	5.4×10^{-5}
	cg14928451	-0.932	0.332	-0.383	0.009				
Isoform e	cg24646556	-1.301	0.552	-0.413	0.026	0.140	5.549	0.026	0.026

Summary of the linear regression analyses (enter method) for variables predicting *DDR1* isoform expression. Only variables showing statistical significance in a previous exploratory linear regression analysis (stepwise method) were included in the model. Independent variables: 5-mC levels, SNPs (rs2267641, rs2844654, rs1264323), PMI, age, sex, brain pH, %glia and BD diagnosis.
†Log transformed variables.
‡Post hoc Benjamini & Hochberg method for multiple testing correction.
%glia: Proportion of glial cells; BD: Bipolar disorder; OC: Occipital cortex; PMI: Postmortem interval.

with nominal p-values, and two (cg22485298 and cg01936707) remained significant after correcting for multiple testing (BH-FDR <0.05). The %5-mC level increase in the BD group ranged from 1.3–44.8%. We also found that the *DDR1* average 5-mC was significantly increased (5.4%, nominal p = 0.009) in the BD group.

We then validated the results by conducting similar analyses in two different sample sets from the DLPFC and prefrontal cortex NeuN+ nuclei (Supplementary Table 6). In glia-DLPFC tissue, we did not find any significant difference in *DDR1* CpGs between the groups, although there was a trend toward hypermethylation in patients with BD compared with HCs, with an increase ranging from 3.6–19%. Conversely, in NeuN+ nuclei, *DDR1* cg24282845 and cg25251478 were hypomethylated in BD patients compared with HCs (-0.5 and -8.6%, nominal p = 0.012 and p = 0.005, respectively), and cg24790028 was slightly hypermethylated in BD patients (0.8%, nominal p = 0.015), but these comparisons were not significant after multiple testing correction. No significant differences were found for *DDR1* average 5-mC between BD and HCs in NeuN+.

DDR1 5-mC levels & *DDR1* mRNA expression

Spearman correlations between *DDR1* 5-mC (avg 5-mC and each CpG) and the mRNA levels for total *DDR1* and for *DDR1* isoforms from the OC tissues were computed (Supplementary Table 7). The bivariate analysis showed that 48 CpGs correlated with *DDR1* isoform mRNA levels; two CpGs negatively correlated with total *DDR1* expression; two CpGs negatively correlated with *DDR1*a mRNA; four CpGs positively correlated with *DDR1*b mRNA; six CpGs negatively correlated with *DDR1*c; 43 CpGs and *DDR1* average 5-mC negatively correlated with *DDR1*d; and one CpG negatively correlated with *DDR1*e. Taking this information into account, a linear regression analysis was performed to test whether *DDR1* 5-mC levels were differentially associated with each *DDR1* mRNA transcript (total *DDR1* mRNA and each of the five isoforms) in BD patients compared with HCs, including relevant covariables (Table 2).

The most significant result (model adjp = 5.9×10^{-6} and adjR^2 = 0.719) was found for *DDR1*b. First, cg25943433 5-mC levels were directly associated with *DDR1*b mRNA levels. Second, BD diagnosis and the rs2267641_AC genotype were inversely associated (β = -0.493, p = 0.001 and β = -0.849, p = 2.5×10^{-6}) with isoform mRNA. However, the interaction between BD diagnosis and the rs2267641_AC genotype was directly associated (β = 0.601, p = 5.0×10^{-6} and β = 0.656, p = 0.001, respectively) with *DDR1*b mRNA levels. In summary, BD patients had lower levels of *DDR*1b mRNA, but the subgroup of BD patients carrying the rs2267641_AC genotype and with high levels of cg25943433 5-mC showed higher levels of *DDR1*b than HC carrying the rs2267641_AC genotype.

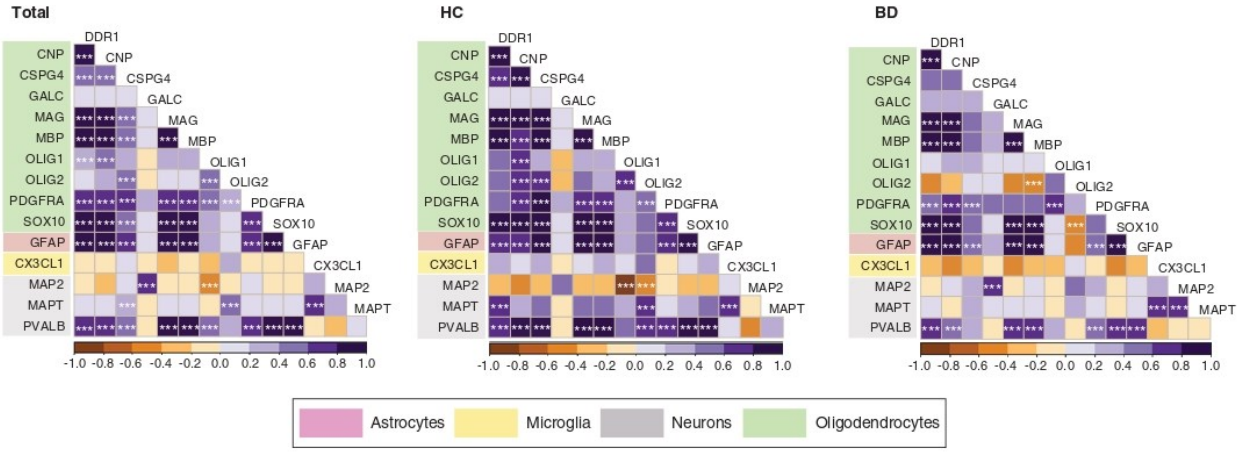


Figure 1. Comethylation of *DDR1* with conventional brain cell type gene markers in occipital cortex tissue from patients with bipolar disorder and healthy controls. Correlograms for average methylation levels between *DDR1* and conventional oligodendrocyte and myelin genes and gene markers for astrocytes, microglia and neurons in occipital cortex tissue. Each significant p-value after adjustment by the Benjamini and Hochberg method (false discovery rate <0.05) is associated with a symbol.
***p < 0.001; **p < 0.01; *p < 0.05.
BD: Bipolar disorder; HC: Healthy control.

The second most significant result (model adjp = 5.4×10^{-5} and adjR2 = 0.535) was found for *DDR1*d, which, although there was no significant difference in expression between BD patients and HCs, showed a strong negative association with cg16111190 and cg14928451 (β = -0.536, p = 0.001 and β = -0.383, p = 0.009, respectively).

*DDR1*c was positively associated with the presence of the rs2264323_C allele, as previously shown [16]; in addition, here, we also found a significant negative association with cg25943433 (model adjp = 0.002 and adjR^2 = 0.361).

*DDR1*a mRNA levels were inversely associated with cg24282845 5-mC levels and brain pH (β = -0.359, p = 0.042 and β = -0.365, p = 0.039, respectively). *DDR1*e mRNA levels were inversely associated with cg24646556 (β = -0.413, p = 0.026). Finally, total *DDR1* mRNA levels were inversely associated with cg18093866 5-mC levels (β = -0.442, p = 0.016). A regression analysis to validate the association between *DDR1* mRNA and 5-mC levels in DLPFC tissue was not carried out since no significant correlations in the previous bivariate analysis were found between 5-mC and the mRNA levels. Instead, in the NeuN+ samples, we found that *DDR1* total mRNA was directly associated (model p = 0.002, adjR^2 = 0.355) with cg01598675 (β = 0.367, p = 0.035) and negatively associated with BD diagnosis (β = -0.422, p = 0.017). Notably, in these two datasets, only *DDR1* total mRNA expression was available.

DDR1 comethylation with myelin genes

To test our hypothesis that *DDR1* comethylates with myelin genes, pairwise correlations were computed in the OC data. We carried out comethylation analysis using two complementary approaches. On the one hand, we tested for an association by computing correlation coefficients using the average 5-mC level in each gene. On the other hand, we computed correlation coefficients using the 5-mC levels in each CpG site in all genes. Arbitrarily, Spearman's coefficients ≥0.75 with adjusted (BH) p-value < 0.05 were selected as a measure of relevant comethylation in both scenarios. The analysis of the average 5-mC levels per gene in the total OC sample (Figure 1) showed a strong positive correlation between *DDR1* and the myelin genes *CNP, CSPG4, MAG, MBP, PDGFRA* and *SOX10* and a moderate positive correlation with *OLIG1*. *DDR1* methylation also showed a positive correlation with *GFAP* (astrocytes) and *PVALB* (neurons) but did not correlate with the *GALC* and *OLIG2* myelin markers. When we analyzed the BD and HC groups separately, the most relevant change was that *DDR1-CSPG4* comethylation was high in HCs but not in patients with BD (Figure 1). The results of the comethylation analysis for individual CpG 5-mC levels in OC are shown in Supplementary Table 8. We found that 66 of the 90 (73.3%) *DDR1* CpGs were significantly correlated (r ≥ 0.75 and adjusted (BH) p-value <0.0001) with CpGs of the myelin genes selected. The results of the comethylation analysis in the validation samples (DLPFC and NeuN+) are shown in Supplementary Figure 2. In the DLPFC (total n = 8: 4 HC and 4 BD), no significant correlations were

observed between *DDR1* methylation and any gene in the total sample or in the HC subgroup. Conversely, in the BD group, *DDR1* methylation was inversely correlated with *GALC* (myelin) and positively correlated with *SOX10* (myelin) and *MAP2* (neuron). In the NeuN+ total sample, *DDR1* methylation positively correlated with *CNP, MAG* and *SOX10* (myelin); *GFAP* (astrocyte); and *PVALB* (neuron). The same pattern was observed when stratifying the sample by diagnosis. Notably, in NeuN+, a strong positive correlation was observed between *CNP, MAG* and *SOX10* (myelin genes), and a strong negative correlation was observed between *CNP, MAG* (myelin) and *MAP2* (neuron). The results of individual CpG comethylation in the validation samples (DLPFC and NeuN+) are provided in Supplementary Table 9. In the DLPFC, the two *DDR1* CpGs included in the analysis did not significantly correlate with any of the myelin gene CpGs. In the NeuN+ nuclei, 29 of the 99 (29.3%) *DDR1* CpGs were significantly correlated with the myelin genes *CSPG4, MAG, MBP, OLIG2* and *SOX10*.

Transcription factor-binding sites & regulatory elements matching *DDR1* methylated CpGs

Figure 2 shows the chromosomal position of each CpG with a relevant finding in the present study as well as the relative position of regulatory elements and Transcription factor-binding sites (TFBSs) matching each CpG. *DDR1* cg18093866 and cg24646556 associated with *DDR1* mRNA levels and cg22485298 hypermethylation in patients with BD were located in the promoter region of the gene (chr6: 30847554-30856766) matching the DNase I hypersensitivity regions and overlapped with the binding regions of the histone acetylase and methylase enzymes (acetylase 27th lysine residue of the histone H3 [H3K27ac] and the methylase trimethylation at the fourth lysine residue of the histone H3 protein [H3K4 me3]). These three CpGs overlapped with the EGR1 and POLR2A binding sites, and cg22485298 also overlapped with SAP30 and SIN3A, which form part of the histone deacetylase complex. Moreover, cg18093866 overlapped with E2F1, a transcription factor that plays an important role in the control of the cell cycle, and TFAP2C, a proximal promoter transcription activator. In exon 8, cg16111190 (associated with *DDR1*d mRNA levels) and cg01936707 (hypermethylated in patients with BD) overlapped with the binding site for CTCF, which is known to have transcriptional activating or repressing functions and to create chromatin loops. Three CpGs (cg24282845 associated with *DDR1* mRNA levels, cg14928451 associated with *DDR1*d mRNA levels and cg01598675 associated with *DDR1* mRNA levels in NeuN+ nuclei) were located in exon 15 without matching TFBSs but very close to miR binding sites (Figure 2B). Finally, we found that cg25943433 was located at the end of the gene (exon 17) and overlapped with EGR1 and the *DDR1* 8-mer binding sites for miR-199-5p. Notably, four out of seven of the CpGs associated with *DDR1* mRNA expression were found to be located within exons 15–17 in the terminal region of the gene. A detailed description of each transcription factor is provided in Supplementary Table 10.

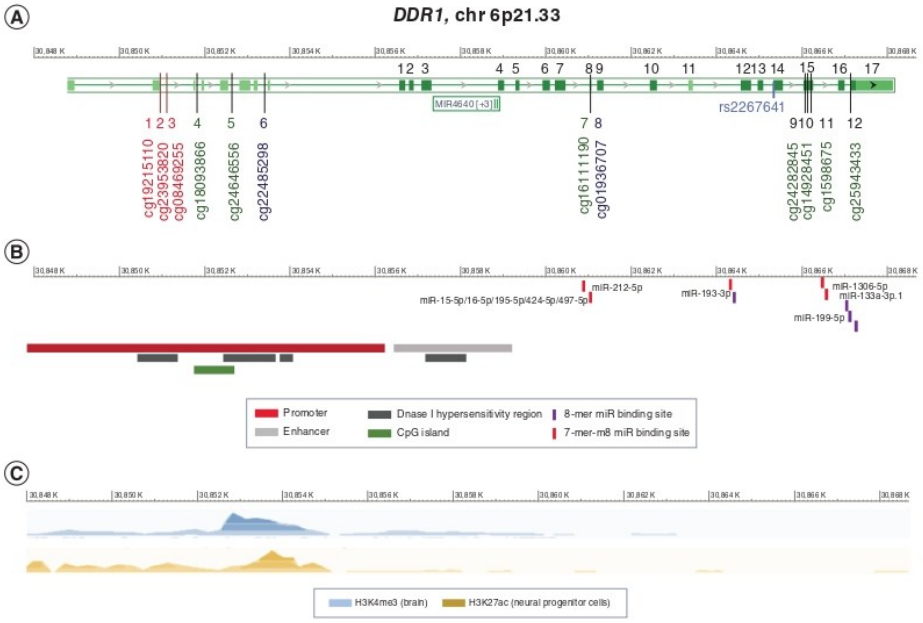
Discussion

Differential methylation of *DDR1* in patients with BD

Our findings provide the first evidence that *DDR1* methylation is altered in the brain tissues of patients with BD. Specifically, two *DDR1* CpGs were hypermethylated in glia-OC. This finding was partially supported by the results in glia-DLPFC, showing *DDR1* hypermethylation in patients with BD compared with HCs; however, these differences were not significant, probably due to the small sample size (HC = 4; BD = 4). Conversely, we found two nominally significant hypomethylated *DDR1* CpGs in NeuN+ (neurons) from patients with BD. Viana and colleagues [36] reported that eight *DDR1* CpGs were hypomethylated in SZ patients in four brain regions (prefrontal cortex, striatum, hippocampus and cerebellum), controlling for the derived neuronal composition. We previously reported hypermethylation of *DDR1* CpG cg19215110 in the DLPFC of patients with SZ without controlling for the cell composition [16], and regarding peripheral blood tissue, we observed hypermethylation in two *DDR1* CpGs (cg19215110 and cg23953820), which was associated with psychological and biological stress markers [16]. Moreover, these two sites overlapped with the glucocorticoid receptor DNA-binding sites (Figure 2). Clive and colleagues [34] found a *DDR1* CpG (cg08469255) hypermethylated and associated with a biosignature of inflammation and hypothalamic-pituitary-adrenal axis dysregulation in a study of suicidal predictive factors.

Association of *DDR1* methylation & diagnostic status with *DDR1* gene expression

Here, we show that patients with BD had decreased *DDR1*b expression levels that were positively associated with methylation at cg25943433 in OC. On the other hand, total *DDR1* and *DDR1*a, -c, -d and -e mRNA expression, although not differentially expressed in patients, was inversely associated with *DDR1* methylation. We recently demonstrated an inverse relationship between *DDR1* 5-mC levels (cg14279856) and *DDR1*c expression in DLPFC



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	CpG	TFBS[1] with signal intensity 1	Findings
1	cg19215110	POLR2A, NR3C1	DM (hyper) in SZ (blood and brain)[2]
2	cg23953820	POLR2A, PAX5, NR3C1	DM (hyper) in SZ (blood)[2]
3	cg08469255	POLR2A, PAX5, EGR1	Associated with suicidal behavior[3]
4	cg18093866	E2F1, EGR1, POLR2A, TFAP2C	Associated (-) to total *DDR1* mRNA levels in glia-OC
5	cg24646556	EGR1, POLR2A	Associated (-) to *DDR1e* mRNA levels in glia-OC
6	cg22485298	EGR1, POLR2A, SAP30, SIN3A	DM (hyper) in BD glia-OC
7	cg16111190	CTCF	Associated (-) to *DDR1*d mRNA levels in glia-OC
8	cg01936707	CTCF	DM (hyper) in BD glia-OC
9	cg24282845	None	Associated (-) to *DDR1a* mRNA levels in glia-OC
10	cg14928451	None	Associated (-) to *DDR1*d mRNA levels in glia-OC
11	cg01598675	None	Associated (+) to *DDR1*d mRNA in NeuN+
12	cg25943433	EGR1	Associated to *DDR1b* (+) and *DDR1c* (-) mRNA levels in glia-OC

DM: differentially methylated; NeuN+: neuronal nuclei; SZ: schizophrenia
Blue: differentially methylated in BD patients; green: associated to *DDR1* mRNA expression; red: not included in the present study.
[1]Transcription factor ChIP-seq clusters (161 factors. The signal intensity 1 corresponds to the maximum signal strength observed in any cell type contributing to the cluster) from ENCODE project and The Open Regulatory Annotation database (ORegAnno).
[2]Garcia-Ruiz et al., 2020.
[3]Clive et al., 2016.

Figure 2. Overlap of *DDR1* CpG sites with relevant results with transcriptional regulatory element-binding sites. (A) Vertical lines numbered from 1 to 12 represent the genomic position of *DDR1* CpGs assessed with a relevant finding in the present study (black lines and numbers) and previously identified in psychiatric conditions (red lines and numbers) [16,34]. The locus for rs2267641 is also shown. **(B)** Graphical representation of regulatory elements of promoters (red rectangles); enhancers (gray rectangles) from the GeneHancer database showing the higher confidence score in both cases; and DNase I hypersensitivity sites (black rectangles) from ENCODE. CpG island is indicated with a green rectangle identified by the USCS Genome Browser. Effective miRNA target sites 8-mer (violet) and 7-mer-m8 (red) are shown according to TargetScanHuman (v7.2) [35]. **(C)** NCBI genome browser view of methylase trimethylation at the fourth lysine residue of the histone H3 protein mark (H3K4 me3) (blue) corresponding to ChIP-Seq analysis of adult human brain tissue (GSM1586388) and acetylase 27th lysine residue of the histone H3 mark (H3K27ac) (yellow) corresponding to ChIP-Seq analysis of neural progenitor cells from human embryonic stem cells (cell line H1) (GSM767343). **(D)** *DDR1* CpG code numbers for the Infinium MethylationEPIC BeadChip (Illumina) shown in **(A)**, the matched transcription factor binding sites and a summary of the findings.
TFBS: Transcription factor binding site; NeuN+: Neuronal nuclei.

tissue in SZ [16]. Notably, we previously observed that the relationship between the expression of *DDR1*c and *DDR1*b mRNA is always inverse [20,21]. Hypermethylation of *DDR1* has been extensively studied in cancer cells and is always associated with lower mRNA levels [37–39]. Studies in neuropsychiatric disorders have reported high levels of methylation associated with low mRNA expression at several loci. For instance, Chen and colleagues [40] found that methylation at several CpGs of four genes associated with psychiatric disorders (*COMT, RELN, OPRM1, SLC1A4*) in the brains of SZ and BD patients was associated with a decrease in its expression. Focusing on myelination, the gene coding for *SOX10*, an oligodendrocyte-specific transcription factor, was found to be hypermethylated in the brains of patients with SZ, and hypermethylation correlated with reduced gene expression [6].

In the present study, we found that *DDR1* isoform expression was associated mainly with methylation at CpGs located at the end of the gene. The main result is the direct relationship between methylation at the cg25943433 and *DDR1*b mRNA levels. The 3' end of *DDR1* contains three binding sites for the miRNA miR199-5p, which represses *DDR1* expression [15]. Although differential methylation in the promoter region could modulate gene expression independently of the isoform, differential methylation at the end of the gene could modulate isoform expression. Further studies are needed to elucidate the mechanisms underlying these associations.

Comethylation of *DDR1* with conventional myelin genes

DNA methylation is an important regulator of the differentiation of oligodendrocytes in myelination and remyelination [41]. Here, we report evidence on the comethylation of *DDR1* in brain tissue with a group of conventional myelin genes, adding further support to the involvement of *DDR1* in myelination. In OC, *DDR1* comethylates with *OLIG1* and *SOX10* (oligodendrocyte transcription factors) and with *CNP, MAG, MBP* and *PDGFRA*, which code for relevant oligodendrocyte proteins and important myelin components. We previously showed a high correlation of mRNA levels of *DDR1* (specifically *DDR1*c) with *OLIG2* and *MAG* in the human brain [21] and tissue colocalization of *DDR1* with myelin proteins such as MBP [20]. In OC, *DDR1* also comethylated with *GFAP* (astrocytes). Comethylation with *GFAP* was expected to be in accordance with our previous result on immune colocalization of *DDR1* and *GFAP* in the human brain cortex [20]. Notably, in OC, *DDR1* methylation was positively correlated with *PVALB* (neurons); however, since *DDR1* is apparently not expressed in neurons, this result is difficult to interpret. In NeuN+ nuclei, *DDR1* showed a strong negative correlation with *MAP2* and *MAPT* neuronal markers and *CX3CL1* (microglia). Altogether, these results of strong comethylation of *DDR1* with different cell type markers indicate that it may be related to cell specialization and that *DDR1* must be activated in a certain cell type (e.g., oligodendrocytes) and at certain times of the cell cycle [15].

Gene localization of the *DDR1* CpGs with relevant results in the present study

Three *DDR1* CpGs are located in the promoter region of the gene overlapping with DNase I hypersensitivity regions and with CpG island shores, and one of them is located in a CpG island. Four *DDR1* CpGs matched the *EGR1* binding sequences distributed along the gene. *EGR1* is a transcription factor known to inhibit oligodendrocyte differentiation [42,43]. Six *DDR1* CpGs, including two from our previous article [16], overlapped with *POLR2A*, and one of them (cg18093866) was inversely associated with total glia-OC *DDR1* mRNA. This suggests that methylation variation in these CpGs could modulate transcription activation at *DDR1*. Interestingly, this region also has a binding site for a transcription repressor, *SIN3A*, which is involved in neuronal axonal elongation. Two CpGs (cg16111190 associated with *DDR1*d mRNA levels and cg01936707 hypermethylated in patients with BD glia-OC) overlapped with the CTCF binding site. CTCF is a zinc-finger DNA-binding protein that mediates interactions between distant sequences in the genome. As a consequence, CTCF regulates enhancer–promoter interactions, alternative splicing, recombination and DNA repair [44].

In summary, hypermethylation of *DDR1* is found in the promoter region of the gene and in exon 8 matching the CTCF binding site. On the other hand, two *DDR1* CpGs were also located in the promoter region associated with gene expression, and one of them was associated with total *DDR1* mRNA. Finally, most of the CpGs associated with *DDR1* isoform-dependent expression are located at the end of the gene, suggesting that it could match splicing regulatory sites and several miRNA-binding sites, such as those for miR199-5p RNA.

These findings should be interpreted in consideration of several limitations. First, the study main sample was limited to OC. Although functional [45] and structural [46–50] MRI studies have described aberrant activity and cortical thickness deficits in OC in BD, other brain regions have also been involved; therefore, future studies should include and compare methylation profiles in several brain regions. Additionally, other psychiatric diagnostics were included for comparison. Second, the sample size was limited, especially in the DLPFC validation sample

(n = 4 per group). Third, the use of DNA extracted from whole-tissue homogenates can make it difficult to detect changes in methylation since there is evidence that DNA methylation patterns differ considerably between different cell types [51]. Despite our efforts to infer the cell type composition of our sample using an *in silico* technique (deconvolution analyses), this limitation does not allow us to assert methylation in specific cell types, a result that could be relevant for understanding disease-related molecular changes. Fourth, we combined information from different platforms for expression and methylation profiling and data preprocessing, entailing bias that may affect the reliability of our findings [52,53]. Furthermore, some of the methylation probe sets we used in OC did not exactly correspond to the CpG sites investigated in the DLPFC and NeuN+, which prevents replication of the results between samples. Fifth, although we removed the effects of some covariates (e.g., age, sex, brain pH and PMI), our results may still be sensitive to other factors, such as disease status, drug use or abuse, other genetic variants, environmental factors or events related to pathological processes [54–57]. In addition, although we cannot rule out that these methylation changes were the consequence of pharmacological therapies other than antipsychotics, *DDR1* methylation was not found to be affected by medication and alcohol and tobacco use in a previous study [16]. Even if that is so, the results are relevant to understanding the disease and the individual response to medication. We could not control our analyses for mood stabilizers or antidepressants, but in future studies, this information should be collected and controlled for.

Conclusion

In conclusion, we found hypermethylation of *DDR1* CpGs and lower *DDR1*b mRNA levels in glia-OC in BD patients. Furthermore, *DDR1* methylation showed a tendency toward an increase in glia-DLPFC and was decreased in NeuN+ neurons in patients with BD. *DDR1* hypermethylation was associated with higher *DDR1*b and lower *DDR1*a, -c, -d and -e mRNA expression in OC tissue. We also reported *DDR1* comethylation with several myelin genes, further supporting the involvement of *DDR1* in myelination.

Future perspective

Biomarkers based on epigenetic changes in certain genes, such as *DDR1*, will be useful in stratifying and staging psychiatric patients and providing more accurate diagnosis and personalized treatments. This is the first study reporting *DDR1* hypermethylation associated with BD and specific isoform expression. Additionally, evidence of *DDR1* comethylation with the most important myelin genes adds further support for the role of this receptor in myelination. Future research is necessary to confirm these results, and experimental designs should focus on elucidating the role of *DDR1* in myelination and neuroinflammation in the context of BD pathophysiology. Our next steps will focus on the study of blood *DDR1* methylation in a larger sample of patients with BD diagnosis and on the relationship between *DDR1* and myelin integrity in BD.

Summary points

- We found increased 5-mC levels at two *DDR1* CpG sites in occipital cortex tissues from patients with bipolar disorder (BD) diagnosis compared with healthy controls.
- One hypermethylated *DDR1* CpG is located in the promoter region, and the other is located in exon 8.
- Patients with BD had decreased *DDR1*b expression levels that were positively associated with methylation at cg25943433 in occipital cortex tissue.
- The presence of the rs2261647_AC genotype in healthy controls but not in BD patients eliminates the positive correlation between cg25943433 5-mC and *DDR1*b mRNA levels.
- Total *DDR1* and *DDR1*a, -c, -d and -e mRNA expression was inversely associated with *DDR1* methylation at *DDR1* cg18093866, cg24282845, cg25943433, cg16111190-cg14928451 and cg24646556 sites, respectively.
- We found that *DDR1* isoform expression was associated mainly with methylation at CpGs located at the promoter region, exon 8 and the end of the gene.
- In occipital cortex, *DDR1* shows strong comethylation with conventional myelin genes (*CNP, MAG, MBP, OLIG1, PDGFRA* and *SOX10*).

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/epi-2021-0006

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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Supplementary material Article 2

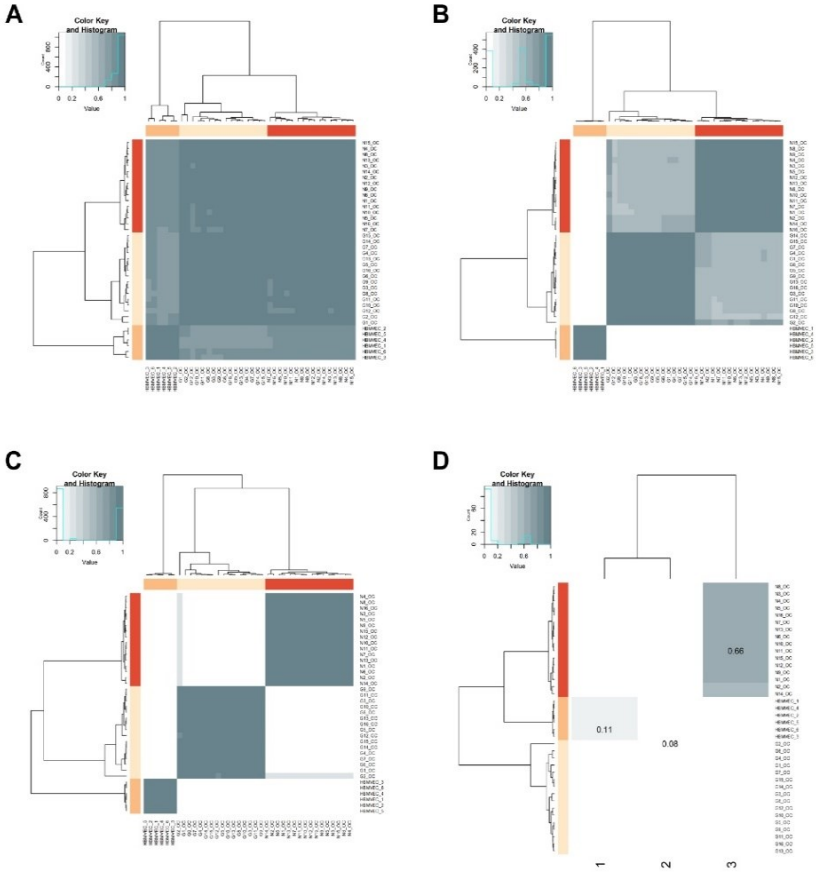

Figure S1. Cell-type deconvolution analysis in bulk tissue from whole-methylome data of OC by the epigenomic deconvolution (EDec) technique.
Heatmaps showing the results of the different steps to deconvolute the methylation profiles of OC samples (Onuchic et al., 2016 and Material and Methods section). Color intensity reflect the strength of the correlations. **A**: Heatmap visualization of pairwise Pearson correlations of the methylation profiles of the three reference cell type classes: glial cells, neurons, and HBMVECs based on hierarchical clustering. **B**: Heatmap visualization of pairwise Pearson correlations of 500 selected marker loci from reference methylation profiles by EDec stage 0 based on T-test comparations of each reference class against all other samples (marker_ovr method). **C:** Heatmap visualization of pairwise Pearson correlations of 500 selected marker loci from reference methylation profiles by EDec stage 0 based on T-test comparations between each pair of reference classes (marker_ep method). **D:** Visualization of the matrix of estimated proportions of constituent cell-types in bulk tissues of OC samples by EDec stage 1 using a three cell-type model and the markers_ovr method.

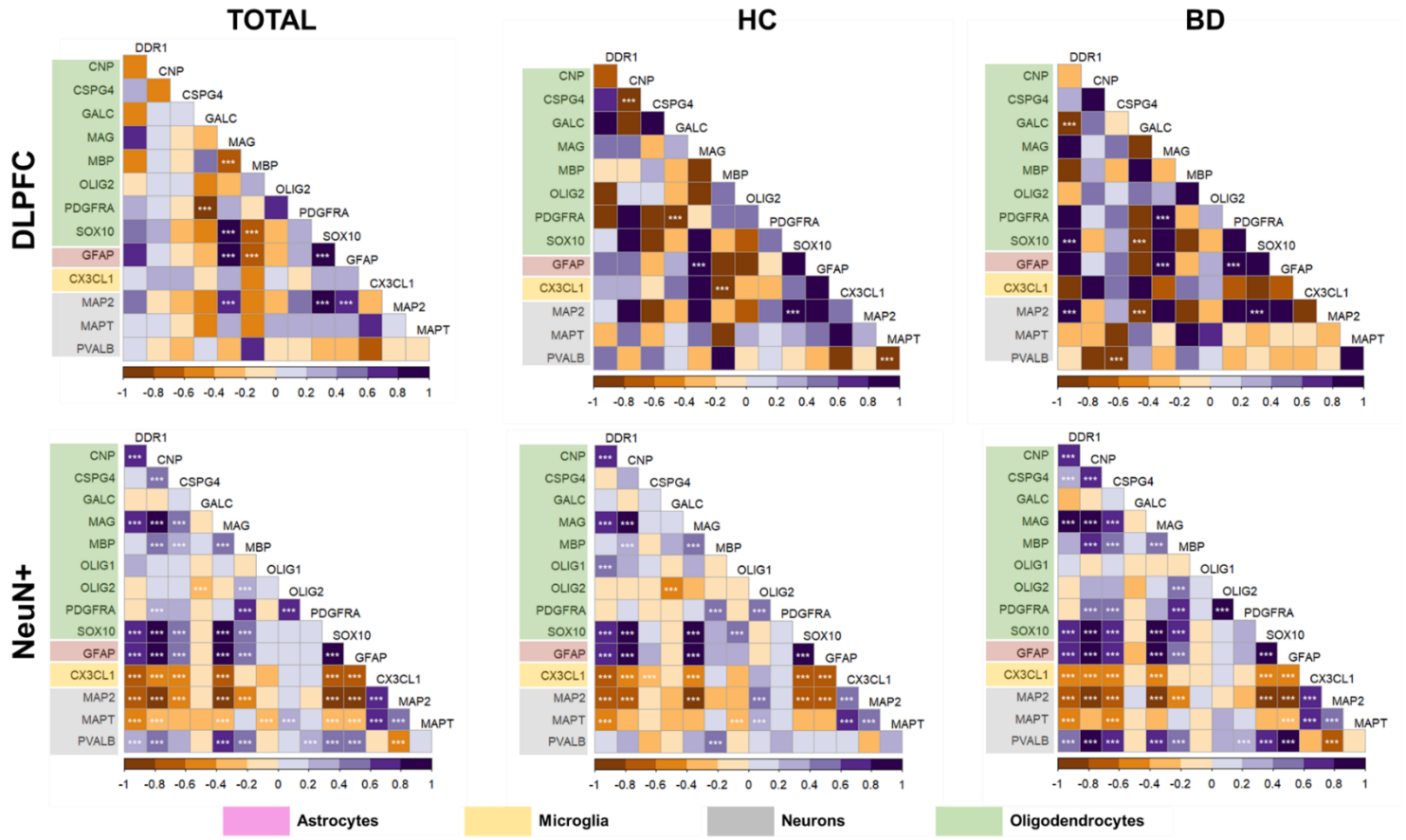

Figure S2. Comethylation of DDR1 with conventional brain cell type gene markers in DLPFC and NeuN+ tissues from patients with BD and HCs.
Correlograms for the average methylation levels between DDR1 and conventional oligodendrocyte and myelin genes and gene markers for astrocytes, microglia, and neurons in OC tissues. Each significant *p*-value after adjustment by the BH method (FDR 0.05) is associated with a symbol (***p<0.001, **p<0.01, *p<0.05). Abbreviations: DLPFC: Dorsolateral prefrontal cortex; NeuN+: Neuronal nuclei; 5-mC: 5-methylcytosine; HC: Healthy controls; BD: Bipolar disorder; BH: Benjamini & Hochberg method; FDR: False discovery rate.

Table S1. Dataset sample description

	OC			DLPFC			NeuN+		
	HC	**BD**	***p*-value[a]**	**HC**	**BD**	***p*-value[a]**	**HC**	**BD**	***p*-value[a]**
Sociodemographic characteristics									
N	14	15	NA	4	4	NA	27	26	NA
Sex (M/F)	9/5	9/6	0.812	3/1	3/1	1,000	24/3	14/12	0.005
Age (years), means ± SDs	48.17 ± 10.7	42.3 ± 11.2	0.288	40.5 ± 7.2	46.0 ± 11.8	0.457	47.3 ± 9.6	48.8 ± 14.1	0.652
Brain tissue integrity indicators									
Brain pH	6.3 ± 0.2	6.2 ± 0.2	0.356	6.7 ± 0.3	6.7 ± 0.1	0.775	NA	NA	NA
PMI	23.7 ± 9.9	32.5 ± 16.1	0.315	24.2 ± 2.6	33.0 ± 18.0	0.686	18.4 ± 5.9	17.6 ± 7.1	0.666
Experimental profiling methods									
DNA methylation	Illumina Infinium MethylationEPIC			Illumina HumanMethylation27 v.1.2			Illumina Infinium MethylationEPIC		
Gene expression	Custom TaqMan® assay (Applied Biosystems)			Affymetrix Human Genome U133 Plus 2.0			Illumina NextSeq® 500 System		

[a]t-test and Mann-Whitney tests for normal and nonnormally distributed variables, respectively, and $\chi 2$ test to compare the frequencies of categorical variables.
Abbreviations: DLPFC: Dorsolateral prefrontal cortex; NA: Not applicable; NeuN+: Neuronal nuclei; OC: Occipital cortex; PMI: Postmortem interval; SD: Standard deviation.

Table S2. Selected myelin, astrocyte, microglia and neuron gene markers

Gene symbol	Gene name	Chr.	Genomic location (GRCh38/hg38)	Genomic location (GRCh37/hg19)	Cell type marker
CNP	2',3'-Cyclic Nucleotide 3' Phosphodiesterase	17	41,966,741-41,977,740	40,118,759-40,129,754	Myelin
CSPG4	Chondroitin Sulfate Proteoglycan 4	15	75,674,322-75,712,848	75,966,663-76,005,189	Myelin
GALC	Galactosylceramidase	14	87,837,820-87,993,665	88,304,164-88,460,009	Myelin
MAG	Myelin Associated Glycoprotein	19	35,292,086-35,313,807	35,782,989-35,804,710	Myelin
MBP	Myelin Basic Protein	18	76,978,827-77,133,708	74,690,783-74,845,639	Myelin
OLIG1	OligodendrocyteTranscription Factor 1	21	33,070,141-33,072,422	34,442,450-34,444,728	Myelin
OLIG2	OligodendrocyteTranscription Factor 2	21	33,025,908-33,029,196	34,398,153-34,401,504	Myelin
PDGFRA	Platelet-Derived Growth Factor Receptor Alpha	4	54,229,097-54,298,245	55,095,264-55,164,414	Myelin
SOX10	SRY-Box Transcription Factor 10	22	37,970,686-37,987,422	38,366,693-38,383,429	Myelin
GFAP	Glial FibrillaryAcidicProtein	17	44,903,159-44,916,937	42,982,376-42,994,305	Astrocyte
CX3CL1	C-X3-C Motif Chemokine Ligand 1	16	57,372,461-57,385,048	57,406,370-57,418,960	Microglia
MAP2	Microtubule-Associated Protein 2	2	209,424,047-209,734,118	210,288,771-210,598,842	Neuron
MAPT	Microtubule-Associated Protein Tau	17	45,894,382-46,028,334	43,971,748-44,105,700	Neuron
PVALB	Parvalbumin	22	36,800,684-36,819,479	37,196,728-37,215,523	Neuron

Table S5. Matrix of estimated proportions of constituent cell types in the OC sample by EDec stage 1[a] using a 3 cell-type models and markers_ovr[b]

Sample_Id	HBMVEC	Glia	Neuron
UK.1OCCIP2	19.8%	44.1%	36.1%
UK.1OCCIP4	53.3%	37.7%	9.0%
UK.1OCCIP5	24.4%	16.3%	59.3%
UK.1OCCIP6	45.0%	35.9%	19.1%
UK.1OCCIP7	50.0%	29.3%	20.7%
UK.1OCCIP8	40.4%	33.9%	25.7%
UK.1OCCIP9	37.3%	17.6%	45.1%
UK.1OCCIP14	42.5%	34.4%	23.2%
UK.1OCCIP15	25.3%	14.2%	60.5%
UK.1OCCIP17	45.8%	19.6%	34.6%
UK.1OCCIP24	0.0%	1.2%	98.8%
UK.1OCCIP27	26.5%	29.7%	43.8%
UK.1OCCIP31	33.9%	20.7%	45.3%
UK.1OCCIP35	37.9%	13.2%	48.9%
UK.1OCCIP36	49.1%	32.3%	18.5%
UK.1OCCIP41	29.6%	17.2%	53.2%
UK.1OCCIP45	37.8%	46.5%	15.8%
UK.1OCCIP46	36.3%	25.1%	38.6%
UK.1OCCIP47	62.0%	38.0%	0.0%
UK.1OCCIP49	20.0%	65.7%	14.3%
UK.1OCCIP50	9.0%	9.6%	81.3%
UK.1OCCIP51	37.1%	23.1%	39.8%
UK.1OCCIP53	57.9%	0.0%	42.1%
UK.1OCCIP54	44.4%	35.5%	20.1%
UK.1OCCIP55	38.9%	25.6%	35.5%
UK.1OCCIP56	0.0%	70.4%	29.6%
UK.1OCCIP57	39.3%	33.9%	26.9%
UK.1OCCIP58	33.5%	21.2%	45.3%
UK.1OCCIP59	35.0%	19.1%	45.9%
Average cell type proportion	34.90%	28.00%	37.10%

[a]Cell type specific analysis of complex tissues by the EDec method.
[b]Selected loci that define cell type identity based on T-test comparations of each class of reference against all other samples. Abbreviations: EDec: Epigenomic deconvolution method; HBMVEC: Human brain microvascular endothelial cells; OC: Occipital cortex.

Table S6. *DDR1* CpG sites with 5-mC levels differentially methylated between patients with BD and HCs in DLPFC and NeuN+ nuclei from the FC tissues

Dataset	CpG	HC	BD	%variation	*p*-value	Adj *p*-value[a]
DLPFC (BD=4, HC=4)	DDR1 avg 5-mC	0.362 ± 0.015	0.381 ± 0.025	5.2%	0.197	NA
	cg11977634	0.079 ± 0.007	0.094 ± 0.007	19.0%	0.754	NA
	cg03270204	0.644 ± 0.033	0.667 ± 0.048	3.6%	0.353	NA
NeuN+ nuclei (BD=26, HC=27)	DDR1 avg 5-mC	0.615 ± 0.016	0.614 ± 0.018	-0.2%	0.498	NA
	cg24282845	0.955 ± 0.006	0.950 ± 0.008	-0.5%	0.012	0.500
	cg24790028	0.881 ± 0.018	0.888 ± 0.013	0.8%	0.015	0.500
	cg25251478	0.163 ± 0.018	0.149 ± 0.012	-8.6%	0.005	0.500

[a]F-test LRM comparing 5-mC levels (M-values) between cases and controls using sex, age, brain pH, PMI, and %glia as covariables in DLPFC and age, sex, and PMI in NeuN+ model. [b]Post hoc chberg method for multiple testing correction.
Abbreviations: 5-mC: 5-methylcytosine; BD: Bipolar disorder; DLPFC: Dorsolateral prefrontal cortex; FC: Frontal cortex; HCs: Healthy controls; LRM: Linear regression model; NeuN+: Neuronal nuclei; PMI: Postmortem interval.

Table S7. Significant correlations between *DDR1* 5-mC levels and *DDR1* isoform mRNA levels in OC tissue

DDR1 5-mC	*DDR1* transcript	ρ[a]	*p*-value	Adj *p*-value[b]
cg16111190	Total mRNA	-0.46	0.013	0.031
cg18093866	Total mRNA	-0.43	0.021	0.047
cg24282845	a	-0.48	0.008	0.020
cg06012011	a	-0.43	0.021	0.048
cg25943433	b	0.63	0.000	0.001
cg08913013	b	0.53	0.003	0.009
cg02696067	b	0.49	0.007	0.019
cg18577693	b	0.47	0.010	0.026
cg18577693	c	-0.53	0.003	0.009
cg08913013	c	-0.45	0.014	0.032
cg15720085	c	-0.45	0.015	0.036
cg02696067	c	-0.44	0.017	0.040
cg25943433	c	-0.44	0.018	0.040
cg24282845	c	-0.43	0.019	0.044
cg16111190	d	-0.64	0.000	0.001
cg08913013	d	-0.59	0.001	0.003
cg19215110	d	-0.59	0.001	0.003
cg01936707	d	-0.57	0.001	0.004
cg14928451	d	-0.56	0.001	0.005
cg08673763	d	-0.55	0.002	0.007
cg11676038	d	-0.54	0.002	0.007
cg13329862	d	-0.54	0.002	0.007
cg12669395	d	-0.54	0.003	0.008
cg16215084	d	-0.53	0.003	0.009
cg00934322	d	-0.52	0.004	0.011
cg24566261	d	-0.52	0.004	0.011
cg01598675	d	-0.52	0.004	0.012
cg14790552	d	-0.52	0.004	0.012
cg07908039	d	-0.51	0.004	0.012
cg08951271	d	-0.51	0.005	0.013
cg07979747	d	-0.50	0.005	0.014
cg14058861	d	-0.50	0.005	0.014
cg00034425	d	-0.50	0.005	0.015
cg21677258	d	-0.50	0.006	0.016
cg02695062	d	-0.49	0.007	0.019
cg09822812	d	-0.49	0.007	0.019
cg25251478	d	-0.49	0.008	0.020
cg27237814	d	-0.48	0.008	0.020
cg19591099	d	-0.48	0.008	0.020
cg27593250	d	-0.47	0.010	0.025
cg16993957	d	-0.47	0.010	0.025
cg07912416	d	-0.47	0.011	0.026
cg17176005	d	-0.46	0.011	0.027
cg25655106	d	-0.46	0.011	0.028
cg25943433	d	-0.46	0.012	0.028
cg15720085	d	-0.46	0.012	0.028
cg16797094	d	-0.46	0.012	0.029

Table S7. Significant correlations between *DDR1* 5-mC levels and *DDR1* isoform mRNA levels in OC tissue *(Continued)*

***DDR1* 5-mC**	***DDR1* transcript**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
cg17604312	d	-0.45	0.013	0.032
cg11530564	d	-0.45	0.014	0.033
cg18577693	d	-0.45	0.014	0.033
cg06501109	d	-0.45	0.014	0.034
cg13351860	d	-0.45	0.015	0.035
cg05703744	d	-0.44	0.016	0.037
cg20560640	d	-0.44	0.017	0.039
cg12847793	d	-0.44	0.018	0.042
cg24727290	d	-0.43	0.019	0.044
cg06200824	d	-0.43	0.021	0.048
DDR1 avg 5-mC	d	-0.55	0.002	0.006
cg24646556	e	-0.46	0.013	0.031

[a]Spearman Correlation.
[b]Post hoc Benjamini & Hochberg method for multiple testing correction.
Abbreviations: 5-mC: 5-methylcytosine; Avg: Average; mRNA: Messenger mRNA; OC: Occipital cortex.

Table S10. Transcription factor-binding regions matching with *DDR1* CpG loci differentially methylated in OC samples from patients with BD

Acronym[a]	Name	Function[b]
ASH2L	ASH2 Like, Histone Lysine Methyltransferase Complex Subunit	Transcriptional regulator. Component or associated component of some histone methyltransferase complexes which regulates transcription through recruitment of those complexes to gene promoters.
ATF3	Activating Transcription Factor 3	This protein binds the cAMP response element (CRE) (consensus: 5'-GTGACGT[AC][AG]-3'), a sequence present in many viral and cellular promoters. Represses transcription from promoters with ATF sites. It may repress transcription by stabilizing the binding of inhibitory cofactors at the promoter.
CTCF	CCCCTC-Binding Factor	Member of the BORIS + CTCF gene family and encodes a transcriptional regulatory protein with 11 highly conserved zinc finger domains. Depending on the context this protein can bind to a histone acetyltransferase (HAT)-containing complex and function as a transcriptional activator or bind to a histone deacetylase-containing complex (HDAC) and function as a transcriptional repressor. If the protein is bound to a transcriptional insulator element, it can block communication between enhancers and upstream promoters, thereby regulating imprinted expression
E2F1	E2F Transcription Factor	Member of the E2F family of transcription factors. The E2F family plays a crucial role in the control of cell cycle. It can mediate both cell proliferation and p53-dependent/independent apoptosis.
EGR1	Early Growth Response 1	Transcriptional regulator involved in differentiation and mitogenesis. Recognizes and binds to the DNA sequence 5'-GCG(T/G)GGGCG-3'(EGR-site) in the promoter region of target genes. Binds double-stranded target DNA, irrespective of the cytosine methylation status. Plays a role in the regulation of cell survival, proliferation and cell death.
FOS	Fos Proto-Oncogene, AP-1 Transcription Factor Subunit	DNA-binding transcription factor activity and transcription factor binding. Regulator of cell proliferation, differentiation, and transformation.
FOSL1	FOS Like 1, AP-1 Transcription Factor Subunit	The Fos gene family consists of 4 members: FOS, FOSB, FOSL1, and FOSL2. These genes encode leucine zipper proteins that can dimerize with proteins of the JUN family, thereby forming the transcription factor complex AP-1. As such, the FOS proteins have been implicated as regulators of cell proliferation, differentiation, and transformation. Has a critical function in regulating the development of cells destined to form and maintain the skeleton. It is thought to have an important role in signal transduction, cell proliferation and differentiation. In growing cells, activates phospholipid synthesis.
FOSL2	FOS Like 2, AP-1 Transcription Factor Subunit	

Table S10. Transcription factor-binding regions matching with *DDR1* CpG loci differentially methylated in OC samples from patients with BD *(Continued)*

HDAC2	Histone Deacetylase 2	Deacetylation of lysine residues at the N-terminal regions of core histones (H2A, H2B, H3 and H4). Thus, it plays an important role in transcriptional regulation, cell cycle progression and developmental events.
JUN	Jun Proto-Oncogene, AP-1 Transcription Factor Subunit	Functional component of the AP1 transcription factor complex that recognizes and binds to the enhancer heptamer motif 5'-TGA[CG]TCA-3'. Among its related pathways are oxytocin signaling pathway and CCR5 pathway in macrophages.
JUND	JunD Proto-Oncogene, AP-1 Transcription Factor Subunit	Functional component of the AP1 transcription factor complex. This protein has been proposed to protect cells from p53-dependent senescence and apoptosis.
MCM2	Minichromosome Maintenance Complex Component 2	The protein encoded by this gene is one of the highly conserved mini-chromosome maintenance proteins (MCM) that are involved in the initiation of eukaryotic genome replication. The hexameric protein complex formed by MCM proteins is a key component of the pre-replication complex (pre_RC) and may be involved in the formation of replication forks and in the recruitment of other DNA replication related proteins.
POLR2A	RNA Polymerase II Subunit A	DNA-directed 5'-3' RNA polymerase activity. Encodes the largest subunit of RNA polymerase II, the polymerase responsible for synthesizing messenger RNA in eukaryotes.
SAP30	Sin3A Associated Protein 30	The protein encoded by this gene is a component of the histone deacetylase complex, which includes SIN3, SAP18, HDAC1, HDAC2, RbAp46, RbAp48, and other polypeptides. Regulator of eukaryotic gene expression.
SIN3A	SIN3 Transcription Regulator Family Member A	DNA-binding transcription factor activity. Transcriptional repressor. Regulator of cell cycle progression. Required for cortical neuron differentiation and callosal axon elongation.
TFAP2C	Transcription Factor AP-2 Gamma	Sequence-specific (5'-GCCNNNGGC-3') DNA-binding protein that regulates transcription of selected genes. The protein can act as either a homodimer or heterodimer with other family members and is induced during retinoic acid-mediated differentiation.

Data from Transcription Factor ChIP-seq Clusters (161 factors. The signal intensity corresponds to the maximum signal strength observed in any cell type contributing to the cluster) from ENCODE project and The Open Regulatory Annotation database (ORegAnno). [a]Transcription factor (gene name) that bind to the *DDR1* GpG sequence. [b]Information adapted from Gene Cards.

Associations of altered leukocyte DDR1 promoter methylation and childhood trauma with bipolar disorder and suicidal behavior in euthymic patients

Garcia-Ruiz B, Jiménez E, Aranda S, Verdolini N, Gutiérrez-Zotes A, Sáez C, Losantos E, Alonso-Lana S, Fatjó-Vilas M, Sarró S, Torres Ll, Panicalli F, del Mar Bonnin C, Pomarol-Clotet E, Vieta E, Vilella E. *Clinical Epigenetics* (enviado)

Falta el Artículo 3; contenido confidencial.

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RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
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V. DISCUSIÓN

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Falta el resumen gráfico y el capítulo Discusión; contenido confidencial.

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VI. CONCLUSIONES

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Las conclusiones que se derivan de los trabajos presentados en esta tesis doctoral son las siguientes:

En ADN procedente de leucocitos periféricos:

Faltan las conclusiones derivadas de este apartado (conclusiones 1-5); contenido confidencial.

En ADN procedente de tejido cerebral:

6. En la CPFDL procedente de pacientes con ESQ y en la CO procedente de pacientes con TB se observa hipermetilación en las regiones R3 y R4 del promotor de *DDR1* respectivamente, resultados similares a los encontrados en leucocitos periféricos.

7. En dos muestras de validación, la tendencia a la hipermetilación en la R4 del promotor de *DDR1* en la CPFDL de pacientes con TB estaría en línea con la hipermetilación que observamos en la CPFDL en la ESQ y en la CO en el TB. Asimismo, la reducción de los niveles de mADN de *DDR1* en la R4 del promotor observada en núcleos neuronales aislados de la CF de pacientes con TB se correspondería con la hallada en la misma región en leucocitos periféricos de pacientes con TBe.

8. La mADN de *DDR1* presenta una relación inversa con la expresión de la isoforma *DDR1*c en tejido de la CPFDL en la ESQ y con la expresión total de ARNm de *DDR1* y de las isoformas *DDR1*a, -c, -d y -e en tejido cerebral de la CO en el TB, poniendo de relieve el papel regulador de la mADN de *DDR1* en la expresión del gen.

9. La mADN de *DDR1-DT* (R1) presenta una relación directa con la isoforma *DDR1*b lo que sugiere que este gen podría estar implicado en el *splicing* alternativo de *DDR1.*

10. La mADN en la región promotora de *DDR1* podría modular la expresión génica independientemente de la isoforma, y la mADN en el extremo final de la región

codificante podría estar más relacionada con la modulación de la expresión de sus isoformas.

11. *DDR1* cometila con un conjunto de genes que codifican proteínas relevantes de OLs y componentes importantes para la síntesis y el mantenimiento de la mielina en tejido cerebral, lo que refuerza su papel en el proceso de mielinización.

Conclusión final:

12. Los pacientes con ESQ y TB muestra patrones alterados de mADN de *DDR1* tanto en sangre como en tejido cerebral que se relacionan con la expresión del gen y con variables fenotípicas de gravedad del trastorno.

VII. REFERENCIAS BIBLIOGRÁFICAS

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UNIVERSITAT ROVIRA I VIRGILI
RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
Beatriz García Ruiz

VIII. ANEXOS

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RELACIÓN ENTRE EL ESTRÉS Y LA ADVERSIDAD EN LA VIDA TEMPRANA CON LA METILACIÓN DE DDR1 EN EL TRASTORNO MENTAL GRAVE
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Anexo 1. Artículo 2: Table S3. 500 selected marker loci (marker_ovr[a]) by EDec stage 0

Table S3. 500 selected marker loci (marker_ovr[a]) by EDec stage 0

Number loci	CpG	Number loci	CpG	Number loci	CpG	Number loci	CpG
1	cg26662324	126	cg00795927	251	cg00288598	376	cg11771735
2	cg08750440	127	cg08203192	252	cg05403655	377	cg15304425
3	cg18222083	128	cg15624160	253	cg19860734	378	cg00758881
4	cg06683719	129	cg07753525	254	cg01898377	379	cg24162959
5	cg22471112	130	cg20445094	255	cg11763830	380	cg10674754
6	cg02069524	131	cg20659057	256	cg03202732	381	cg07301508
7	cg13146674	132	cg10677372	257	cg04179740	382	cg02430732
8	cg06255601	133	cg26101086	258	cg13962347	383	cg17095958
9	cg21671658	134	cg14669524	259	cg16162970	384	cg09800974
10	cg03556243	135	cg10787000	260	cg01128736	385	cg06420512
11	cg18454133	136	cg06968674	261	cg06526980	386	cg03109729
12	cg06815411	137	cg21598117	262	cg21205978	387	cg08633881
13	cg22809856	138	cg05409391	263	cg16528895	388	cg00144425
14	cg11423206	139	cg18776945	264	cg03516335	389	cg03352153
15	cg21514164	140	cg14755417	265	cg09365147	390	cg21236414
16	cg18957751	141	cg01694276	266	cg13496662	391	cg27251686
17	cg07153588	142	cg27205902	267	cg27570256	392	cg06286604
18	cg09671951	143	cg14470792	268	cg16614527	393	cg19647607
19	cg22511413	144	cg10659480	269	cg10760299	394	cg18207099
20	cg15405572	145	cg02554051	270	cg02000275	395	cg19444998
21	cg00968638	146	cg01923516	271	cg16699540	396	cg02679662
22	cg09803321	147	cg22938135	272	cg20388732	397	cg19760666
23	cg09000385	148	cg13021479	273	cg14484885	398	cg23544472
24	cg18215449	149	cg19658522	274	cg14546128	399	cg08609400
25	cg11225090	150	cg22086566	275	cg18920088	400	cg06295071
26	cg25283465	151	cg04228083	276	cg13475995	401	cg13898166
27	cg22481960	152	cg26190686	277	cg14802771	402	cg16496814
28	cg16895672	153	cg21529164	278	cg18184053	403	cg02057688
29	cg03779374	154	cg25670583	279	cg08594554	404	cg24246360
30	cg15910502	155	cg05194636	280	cg19552640	405	cg04434909
31	cg10553890	156	cg20553577	281	cg15384589	406	cg13495918
32	cg24008544	157	cg08149865	282	cg15300753	407	cg05888551
33	cg12192749	158	cg06603561	283	cg00710180	408	cg02753404
34	cg20438687	159	cg21551979	284	cg20494738	409	cg24469152
35	cg09750084	160	cg03966955	285	cg00251716	410	cg19322825
36	cg12439977	161	cg06984201	286	cg10321156	411	cg19431009
37	cg13608733	162	cg13909661	287	cg27309098	412	cg09259182
38	cg20483374	163	cg23401796	288	cg11911305	413	cg12749468
39	cg17427639	164	cg04194055	289	cg02872426	414	cg26312950
40	cg17176609	165	cg01307776	290	cg02284297	415	cg12260801
41	cg26930816	166	cg14089832	291	cg14672084	416	cg23950714
42	cg14213590	167	cg24093182	292	cg10896586	417	cg07768103
43	cg07962143	168	cg03773862	293	cg04942251	418	cg16451525
44	cg18832140	169	cg00857862	294	cg09327586	419	cg20293609
45	cg00808305	170	cg01344644	295	cg25412448	420	cg17107691
46	cg13437525	171	cg26284735	296	cg26573923	421	cg09550697

Table S3. 500 selected marker loci (marker_ovr[a]) by EDec stage 0 *(continued)*

Number loci	CpG	Number loci	CpG	Number loci	CpG	Number loci	CpG
47	cg27405988	172	cg11868461	297	cg06454084	422	cg15028458
48	cg13767001	173	cg01751245	298	cg10948630	423	cg09026722
49	cg05032848	174	cg26606551	299	cg12608692	424	cg19640303
50	cg02515422	175	cg12842791	300	cg01112778	425	cg10965178
51	cg04990202	176	cg22094781	301	cg25436634	426	cg19232929
52	cg17656763	177	cg24736734	302	cg05037389	427	cg10823804
53	cg05033239	178	cg06433467	303	cg18749563	428	cg04059762
54	cg04564000	179	cg10911054	304	cg08569979	429	cg09365002
55	cg27661846	180	cg00409696	305	cg20654468	430	cg09476092
56	cg05401447	181	cg08467103	306	cg12754495	431	cg03582419
57	cg21037265	182	cg07340025	307	cg16274899	432	cg02286008
58	cg17531849	183	cg10808934	308	cg05711023	433	cg13208899
59	cg03781098	184	cg20358011	309	cg11804725	434	cg14839087
60	cg04115680	185	cg08998950	310	cg08906015	435	cg08959039
61	cg16286735	186	cg04236915	311	cg24624505	436	cg03306486
62	cg22437153	187	cg23841186	312	cg26952803	437	cg13024471
63	cg15026277	188	cg16596440	313	cg09462089	438	cg26796518
64	cg17886420	189	cg09371112	314	cg07152925	439	cg13501446
65	cg03655701	190	cg11827514	315	cg14689338	440	cg09791621
66	cg08220149	191	cg04942791	316	cg06100756	441	cg24028634
67	cg15096829	192	cg25508319	317	cg26165081	442	cg24773770
68	cg24757533	193	cg26126295	318	cg15035590	443	cg04339692
69	cg00460983	194	cg09884146	319	cg21860045	444	cg05106892
70	cg24940138	195	cg10113526	320	cg22373519	445	cg17746570
71	cg08647349	196	cg02272851	321	cg04421271	446	cg10511890
72	cg12829325	197	cg11012153	322	cg12651286	447	cg07139509
73	cg06930722	198	cg09372525	323	cg06154903	448	cg05971592
74	cg21211480	199	cg27149179	324	cg10772263	449	cg01973676
75	cg24375409	200	cg06545268	325	cg18574274	450	cg27366766
76	cg10470891	201	cg23138413	326	cg01657761	451	cg27260080
77	cg20918393	202	cg07006935	327	cg17369406	452	cg06943912
78	cg17966560	203	cg21425296	328	cg01309726	453	cg14361672
79	cg00414166	204	cg02458188	329	cg26064794	454	cg18196829
80	cg24166450	205	cg07301044	330	cg03952520	455	cg19108747
81	cg13029400	206	cg26721759	331	cg06388363	456	cg04709736
82	cg17684207	207	cg04470054	332	cg15656501	457	cg17534029
83	cg21297493	208	cg01135165	333	cg19187110	458	cg16217297
84	cg12646786	209	cg03024720	334	cg16809457	459	cg17826530
85	cg05940691	210	cg16320427	335	cg12491643	460	cg13436110
86	cg01462184	211	cg13056990	336	cg05766064	461	cg07639376
87	cg09998451	212	cg12217954	337	cg01842321	462	cg07420137
88	cg01553231	213	cg27484412	338	cg14414203	463	cg16959787
89	cg22155376	214	cg22679813	339	cg18088587	464	cg10615591
90	cg12033075	215	cg24312105	340	cg15154339	465	cg15972148
91	cg15597480	216	cg00004700	341	cg18617669	466	cg04873098
92	cg06413196	217	cg05474726	342	cg25824218	467	cg25739366
93	cg05402634	218	cg25633678	343	cg13705674	468	cg24018174
94	cg02591564	219	cg03789372	344	cg11864201	469	cg17362483

Table S3. 500 selected marker loci (marker_ovr[a]) by EDec stage 0 *(continued)*

Number loci	CpG	Number loci	CpG	Number loci	CpG	Number loci	CpG
95	cg15320905	220	cg00362657	345	cg16927285	470	cg22391718
96	cg05003723	221	cg14345676	346	cg04850059	471	cg00009750
97	cg07592809	222	cg26335577	347	cg14418582	472	cg05740262
98	cg07055259	223	cg17943672	348	cg08832723	473	cg05124021
99	cg13470557	224	cg17526103	349	cg14197892	474	cg03827835
100	cg07197585	225	cg16464373	350	cg01703355	475	cg08356028
101	cg05230834	226	cg19807286	351	cg01134758	476	cg27450668
102	cg20229025	227	cg24022152	352	cg09729395	477	cg00524561
103	cg18041123	228	cg02226645	353	cg21434376	478	cg06866451
104	cg01963754	229	cg00768487	354	cg07295003	479	cg01471232
105	cg21130463	230	cg14931884	355	cg23915679	480	cg18520125
106	cg04404310	231	cg03935060	356	cg13603805	481	cg08244518
107	cg19118904	232	cg08030922	357	cg05945030	482	cg17412901
108	cg00256675	233	cg11555420	358	cg25983629	483	cg25623473
109	cg22686523	234	cg01517740	359	cg19252369	484	cg19333963
110	cg21396630	235	cg23501051	360	cg17025459	485	cg18633230
111	cg13276570	236	cg04104463	361	cg05941641	486	cg00871207
112	cg01523712	237	cg24587185	362	cg23906001	487	cg07573872
113	cg04571522	238	cg16281600	363	cg18400181	488	cg03155200
114	cg24445388	239	cg06889535	364	cg17517997	489	cg23928126
115	cg02490942	240	cg07581070	365	cg01120369	490	cg01312394
116	cg26814635	241	cg02077216	366	cg27100547	491	cg07754940
117	cg11068784	242	cg25900085	367	cg13151811	492	cg08418670
118	cg18242139	243	cg23028740	368	cg10383447	493	cg17126924
119	cg12093060	244	cg17510385	369	cg20480899	494	cg03033182
120	cg02760280	245	cg24107728	370	cg06893379	495	cg06878548
121	cg27308218	246	cg03611487	371	cg18890825	496	cg10207553
122	cg07233230	247	cg23305899	372	cg05870398	497	cg03065175
123	cg18456456	248	cg23068558	373	cg26205216	498	cg17540192
124	cg04347414	249	cg04362790	374	cg06354692	499	cg08094614
125	cg11093142	250	cg11235594	375	cg18856501	500	cg14518185

[a]Selected loci that define cell type identity based on T-test comparations of each reference class against all other samples.
Abbreviations: EDec: Epigenomic deconvolution method; OC: Occipital cortex.

Anexo 2. Artículo 2: Table S4. 500 selected marker loci (marker_ep[a]) by EDec stage 0

Table S4. 500 selected marker loci (marker_epa) by EDec stage 0

Number loci	CpG	Number loci	CpG	Number loci	CpG	Number loci	CpG
1	cg21297493	126	cg26755097	251	cg00022024	376	cg02668248
2	cg23350336	127	cg21130463	252	cg00030909	377	cg07420137
3	cg26607828	128	cg25834419	253	cg00041865	378	cg22711792
4	cg23201549	129	cg14457472	254	cg00076216	379	cg13434411
5	cg12927498	130	cg20560075	255	cg00098182	380	cg10927841
6	cg26284390	131	cg23693289	256	cg00100680	381	cg07482202
7	cg24843443	132	cg03805475	257	cg00101713	382	cg03331514
8	cg09301222	133	cg05230834	258	cg00120358	383	cg07434271
9	cg18215449	134	cg11714334	259	cg00136822	384	cg21593001
10	cg06383124	135	cg11245569	260	cg00144425	385	cg24956391
11	cg20107759	136	cg10224600	261	cg00158654	386	cg12605662
12	cg22105332	137	cg01454752	262	cg00163459	387	cg18396811
13	cg09365147	138	cg10755058	263	cg00172074	388	cg20327845
14	cg09225230	139	cg15564619	264	cg00172189	389	cg16622899
15	cg14217558	140	cg05016746	265	cg00172225	390	cg16627786
16	cg24757533	141	cg27404023	266	cg00179663	391	cg03531247
17	cg05999245	142	cg02226645	267	cg00187059	392	cg12140144
18	cg26444623	143	cg24105081	268	cg00187503	393	cg11767757
19	cg13029400	144	cg08203192	269	cg00199519	394	cg04484550
20	cg12646786	145	cg22212414	270	cg00204802	395	cg12177944
21	cg24065770	146	cg04880138	271	cg00222625	396	cg23521140
22	cg07427605	147	cg21053323	272	cg00237586	397	cg01829163
23	cg14914220	148	cg18572413	273	cg00249974	398	cg10137837
24	cg15346168	149	cg26309929	274	cg00300808	399	cg14058100
25	cg13792579	150	cg24724428	275	cg00308438	400	cg26556385
26	cg27539986	151	cg08061598	276	cg00323861	401	cg07180475
27	cg26090652	152	cg20478148	277	cg00334399	402	cg03263514
28	cg09671951	153	cg20441502	278	cg00353659	403	cg11549953
29	cg18880897	154	cg27272679	279	cg00359423	404	cg10591771
30	cg27376136	155	cg22155376	280	cg00374056	405	cg10836101
31	cg22481960	156	cg04104463	281	cg00389577	406	cg04313875
32	cg06930722	157	cg06590946	282	cg00432059	407	cg27115863
33	cg17321883	158	cg09436545	283	cg00449608	408	cg06889535
34	cg03779374	159	cg14076195	284	cg00454592	409	cg06899985
35	cg08663159	160	cg14876077	285	cg00469083	410	cg12121643
36	cg25076767	161	cg20577205	286	cg00487533	411	cg15628518
37	cg01867433	162	cg08599792	287	cg00495035	412	cg17807131
38	cg24064264	163	cg20595750	288	cg00530870	413	cg14712531
39	cg00162231	164	cg11246938	289	cg00571067	414	cg08230483
40	cg00159523	165	cg17733616	290	cg00589581	415	cg19893585
41	cg24180402	166	cg02286008	291	cg00591890	416	cg03061122
42	cg27043630	167	cg24707573	292	cg00598866	417	cg01113680
43	cg09939831	168	cg03209642	293	cg00599273	418	cg01120369
44	cg19954537	169	cg18193764	294	cg00621247	419	cg01134758
45	cg17298239	170	cg09791621	295	cg00622516	420	cg01144436
46	cg04850765	171	cg04173586	296	cg00627361	421	cg01158161

Table S4. 500 selected marker loci (marker_ep[a]) by EDec stage 0 *(continued)*

Number loci	CpG	Number loci	CpG	Number loci	CpG	Number loci	CpG
47	cg19383430	172	cg13421412	297	cg00643814	422	cg01166299
48	cg06815411	173	cg01889143	298	cg00646621	423	cg01168776
49	cg13146674	174	cg04659689	299	cg00666124	424	cg01243992
50	cg12829325	175	cg17107691	300	cg00695265	425	cg01312412
51	cg18201077	176	cg25019648	301	cg00703902	426	cg01331309
52	cg17684207	177	cg21820652	302	cg00720375	427	cg01384290
53	cg08988364	178	cg12348588	303	cg00734567	428	cg01392772
54	cg20554488	179	cg24773770	304	cg00767948	429	cg01421830
55	cg07382923	180	cg21610221	305	cg00789812	430	cg01422881
56	cg01566127	181	cg04417773	306	cg00789960	431	cg01434672
57	cg07966140	182	cg19706320	307	cg00793227	432	cg01454305
58	cg09159285	183	cg14149007	308	cg00804934	433	cg01454612
59	cg12794421	184	cg00463982	309	cg00806644	434	cg01502653
60	cg23864632	185	cg09675196	310	cg00820740	435	cg01532392
61	cg12542255	186	cg17540192	311	cg00826638	436	cg01546248
62	cg00261781	187	cg15028458	312	cg00828709	437	cg01556514
63	cg20814026	188	cg07139509	313	cg00842122	438	cg01576459
64	cg09689449	189	cg05212706	314	cg00853103	439	cg01606770
65	cg05330668	190	cg09335713	315	cg00864474	440	cg01607444
66	cg05438508	191	cg15043384	316	cg00867461	441	cg01608493
67	cg01425054	192	cg13323489	317	cg00890649	442	cg01631596
68	cg20918393	193	cg22463795	318	cg00894559	443	cg01667018
69	cg13294849	194	cg22365240	319	cg00917373	444	cg01680674
70	cg09463900	195	cg01678084	320	cg00919806	445	cg01682157
71	cg19605920	196	cg15202102	321	cg00921219	446	cg01691160
72	cg22893247	197	cg21211480	322	cg00932141	447	cg01703355
73	cg16528895	198	cg19108747	323	cg00942495	448	cg01732495
74	cg09386954	199	cg01178680	324	cg00977842	449	cg01775492
75	cg02503159	200	cg09026722	325	cg00997931	450	cg01804183
76	cg07323350	201	cg04709736	326	cg01005365	451	cg01812328
77	cg14280424	202	cg05845757	327	cg01006587	452	cg01813738
78	cg05401447	203	cg10098021	328	cg01025185	453	cg01842321
79	cg22125968	204	cg09456094	329	cg01035260	454	cg01866770
80	cg02582203	205	cg10292154	330	cg01075555	455	cg01880399
81	cg02172579	206	cg19537719	331	cg01092108	456	cg01880569
82	cg06368590	207	cg02119938	332	cg01093202	457	cg01886855
83	cg02458945	208	cg16776065	333	cg15316843	458	cg01892980
84	cg24662107	209	cg06970884	334	cg24348240	459	cg01899074
85	cg25900085	210	cg18196829	335	cg00498591	460	cg01914555
86	cg00630164	211	cg10823804	336	cg08499046	461	cg01915642
87	cg06550177	212	cg19333963	337	cg18055623	462	cg01937267
88	cg05403655	213	cg02125316	338	cg08384314	463	cg01954957
89	cg01623261	214	cg03634854	339	cg18987410	464	cg01965462
90	cg22897141	215	cg05721365	340	cg25633678	465	cg01995393
91	cg15126544	216	cg10285466	341	cg13341668	466	cg02007786
92	cg17002851	217	cg26796518	342	cg03487027	467	cg02032696
93	cg15292765	218	cg25739366	343	cg07316846	468	cg02042823
94	cg16732616	219	cg10169241	344	cg22272840	469	cg02057688
95	cg05103387	220	cg20293609	345	cg25386676	470	cg02068832

Table S4. 500 selected marker loci (marker_ep[a]) by EDec stage 0 *(continued)*

Number loci	CpG	Number loci	CpG	Number loci	CpG	Number loci	CpG
96	cg11736230	221	cg12350325	346	cg19470372	471	cg02088197
97	cg21656205	222	cg04150136	347	cg00880290	472	cg02106712
98	cg19066520	223	cg17560015	348	cg24500959	473	cg02114341
99	cg07222505	224	cg07458308	349	cg05542681	474	cg02129712
100	cg24455365	225	cg02903822	350	cg21762523	475	cg02133070
101	cg19447962	226	cg09365002	351	cg24925929	476	cg02136622
102	cg00920668	227	cg03953626	352	cg04243827	477	cg02151535
103	cg22714290	228	cg06436854	353	cg18404706	478	cg02159654
104	cg21762788	229	cg18586886	354	cg03827835	479	cg02166725
105	cg15140703	230	cg16398761	355	cg24766821	480	cg02175309
106	cg04734712	231	cg09157302	356	cg26540315	481	cg02217063
107	cg05940691	232	cg01514538	357	cg18520125	482	cg02219607
108	cg11460820	233	cg08959039	358	cg05516327	483	cg02242345
109	cg23501051	234	cg01263386	359	cg24028634	484	cg02271603
110	cg05447023	235	cg04115680	360	cg15105326	485	cg02278959
111	cg15149655	236	cg26505691	361	cg06943912	486	cg02279471
112	cg13438961	237	cg22481632	362	cg11536474	487	cg02303592
113	cg23363971	238	cg15496956	363	cg09074856	488	cg02335863
114	cg09657963	239	cg03306486	364	cg11355217	489	cg02347859
115	cg17276002	240	cg04004830	365	cg25020286	490	cg02356993
116	cg27602828	241	cg14557185	366	cg19068510	491	cg02368469
117	cg15123692	242	cg19389001	367	cg02297063	492	cg02378074
118	cg15384598	243	cg26465602	368	cg04742550	493	cg02397179
119	cg25327888	244	cg07065220	369	cg13024471	494	cg02401614
120	cg06484415	245	cg24375409	370	cg00295794	495	cg02412684
121	cg08455778	246	cg24792289	371	cg14972155	496	cg02419321
122	cg03339668	247	cg17534029	372	cg03517024	497	cg02421824
123	cg13826247	248	cg10615591	373	cg02390319	498	cg02430732
124	cg18173726	249	cg00010672	374	cg06100807	499	cg02432101
125	cg14931884	250	cg00019838	375	cg04875128	500	cg02466008

[a]Selected loci that define cell type identity based on T-test comparations between each pair of reference classes.
Abbreviations: EDec: Epigenomic deconvolution method; OC: Occipital cortex.

Anexo 3. Artículo 2: Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues

DDR1 CpG	Gene CpG	Cell type marker	ρ[a]	*p*-value	Adj *p*-value[b]
DDR1_cg00466425	CNP_cg01443071	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg01936707	CNP_cg01443071	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg05703744	CNP_cg01443071	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg06200824	CNP_cg01443071	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg06501109	CNP_cg01443071	Myelin	0.82	4.50E-08	1.27E-06
DDR1_cg07912416	CNP_cg01443071	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg07979747	CNP_cg01443071	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg08673763	CNP_cg01443071	Myelin	0.87	1.18E-09	4.87E-08
DDR1_cg08951271	CNP_cg01443071	Myelin	0.94	3.24E-14	7.65E-12
DDR1_cg11530564	CNP_cg01443071	Myelin	0.86	1.87E-09	7.34E-08
DDR1_cg11676038	CNP_cg01443071	Myelin	0.94	1.03E-13	1.89E-11
DDR1_cg12669395	CNP_cg01443071	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg13329862	CNP_cg01443071	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg13351860	CNP_cg01443071	Myelin	0.86	3.32E-09	1.22E-07
DDR1_cg14058861	CNP_cg01443071	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg14790552	CNP_cg01443071	Myelin	0.85	5.50E-09	1.92E-07
DDR1_cg15656686	CNP_cg01443071	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg16111190	CNP_cg01443071	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg16797094	CNP_cg01443071	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg17176005	CNP_cg01443071	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg17604312	CNP_cg01443071	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg18577693	CNP_cg01443071	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg19215110	CNP_cg01443071	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg19591099	CNP_cg01443071	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg21677258	CNP_cg01443071	Myelin	0.91	8.63E-12	7.11E-10
DDR1_cg24636809	CNP_cg01443071	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg24727290	CNP_cg01443071	Myelin	0.85	3.77E-09	1.37E-07
DDR1_cg25613385	CNP_cg01443071	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg25655106	CNP_cg01443071	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg27237814	CNP_cg01443071	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg27593250	CNP_cg01443071	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg00466425	CNP_cg02357631	Myelin	0.85	4.47E-09	1.59E-07
DDR1_cg01936707	CNP_cg02357631	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg05703744	CNP_cg02357631	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg06200824	CNP_cg02357631	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg06501109	CNP_cg02357631	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg07912416	CNP_cg02357631	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg07979747	CNP_cg02357631	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg08673763	CNP_cg02357631	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg08951271	CNP_cg02357631	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg11530564	CNP_cg02357631	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg11676038	CNP_cg02357631	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg12669395	CNP_cg02357631	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg13329862	CNP_cg02357631	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg13351860	CNP_cg02357631	Myelin	0.80	1.64E-07	4.08E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg16111190	CNP_cg02357631	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg16797094	CNP_cg02357631	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg19591099	CNP_cg02357631	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg21677258	CNP_cg02357631	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg24636809	CNP_cg02357631	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg24727290	CNP_cg02357631	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg25655106	CNP_cg02357631	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg27237814	CNP_cg02357631	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg27593250	CNP_cg02357631	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg00466425	CNP_cg09479341	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg01936707	CNP_cg09479341	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg05703744	CNP_cg09479341	Myelin	0.90	2.88E-11	1.96E-09
DDR1_cg06200824	CNP_cg09479341	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg06501109	CNP_cg09479341	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg07912416	CNP_cg09479341	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg07979747	CNP_cg09479341	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg08673763	CNP_cg09479341	Myelin	0.86	2.91E-09	1.08E-07
DDR1_cg08951271	CNP_cg09479341	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg09822812	CNP_cg09479341	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg09965419	CNP_cg09479341	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg11530564	CNP_cg09479341	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg11676038	CNP_cg09479341	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg12669395	CNP_cg09479341	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg12847793	CNP_cg09479341	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg13329862	CNP_cg09479341	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg13351860	CNP_cg09479341	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg14058861	CNP_cg09479341	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg14790552	CNP_cg09479341	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg15656686	CNP_cg09479341	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg16111190	CNP_cg09479341	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg16797094	CNP_cg09479341	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg17176005	CNP_cg09479341	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg17604312	CNP_cg09479341	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg18577693	CNP_cg09479341	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg19215110	CNP_cg09479341	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg19591099	CNP_cg09479341	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg21677258	CNP_cg09479341	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg24566261	CNP_cg09479341	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg24636809	CNP_cg09479341	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg24727290	CNP_cg09479341	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg25655106	CNP_cg09479341	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg27237814	CNP_cg09479341	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg27593250	CNP_cg09479341	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg19018599	CNP_cg09575037	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg19894264	CNP_cg09575037	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg01936707	CNP_cg13917614	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg05703744	CNP_cg13917614	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg06501109	CNP_cg13917614	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg07912416	CNP_cg13917614	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg07979747	CNP_cg13917614	Myelin	0.76	2.20E-06	4.15E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg09965419	CNP_cg13917614	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg11530564	CNP_cg13917614	Myelin	0.83	2.47E-08	7.36E-07
DDR1_cg11676038	CNP_cg13917614	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg12669395	CNP_cg13917614	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg13351860	CNP_cg13917614	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg13695585	CNP_cg13917614	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg14790552	CNP_cg13917614	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg15656686	CNP_cg13917614	Myelin	0.85	3.61E-09	1.32E-07
DDR1_cg16797094	CNP_cg13917614	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg17176005	CNP_cg13917614	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg17604312	CNP_cg13917614	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg21677258	CNP_cg13917614	Myelin	0.81	9.65E-08	2.52E-06
DDR1_cg25655106	CNP_cg13917614	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg00466425	CNP_cg14376548	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg01598675	CNP_cg14376548	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg01936707	CNP_cg14376548	Myelin	0.88	2.37E-10	1.20E-08
DDR1_cg05703744	CNP_cg14376548	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg06200824	CNP_cg14376548	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg06501109	CNP_cg14376548	Myelin	0.82	5.71E-08	1.57E-06
DDR1_cg07912416	CNP_cg14376548	Myelin	0.83	1.99E-08	6.05E-07
DDR1_cg07979747	CNP_cg14376548	Myelin	0.86	1.63E-09	6.49E-08
DDR1_cg08673763	CNP_cg14376548	Myelin	0.87	6.31E-10	2.82E-08
DDR1_cg08951271	CNP_cg14376548	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg11530564	CNP_cg14376548	Myelin	0.87	6.96E-10	3.06E-08
DDR1_cg11676038	CNP_cg14376548	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg12669395	CNP_cg14376548	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg13329862	CNP_cg14376548	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg13351860	CNP_cg14376548	Myelin	0.87	1.30E-09	5.30E-08
DDR1_cg14058861	CNP_cg14376548	Myelin	0.83	3.29E-08	9.53E-07
DDR1_cg14790552	CNP_cg14376548	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg15656686	CNP_cg14376548	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg15720085	CNP_cg14376548	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg16111190	CNP_cg14376548	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg16797094	CNP_cg14376548	Myelin	0.85	7.92E-09	2.66E-07
DDR1_cg17176005	CNP_cg14376548	Myelin	0.82	4.50E-08	1.27E-06
DDR1_cg17604312	CNP_cg14376548	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg18577693	CNP_cg14376548	Myelin	0.81	1.24E-07	3.16E-06
DDR1_cg19215110	CNP_cg14376548	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg19591099	CNP_cg14376548	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg21677258	CNP_cg14376548	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg24566261	CNP_cg14376548	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg24636809	CNP_cg14376548	Myelin	0.85	3.61E-09	1.32E-07
DDR1_cg24727290	CNP_cg14376548	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg25655106	CNP_cg14376548	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg27237814	CNP_cg14376548	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg27593250	CNP_cg14376548	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg00466425	CNP_cg14826331	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg00934322	CNP_cg14826331	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg01936707	CNP_cg14826331	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg05703744	CNP_cg14826331	Myelin	0.91	1.31E-11	1.01E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg06501109	CNP_cg14826331	Myelin	0.82	4.35E-08	1.23E-06
DDR1_cg07908039	CNP_cg14826331	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg07912416	CNP_cg14826331	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg07979747	CNP_cg14826331	Myelin	0.86	1.96E-09	7.64E-08
DDR1_cg08673763	CNP_cg14826331	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg08951271	CNP_cg14826331	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg11530564	CNP_cg14826331	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg11676038	CNP_cg14826331	Myelin	0.95	1.33E-15	7.11E-13
DDR1_cg12669395	CNP_cg14826331	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg13329862	CNP_cg14826331	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg13351860	CNP_cg14826331	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg14058861	CNP_cg14826331	Myelin	0.80	1.45E-07	3.64E-06
DDR1_cg14790552	CNP_cg14826331	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg15656686	CNP_cg14826331	Myelin	0.84	9.28E-09	3.06E-07
DDR1_cg16111190	CNP_cg14826331	Myelin	0.88	2.13E-10	1.10E-08
DDR1_cg16797094	CNP_cg14826331	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg17176005	CNP_cg14826331	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg17604312	CNP_cg14826331	Myelin	0.82	6.74E-08	1.82E-06
DDR1_cg19215110	CNP_cg14826331	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg19591099	CNP_cg14826331	Myelin	0.83	3.41E-08	9.84E-07
DDR1_cg21677258	CNP_cg14826331	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg24636809	CNP_cg14826331	Myelin	0.88	2.64E-10	1.32E-08
DDR1_cg24727290	CNP_cg14826331	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg25613385	CNP_cg14826331	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg25655106	CNP_cg14826331	Myelin	0.91	6.49E-12	5.56E-10
DDR1_cg27237814	CNP_cg14826331	Myelin	0.86	1.96E-09	7.64E-08
DDR1_cg27593250	CNP_cg14826331	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg00466425	CNP_cg16563470	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg00934322	CNP_cg16563470	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg01936707	CNP_cg16563470	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg05703744	CNP_cg16563470	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg06501109	CNP_cg16563470	Myelin	0.80	2.22E-07	5.35E-06
DDR1_cg07908039	CNP_cg16563470	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg07912416	CNP_cg16563470	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg08673763	CNP_cg16563470	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg08951271	CNP_cg16563470	Myelin	0.80	2.22E-07	5.35E-06
DDR1_cg09822812	CNP_cg16563470	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg09965419	CNP_cg16563470	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg11530564	CNP_cg16563470	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg11676038	CNP_cg16563470	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg12669395	CNP_cg16563470	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg12847793	CNP_cg16563470	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg13329862	CNP_cg16563470	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg13351860	CNP_cg16563470	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg13695585	CNP_cg16563470	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg14790552	CNP_cg16563470	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg15656686	CNP_cg16563470	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg16111190	CNP_cg16563470	Myelin	0.82	6.74E-08	1.82E-06
DDR1_cg16797094	CNP_cg16563470	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg17176005	CNP_cg16563470	Myelin	0.75	2.65E-06	4.91E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg17604312	CNP_cg16563470	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg20955507	CNP_cg16563470	Myelin	0.80	2.57E-07	6.12E-06
DDR1_cg21677258	CNP_cg16563470	Myelin	0.83	3.66E-08	1.05E-06
DDR1_cg24636809	CNP_cg16563470	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg24727290	CNP_cg16563470	Myelin	0.80	1.41E-07	3.54E-06
DDR1_cg25655106	CNP_cg16563470	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg27237814	CNP_cg16563470	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg00466425	CNP_cg20212624	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg00934322	CNP_cg20212624	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg01936707	CNP_cg20212624	Myelin	0.82	5.71E-08	1.57E-06
DDR1_cg05703744	CNP_cg20212624	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg06501109	CNP_cg20212624	Myelin	0.78	5.52E-07	1.22E-05
DDR1_cg07187855	CNP_cg20212624	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg07908039	CNP_cg20212624	Myelin	0.76	2.20E-06	4.15E-05
DDR1_cg07912416	CNP_cg20212624	Myelin	0.79	2.89E-07	6.80E-06
DDR1_cg07979747	CNP_cg20212624	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg08673763	CNP_cg20212624	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg08684361	CNP_cg20212624	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg08951271	CNP_cg20212624	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg09822812	CNP_cg20212624	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg09965419	CNP_cg20212624	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg11530564	CNP_cg20212624	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg11676038	CNP_cg20212624	Myelin	0.80	1.69E-07	4.19E-06
DDR1_cg12669395	CNP_cg20212624	Myelin	0.85	5.50E-09	1.92E-07
DDR1_cg12847793	CNP_cg20212624	Myelin	0.83	2.30E-08	6.90E-07
DDR1_cg13329862	CNP_cg20212624	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg13351860	CNP_cg20212624	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg13695585	CNP_cg20212624	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg15656686	CNP_cg20212624	Myelin	0.87	1.30E-09	5.30E-08
DDR1_cg16111190	CNP_cg20212624	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg16797094	CNP_cg20212624	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg17176005	CNP_cg20212624	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg17604312	CNP_cg20212624	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg19215110	CNP_cg20212624	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg20955507	CNP_cg20212624	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg21677258	CNP_cg20212624	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg24636809	CNP_cg20212624	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg24727290	CNP_cg20212624	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg25613385	CNP_cg20212624	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg25655106	CNP_cg20212624	Myelin	0.84	1.27E-08	4.04E-07
DDR1_cg27237814	CNP_cg20212624	Myelin	0.81	1.10E-07	2.82E-06
DDR1_cg27593250	CNP_cg20212624	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg19018599	CNP_cg21248590	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg00466425	CNP_cg25015416	Myelin	0.77	1.10E-06	2.25E-05
DDR1_cg01598675	CNP_cg25015416	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg05703744	CNP_cg25015416	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg07912416	CNP_cg25015416	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg07979747	CNP_cg25015416	Myelin	0.76	1.64E-06	3.21E-05
DDR1_cg08673763	CNP_cg25015416	Myelin	0.86	2.91E-09	1.08E-07
DDR1_cg08951271	CNP_cg25015416	Myelin	0.80	1.54E-07	3.86E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg09822812	CNP_cg25015416	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg09965419	CNP_cg25015416	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg11530564	CNP_cg25015416	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg11676038	CNP_cg25015416	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg12669395	CNP_cg25015416	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg13329862	CNP_cg25015416	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg13351860	CNP_cg25015416	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg14790552	CNP_cg25015416	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg15656686	CNP_cg25015416	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg16111190	CNP_cg25015416	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg16797094	CNP_cg25015416	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg17176005	CNP_cg25015416	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg17604312	CNP_cg25015416	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg19215110	CNP_cg25015416	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg20955507	CNP_cg25015416	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg21677258	CNP_cg25015416	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg24636809	CNP_cg25015416	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg24727290	CNP_cg25015416	Myelin	0.81	1.24E-07	3.16E-06
DDR1_cg25655106	CNP_cg25015416	Myelin	0.86	2.91E-09	1.08E-07
DDR1_cg27237814	CNP_cg25015416	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg00466425	CNP_cg27435103	Myelin	0.90	3.49E-11	2.31E-09
DDR1_cg01936707	CNP_cg27435103	Myelin	0.90	5.71E-11	3.53E-09
DDR1_cg05703744	CNP_cg27435103	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg06200824	CNP_cg27435103	Myelin	0.84	1.53E-08	4.79E-07
DDR1_cg06501109	CNP_cg27435103	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg07912416	CNP_cg27435103	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg07979747	CNP_cg27435103	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg08673763	CNP_cg27435103	Myelin	0.90	3.07E-11	2.07E-09
DDR1_cg08951271	CNP_cg27435103	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg09965419	CNP_cg27435103	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg11530564	CNP_cg27435103	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg11676038	CNP_cg27435103	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg12669395	CNP_cg27435103	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg13329862	CNP_cg27435103	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg13351860	CNP_cg27435103	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg14058861	CNP_cg27435103	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg14790552	CNP_cg27435103	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg15656686	CNP_cg27435103	Myelin	0.86	1.71E-09	6.76E-08
DDR1_cg15720085	CNP_cg27435103	Myelin	0.80	2.35E-07	5.65E-06
DDR1_cg16111190	CNP_cg27435103	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg16797094	CNP_cg27435103	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg17176005	CNP_cg27435103	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg17604312	CNP_cg27435103	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg18577693	CNP_cg27435103	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg19215110	CNP_cg27435103	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg19591099	CNP_cg27435103	Myelin	0.83	2.66E-08	7.86E-07
DDR1_cg21677258	CNP_cg27435103	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg24566261	CNP_cg27435103	Myelin	0.76	1.72E-06	3.35E-05
DDR1_cg24636809	CNP_cg27435103	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg24727290	CNP_cg27435103	Myelin	0.87	1.24E-09	5.08E-08

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg25655106	CNP_cg27435103	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg27237814	CNP_cg27435103	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg27593250	CNP_cg27435103	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg00466425	MAG_cg00162517	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg01598675	MAG_cg00162517	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg01936707	MAG_cg00162517	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg05703744	MAG_cg00162517	Myelin	0.92	1.94E-12	2.03E-10
DDR1_cg06200824	MAG_cg00162517	Myelin	0.81	9.65E-08	2.52E-06
DDR1_cg06501109	MAG_cg00162517	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg07912416	MAG_cg00162517	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg07979747	MAG_cg00162517	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg08673763	MAG_cg00162517	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg08951271	MAG_cg00162517	Myelin	0.92	2.45E-12	2.47E-10
DDR1_cg11530564	MAG_cg00162517	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg11676038	MAG_cg00162517	Myelin	0.95	4.44E-15	1.74E-12
DDR1_cg12669395	MAG_cg00162517	Myelin	0.93	1.53E-13	2.55E-11
DDR1_cg13329862	MAG_cg00162517	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg13351860	MAG_cg00162517	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg14058861	MAG_cg00162517	Myelin	0.77	1.13E-06	2.30E-05
DDR1_cg14790552	MAG_cg00162517	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg15656686	MAG_cg00162517	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg15720085	MAG_cg00162517	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg16111190	MAG_cg00162517	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg16797094	MAG_cg00162517	Myelin	0.87	1.36E-09	5.52E-08
DDR1_cg17176005	MAG_cg00162517	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg17604312	MAG_cg00162517	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg18577693	MAG_cg00162517	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg19215110	MAG_cg00162517	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg19591099	MAG_cg00162517	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg20335906	MAG_cg00162517	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg21677258	MAG_cg00162517	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg24636809	MAG_cg00162517	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg24727290	MAG_cg00162517	Myelin	0.84	1.53E-08	4.79E-07
DDR1_cg25655106	MAG_cg00162517	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg27237814	MAG_cg00162517	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg27593250	MAG_cg00162517	Myelin	0.80	2.57E-07	6.12E-06
DDR1_cg00466425	MAG_cg01349478	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg00934322	MAG_cg01349478	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg01598675	MAG_cg01349478	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg01936707	MAG_cg01349478	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg05703744	MAG_cg01349478	Myelin	0.93	3.55E-13	5.01E-11
DDR1_cg06200824	MAG_cg01349478	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg06501109	MAG_cg01349478	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg07908039	MAG_cg01349478	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg07912416	MAG_cg01349478	Myelin	0.87	8.88E-10	3.80E-08
DDR1_cg07979747	MAG_cg01349478	Myelin	0.86	1.71E-09	6.76E-08
DDR1_cg08673763	MAG_cg01349478	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg08951271	MAG_cg01349478	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg09965419	MAG_cg01349478	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg11530564	MAG_cg01349478	Myelin	0.90	2.38E-11	1.66E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg11676038	MAG_cg01349478	Myelin	0.94	3.24E-14	7.65E-12
DDR1_cg12669395	MAG_cg01349478	Myelin	0.93	1.14E-13	2.04E-11
DDR1_cg12847793	MAG_cg01349478	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg13329862	MAG_cg01349478	Myelin	0.94	6.84E-14	1.37E-11
DDR1_cg13351860	MAG_cg01349478	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg14058861	MAG_cg01349478	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg14790552	MAG_cg01349478	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg15656686	MAG_cg01349478	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg15720085	MAG_cg01349478	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg16111190	MAG_cg01349478	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg16797094	MAG_cg01349478	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg17176005	MAG_cg01349478	Myelin	0.81	7.69E-08	2.05E-06
DDR1_cg17604312	MAG_cg01349478	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg18577693	MAG_cg01349478	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg19215110	MAG_cg01349478	Myelin	0.81	8.48E-08	2.24E-06
DDR1_cg19591099	MAG_cg01349478	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg21677258	MAG_cg01349478	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg24566261	MAG_cg01349478	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg24636809	MAG_cg01349478	Myelin	0.90	3.49E-11	2.31E-09
DDR1_cg24727290	MAG_cg01349478	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg25655106	MAG_cg01349478	Myelin	0.92	2.27E-12	2.31E-10
DDR1_cg27237814	MAG_cg01349478	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg27593250	MAG_cg01349478	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg00466425	MAG_cg02127209	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg01598675	MAG_cg02127209	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg01936707	MAG_cg02127209	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg05703744	MAG_cg02127209	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg06200824	MAG_cg02127209	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg07908039	MAG_cg02127209	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg07912416	MAG_cg02127209	Myelin	0.85	7.92E-09	2.66E-07
DDR1_cg07979747	MAG_cg02127209	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg08673763	MAG_cg02127209	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg08951271	MAG_cg02127209	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg11530564	MAG_cg02127209	Myelin	0.94	6.17E-14	1.26E-11
DDR1_cg11676038	MAG_cg02127209	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg12669395	MAG_cg02127209	Myelin	0.86	1.87E-09	7.34E-08
DDR1_cg13329862	MAG_cg02127209	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg13351860	MAG_cg02127209	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg14790552	MAG_cg02127209	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg15656686	MAG_cg02127209	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg16111190	MAG_cg02127209	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg16797094	MAG_cg02127209	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg17176005	MAG_cg02127209	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg17604312	MAG_cg02127209	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg19215110	MAG_cg02127209	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg21677258	MAG_cg02127209	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg24636809	MAG_cg02127209	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg24727290	MAG_cg02127209	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg25613385	MAG_cg02127209	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg25655106	MAG_cg02127209	Myelin	0.89	6.06E-11	3.72E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg27237814	MAG_cg02127209	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg27593250	MAG_cg02127209	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg01936707	MAG_cg04169912	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg07912416	MAG_cg04169912	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg07979747	MAG_cg04169912	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg08673763	MAG_cg04169912	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg08951271	MAG_cg04169912	Myelin	0.82	6.74E-08	1.82E-06
DDR1_cg11530564	MAG_cg04169912	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg11676038	MAG_cg04169912	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg12669395	MAG_cg04169912	Myelin	0.86	3.32E-09	1.22E-07
DDR1_cg13329862	MAG_cg04169912	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg14790552	MAG_cg04169912	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg15656686	MAG_cg04169912	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg17604312	MAG_cg04169912	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg18577693	MAG_cg04169912	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg19215110	MAG_cg04169912	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg21677258	MAG_cg04169912	Myelin	0.86	3.32E-09	1.22E-07
DDR1_cg24636809	MAG_cg04169912	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg24727290	MAG_cg04169912	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg25655106	MAG_cg04169912	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg27237814	MAG_cg04169912	Myelin	0.75	3.05E-06	5.55E-05
DDR1_cg00466425	MAG_cg05055150	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg01598675	MAG_cg05055150	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg01936707	MAG_cg05055150	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg05703744	MAG_cg05055150	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg06200824	MAG_cg05055150	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg06501109	MAG_cg05055150	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg07908039	MAG_cg05055150	Myelin	0.80	1.97E-07	4.80E-06
DDR1_cg07912416	MAG_cg05055150	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg07979747	MAG_cg05055150	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg08673763	MAG_cg05055150	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg08951271	MAG_cg05055150	Myelin	0.94	4.51E-14	9.90E-12
DDR1_cg09965419	MAG_cg05055150	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg11530564	MAG_cg05055150	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg11676038	MAG_cg05055150	Myelin	0.96	2.22E-16	2.02E-13
DDR1_cg12669395	MAG_cg05055150	Myelin	0.95	9.33E-15	2.95E-12
DDR1_cg12847793	MAG_cg05055150	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg13329862	MAG_cg05055150	Myelin	0.93	1.68E-13	2.75E-11
DDR1_cg13351860	MAG_cg05055150	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg14058861	MAG_cg05055150	Myelin	0.78	5.52E-07	1.22E-05
DDR1_cg14790552	MAG_cg05055150	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg15656686	MAG_cg05055150	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg15720085	MAG_cg05055150	Myelin	0.80	1.69E-07	4.19E-06
DDR1_cg16111190	MAG_cg05055150	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg16797094	MAG_cg05055150	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg17176005	MAG_cg05055150	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg17604312	MAG_cg05055150	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg18577693	MAG_cg05055150	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg19215110	MAG_cg05055150	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg19591099	MAG_cg05055150	Myelin	0.88	2.37E-10	1.20E-08

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg21677258	MAG_cg05055150	Myelin	0.93	1.39E-13	2.37E-11
DDR1_cg24566261	MAG_cg05055150	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg24636809	MAG_cg05055150	Myelin	0.94	4.51E-14	9.90E-12
DDR1_cg24727290	MAG_cg05055150	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg25613385	MAG_cg05055150	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg25655106	MAG_cg05055150	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg27237814	MAG_cg05055150	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg27593250	MAG_cg05055150	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg08913013	MAG_cg05327744	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg11676038	MAG_cg05327744	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg12669395	MAG_cg05327744	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg14790552	MAG_cg05327744	Myelin	0.77	1.18E-06	2.41E-05
DDR1_cg16111190	MAG_cg05327744	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg00466425	MAG_cg05663558	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg01598675	MAG_cg05663558	Myelin	0.78	6.49E-07	1.41E-05
DDR1_cg01936707	MAG_cg05663558	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg05703744	MAG_cg05663558	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg06200824	MAG_cg05663558	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg06501109	MAG_cg05663558	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg07908039	MAG_cg05663558	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg07912416	MAG_cg05663558	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg07979747	MAG_cg05663558	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg08673763	MAG_cg05663558	Myelin	0.85	5.97E-09	2.06E-07
DDR1_cg08951271	MAG_cg05663558	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg09965419	MAG_cg05663558	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg11530564	MAG_cg05663558	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg11676038	MAG_cg05663558	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg12669395	MAG_cg05663558	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg13329862	MAG_cg05663558	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg13351860	MAG_cg05663558	Myelin	0.87	1.30E-09	5.30E-08
DDR1_cg14058861	MAG_cg05663558	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg14790552	MAG_cg05663558	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg15656686	MAG_cg05663558	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg15720085	MAG_cg05663558	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg16111190	MAG_cg05663558	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg16797094	MAG_cg05663558	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg17176005	MAG_cg05663558	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg17604312	MAG_cg05663558	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg18577693	MAG_cg05663558	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg19591099	MAG_cg05663558	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg21677258	MAG_cg05663558	Myelin	0.91	1.50E-11	1.13E-09
DDR1_cg24636809	MAG_cg05663558	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg24727290	MAG_cg05663558	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg25655106	MAG_cg05663558	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg27237814	MAG_cg05663558	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg27593250	MAG_cg05663558	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg07912416	MAG_cg07918620	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg07979747	MAG_cg07918620	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg08673763	MAG_cg07918620	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg08951271	MAG_cg07918620	Myelin	0.78	4.81E-07	1.07E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg12669395	MAG_cg07918620	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg13329862	MAG_cg07918620	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg14790552	MAG_cg07918620	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg16111190	MAG_cg07918620	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg17176005	MAG_cg07918620	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg18577693	MAG_cg07918620	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg19215110	MAG_cg07918620	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg21677258	MAG_cg07918620	Myelin	0.86	1.49E-09	5.99E-08
DDR1_cg24636809	MAG_cg07918620	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg24727290	MAG_cg07918620	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg25655106	MAG_cg07918620	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg00466425	MAG_cg08585489	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg00934322	MAG_cg08585489	Myelin	0.75	3.05E-06	5.55E-05
DDR1_cg01598675	MAG_cg08585489	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg01936707	MAG_cg08585489	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg05703744	MAG_cg08585489	Myelin	0.94	2.93E-14	7.05E-12
DDR1_cg06200824	MAG_cg08585489	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg06501109	MAG_cg08585489	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg07908039	MAG_cg08585489	Myelin	0.78	7.42E-07	1.59E-05
DDR1_cg07912416	MAG_cg08585489	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg07979747	MAG_cg08585489	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg08673763	MAG_cg08585489	Myelin	0.92	1.01E-12	1.19E-10
DDR1_cg08951271	MAG_cg08585489	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg09822812	MAG_cg08585489	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg09965419	MAG_cg08585489	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg11530564	MAG_cg08585489	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg11676038	MAG_cg08585489	Myelin	0.93	2.46E-13	3.73E-11
DDR1_cg12669395	MAG_cg08585489	Myelin	0.95	9.33E-15	2.95E-12
DDR1_cg12847793	MAG_cg08585489	Myelin	0.78	6.85E-07	1.48E-05
DDR1_cg13329862	MAG_cg08585489	Myelin	0.94	1.47E-14	4.13E-12
DDR1_cg13351860	MAG_cg08585489	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg14058861	MAG_cg08585489	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg14790552	MAG_cg08585489	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg15656686	MAG_cg08585489	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg15720085	MAG_cg08585489	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg16111190	MAG_cg08585489	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg16797094	MAG_cg08585489	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg17176005	MAG_cg08585489	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg17604312	MAG_cg08585489	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg18577693	MAG_cg08585489	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg19215110	MAG_cg08585489	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg19591099	MAG_cg08585489	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg21677258	MAG_cg08585489	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg24566261	MAG_cg08585489	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg24636809	MAG_cg08585489	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg24727290	MAG_cg08585489	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg25655106	MAG_cg08585489	Myelin	0.95	9.33E-15	2.95E-12
DDR1_cg27237814	MAG_cg08585489	Myelin	0.89	1.37E-10	7.45E-09
DDR1_cg27593250	MAG_cg08585489	Myelin	0.82	6.74E-08	1.82E-06
DDR1_cg00466425	MAG_cg10618943	Myelin	0.79	3.06E-07	7.17E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg00934322	MAG_cg10618943	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg01936707	MAG_cg10618943	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg05703744	MAG_cg10618943	Myelin	0.88	2.13E-10	1.10E-08
DDR1_cg06501109	MAG_cg10618943	Myelin	0.75	3.05E-06	5.55E-05
DDR1_cg07908039	MAG_cg10618943	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg07912416	MAG_cg10618943	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg07979747	MAG_cg10618943	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg08673763	MAG_cg10618943	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg08951271	MAG_cg10618943	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg09965419	MAG_cg10618943	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg11530564	MAG_cg10618943	Myelin	0.92	2.45E-12	2.47E-10
DDR1_cg11676038	MAG_cg10618943	Myelin	0.87	1.18E-09	4.87E-08
DDR1_cg12669395	MAG_cg10618943	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg13329862	MAG_cg10618943	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg13351860	MAG_cg10618943	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg13695585	MAG_cg10618943	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg14790552	MAG_cg10618943	Myelin	0.86	2.56E-09	9.63E-08
DDR1_cg15656686	MAG_cg10618943	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg16111190	MAG_cg10618943	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg16797094	MAG_cg10618943	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg17176005	MAG_cg10618943	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg17604312	MAG_cg10618943	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg21677258	MAG_cg10618943	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg24566261	MAG_cg10618943	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg24636809	MAG_cg10618943	Myelin	0.81	1.24E-07	3.16E-06
DDR1_cg25613385	MAG_cg10618943	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg25655106	MAG_cg10618943	Myelin	0.88	2.64E-10	1.32E-08
DDR1_cg27237814	MAG_cg10618943	Myelin	0.83	2.30E-08	6.90E-07
DDR1_cg27593250	MAG_cg10618943	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg00466425	MAG_cg11587635	Myelin	0.87	8.88E-10	3.80E-08
DDR1_cg00934322	MAG_cg11587635	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg01936707	MAG_cg11587635	Myelin	0.92	1.01E-12	1.19E-10
DDR1_cg05703744	MAG_cg11587635	Myelin	0.93	2.46E-13	3.73E-11
DDR1_cg06200824	MAG_cg11587635	Myelin	0.80	2.35E-07	5.65E-06
DDR1_cg06501109	MAG_cg11587635	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg07908039	MAG_cg11587635	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg07912416	MAG_cg11587635	Myelin	0.87	6.96E-10	3.06E-08
DDR1_cg07979747	MAG_cg11587635	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg08673763	MAG_cg11587635	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg08684361	MAG_cg11587635	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg08951271	MAG_cg11587635	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg09965419	MAG_cg11587635	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg11530564	MAG_cg11587635	Myelin	0.94	2.33E-14	5.92E-12
DDR1_cg11676038	MAG_cg11587635	Myelin	0.93	3.24E-13	4.65E-11
DDR1_cg12669395	MAG_cg11587635	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg12847793	MAG_cg11587635	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg13329862	MAG_cg11587635	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg13351860	MAG_cg11587635	Myelin	0.94	5.55E-14	1.16E-11
DDR1_cg13695585	MAG_cg11587635	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg14058861	MAG_cg11587635	Myelin	0.76	1.68E-06	3.28E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg14790552	MAG_cg11587635	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg15656686	MAG_cg11587635	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg16111190	MAG_cg11587635	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg16797094	MAG_cg11587635	Myelin	0.94	1.03E-13	1.89E-11
DDR1_cg17176005	MAG_cg11587635	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg17604312	MAG_cg11587635	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg19215110	MAG_cg11587635	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg19591099	MAG_cg11587635	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg21677258	MAG_cg11587635	Myelin	0.93	3.55E-13	5.01E-11
DDR1_cg24636809	MAG_cg11587635	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg24727290	MAG_cg11587635	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg25613385	MAG_cg11587635	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg25655106	MAG_cg11587635	Myelin	0.93	2.04E-13	3.19E-11
DDR1_cg27237814	MAG_cg11587635	Myelin	0.90	3.95E-11	2.57E-09
DDR1_cg27593250	MAG_cg11587635	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg00466425	MAG_cg11902728	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg01936707	MAG_cg11902728	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg05703744	MAG_cg11902728	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg06200824	MAG_cg11902728	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg06501109	MAG_cg11902728	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg07912416	MAG_cg11902728	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg07979747	MAG_cg11902728	Myelin	0.90	5.71E-11	3.53E-09
DDR1_cg08673763	MAG_cg11902728	Myelin	0.86	2.56E-09	9.63E-08
DDR1_cg08684361	MAG_cg11902728	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg08951271	MAG_cg11902728	Myelin	0.93	3.55E-13	5.01E-11
DDR1_cg11530564	MAG_cg11902728	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg11676038	MAG_cg11902728	Myelin	0.95	4.88E-15	1.86E-12
DDR1_cg12669395	MAG_cg11902728	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg12847793	MAG_cg11902728	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg13329862	MAG_cg11902728	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg13351860	MAG_cg11902728	Myelin	0.86	1.71E-09	6.76E-08
DDR1_cg14058861	MAG_cg11902728	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg14790552	MAG_cg11902728	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg15656686	MAG_cg11902728	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg16111190	MAG_cg11902728	Myelin	0.84	9.28E-09	3.06E-07
DDR1_cg16797094	MAG_cg11902728	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg17176005	MAG_cg11902728	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg17604312	MAG_cg11902728	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg18577693	MAG_cg11902728	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg19215110	MAG_cg11902728	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg19591099	MAG_cg11902728	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg21677258	MAG_cg11902728	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg24636809	MAG_cg11902728	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg24727290	MAG_cg11902728	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg25655106	MAG_cg11902728	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg27237814	MAG_cg11902728	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg27593250	MAG_cg11902728	Myelin	0.77	9.16E-07	1.91E-05
DDR1_cg00466425	MAG_cg12402033	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg01936707	MAG_cg12402033	Myelin	0.92	1.01E-12	1.19E-10
DDR1_cg05703744	MAG_cg12402033	Myelin	0.92	2.65E-12	2.64E-10

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg06200824	MAG_cg12402033	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg06501109	MAG_cg12402033	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg07908039	MAG_cg12402033	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg07912416	MAG_cg12402033	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg07979747	MAG_cg12402033	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg08673763	MAG_cg12402033	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg08684361	MAG_cg12402033	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg08951271	MAG_cg12402033	Myelin	0.93	1.14E-13	2.04E-11
DDR1_cg09822812	MAG_cg12402033	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg09965419	MAG_cg12402033	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg11530564	MAG_cg12402033	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg11676038	MAG_cg12402033	Myelin	0.94	3.24E-14	7.65E-12
DDR1_cg12669395	MAG_cg12402033	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg13329862	MAG_cg12402033	Myelin	0.93	3.24E-13	4.65E-11
DDR1_cg13351860	MAG_cg12402033	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg14058861	MAG_cg12402033	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg14790552	MAG_cg12402033	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg15656686	MAG_cg12402033	Myelin	0.87	6.31E-10	2.82E-08
DDR1_cg15720085	MAG_cg12402033	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg16111190	MAG_cg12402033	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg16797094	MAG_cg12402033	Myelin	0.91	1.50E-11	1.13E-09
DDR1_cg17176005	MAG_cg12402033	Myelin	0.81	1.10E-07	2.82E-06
DDR1_cg17604312	MAG_cg12402033	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg18577693	MAG_cg12402033	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg19215110	MAG_cg12402033	Myelin	0.83	3.29E-08	9.53E-07
DDR1_cg19591099	MAG_cg12402033	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg21677258	MAG_cg12402033	Myelin	0.93	2.96E-13	4.31E-11
DDR1_cg24636809	MAG_cg12402033	Myelin	0.94	6.84E-14	1.37E-11
DDR1_cg24727290	MAG_cg12402033	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg25613385	MAG_cg12402033	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg25655106	MAG_cg12402033	Myelin	0.94	4.04E-14	9.10E-12
DDR1_cg27237814	MAG_cg12402033	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg27593250	MAG_cg12402033	Myelin	0.79	3.85E-07	8.81E-06
DDR1_cg00466425	MAG_cg13993734	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg01598675	MAG_cg13993734	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg01936707	MAG_cg13993734	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg05703744	MAG_cg13993734	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg06200824	MAG_cg13993734	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg06501109	MAG_cg13993734	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg07912416	MAG_cg13993734	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg07979747	MAG_cg13993734	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg08673763	MAG_cg13993734	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg08951271	MAG_cg13993734	Myelin	0.92	2.27E-12	2.31E-10
DDR1_cg09810078	MAG_cg13993734	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg09965419	MAG_cg13993734	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg11530564	MAG_cg13993734	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg11676038	MAG_cg13993734	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg12669395	MAG_cg13993734	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg12847793	MAG_cg13993734	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg13329862	MAG_cg13993734	Myelin	0.94	6.17E-14	1.26E-11

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13351860	MAG_cg13993734	Myelin	0.92	1.94E-12	2.03E-10
DDR1_cg14790552	MAG_cg13993734	Myelin	0.86	1.87E-09	7.34E-08
DDR1_cg15656686	MAG_cg13993734	Myelin	0.86	1.49E-09	5.99E-08
DDR1_cg15720085	MAG_cg13993734	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg16111190	MAG_cg13993734	Myelin	0.87	1.36E-09	5.52E-08
DDR1_cg16797094	MAG_cg13993734	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg17176005	MAG_cg13993734	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg17604312	MAG_cg13993734	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg18577693	MAG_cg13993734	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg19215110	MAG_cg13993734	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg19591099	MAG_cg13993734	Myelin	0.80	1.45E-07	3.64E-06
DDR1_cg20955507	MAG_cg13993734	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg21677258	MAG_cg13993734	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg24636809	MAG_cg13993734	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg24727290	MAG_cg13993734	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg25655106	MAG_cg13993734	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg27237814	MAG_cg13993734	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg27593250	MAG_cg13993734	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg00466425	MAG_cg14535518	Myelin	0.93	2.46E-13	3.73E-11
DDR1_cg00934322	MAG_cg14535518	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg01936707	MAG_cg14535518	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg05703744	MAG_cg14535518	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg06200824	MAG_cg14535518	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg06501109	MAG_cg14535518	Myelin	0.81	8.21E-08	2.18E-06
DDR1_cg07908039	MAG_cg14535518	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg07912416	MAG_cg14535518	Myelin	0.88	2.13E-10	1.10E-08
DDR1_cg07979747	MAG_cg14535518	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg08673763	MAG_cg14535518	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg08951271	MAG_cg14535518	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg09965419	MAG_cg14535518	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg11530564	MAG_cg14535518	Myelin	0.87	1.18E-09	4.87E-08
DDR1_cg11676038	MAG_cg14535518	Myelin	0.95	3.33E-15	1.40E-12
DDR1_cg12669395	MAG_cg14535518	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg12847793	MAG_cg14535518	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg13329862	MAG_cg14535518	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg13351860	MAG_cg14535518	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg14058861	MAG_cg14535518	Myelin	0.83	2.86E-08	8.38E-07
DDR1_cg14790552	MAG_cg14535518	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg15656686	MAG_cg14535518	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg15720085	MAG_cg14535518	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg16111190	MAG_cg14535518	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg16797094	MAG_cg14535518	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg17176005	MAG_cg14535518	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg17604312	MAG_cg14535518	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg18577693	MAG_cg14535518	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg19215110	MAG_cg14535518	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg19591099	MAG_cg14535518	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg21677258	MAG_cg14535518	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg24566261	MAG_cg14535518	Myelin	0.83	3.66E-08	1.05E-06
DDR1_cg24636809	MAG_cg14535518	Myelin	0.91	1.40E-11	1.06E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg24727290	MAG_cg14535518	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg25655106	MAG_cg14535518	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg27237814	MAG_cg14535518	Myelin	0.87	6.31E-10	2.82E-08
DDR1_cg27593250	MAG_cg14535518	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg00466425	MAG_cg14952359	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg01936707	MAG_cg14952359	Myelin	0.77	1.13E-06	2.30E-05
DDR1_cg05703744	MAG_cg14952359	Myelin	0.80	1.85E-07	4.55E-06
DDR1_cg06200824	MAG_cg14952359	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg06501109	MAG_cg14952359	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg07912416	MAG_cg14952359	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg07979747	MAG_cg14952359	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg08673763	MAG_cg14952359	Myelin	0.86	2.56E-09	9.63E-08
DDR1_cg08951271	MAG_cg14952359	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg11530564	MAG_cg14952359	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg11676038	MAG_cg14952359	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg12669395	MAG_cg14952359	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg13329862	MAG_cg14952359	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg13351860	MAG_cg14952359	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg14058861	MAG_cg14952359	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg14790552	MAG_cg14952359	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg15656686	MAG_cg14952359	Myelin	0.82	7.20E-08	1.94E-06
DDR1_cg16111190	MAG_cg14952359	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg16797094	MAG_cg14952359	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg17176005	MAG_cg14952359	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg17604312	MAG_cg14952359	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg18577693	MAG_cg14952359	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg21677258	MAG_cg14952359	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg24636809	MAG_cg14952359	Myelin	0.83	2.86E-08	8.38E-07
DDR1_cg24727290	MAG_cg14952359	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg25613385	MAG_cg14952359	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg25655106	MAG_cg14952359	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg27237814	MAG_cg14952359	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg00466425	MAG_cg15005368	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg01936707	MAG_cg15005368	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg05703744	MAG_cg15005368	Myelin	0.87	6.31E-10	2.82E-08
DDR1_cg06200824	MAG_cg15005368	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg06501109	MAG_cg15005368	Myelin	0.82	6.31E-08	1.72E-06
DDR1_cg07912416	MAG_cg15005368	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg07979747	MAG_cg15005368	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg08673763	MAG_cg15005368	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg08684361	MAG_cg15005368	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg08951271	MAG_cg15005368	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg09965419	MAG_cg15005368	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg11530564	MAG_cg15005368	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg11676038	MAG_cg15005368	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg12669395	MAG_cg15005368	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg13329862	MAG_cg15005368	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg13351860	MAG_cg15005368	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg14790552	MAG_cg15005368	Myelin	0.82	4.35E-08	1.23E-06
DDR1_cg15656686	MAG_cg15005368	Myelin	0.86	3.46E-09	1.27E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg15720085	MAG_cg15005368	Myelin	0.78	5.52E-07	1.22E-05
DDR1_cg16111190	MAG_cg15005368	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg16797094	MAG_cg15005368	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg17604312	MAG_cg15005368	Myelin	0.83	3.66E-08	1.05E-06
DDR1_cg19591099	MAG_cg15005368	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg21677258	MAG_cg15005368	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg24636809	MAG_cg15005368	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg24727290	MAG_cg15005368	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg25655106	MAG_cg15005368	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg27237814	MAG_cg15005368	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg27593250	MAG_cg15005368	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg00466425	MAG_cg15485216	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg01936707	MAG_cg15485216	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg07979747	MAG_cg15485216	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg08673763	MAG_cg15485216	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg08951271	MAG_cg15485216	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg11530564	MAG_cg15485216	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg11676038	MAG_cg15485216	Myelin	0.88	2.37E-10	1.20E-08
DDR1_cg12669395	MAG_cg15485216	Myelin	0.80	2.57E-07	6.12E-06
DDR1_cg13329862	MAG_cg15485216	Myelin	0.81	8.76E-08	2.31E-06
DDR1_cg13351860	MAG_cg15485216	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg14058861	MAG_cg15485216	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg16111190	MAG_cg15485216	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg19591099	MAG_cg15485216	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg21677258	MAG_cg15485216	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg24636809	MAG_cg15485216	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg24727290	MAG_cg15485216	Myelin	0.77	1.18E-06	2.41E-05
DDR1_cg25655106	MAG_cg15485216	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg27237814	MAG_cg15485216	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg27593250	MAG_cg15485216	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg00466425	MAG_cg15761414	Myelin	0.84	1.27E-08	4.04E-07
DDR1_cg01598675	MAG_cg15761414	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg01936707	MAG_cg15761414	Myelin	0.84	1.32E-08	4.19E-07
DDR1_cg05703744	MAG_cg15761414	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg06200824	MAG_cg15761414	Myelin	0.85	6.22E-09	2.14E-07
DDR1_cg07908039	MAG_cg15761414	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg07912416	MAG_cg15761414	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg07979747	MAG_cg15761414	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg08673763	MAG_cg15761414	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg08951271	MAG_cg15761414	Myelin	0.86	1.49E-09	5.99E-08
DDR1_cg09965419	MAG_cg15761414	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg11530564	MAG_cg15761414	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg11676038	MAG_cg15761414	Myelin	0.85	4.47E-09	1.59E-07
DDR1_cg12669395	MAG_cg15761414	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg13329862	MAG_cg15761414	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg13351860	MAG_cg15761414	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg13695585	MAG_cg15761414	Myelin	0.79	4.55E-07	1.02E-05
DDR1_cg14790552	MAG_cg15761414	Myelin	0.85	3.61E-09	1.32E-07
DDR1_cg15656686	MAG_cg15761414	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg16111190	MAG_cg15761414	Myelin	0.85	3.61E-09	1.32E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg16797094	MAG_cg15761414	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg17176005	MAG_cg15761414	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg17604312	MAG_cg15761414	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg18577693	MAG_cg15761414	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg19215110	MAG_cg15761414	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg19591099	MAG_cg15761414	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg21677258	MAG_cg15761414	Myelin	0.95	3.77E-15	1.53E-12
DDR1_cg24566261	MAG_cg15761414	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg24636809	MAG_cg15761414	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg24727290	MAG_cg15761414	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg25655106	MAG_cg15761414	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg27237814	MAG_cg15761414	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg00466425	MAG_cg17096126	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg01936707	MAG_cg17096126	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg05703744	MAG_cg17096126	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg06200824	MAG_cg17096126	Myelin	0.81	8.48E-08	2.24E-06
DDR1_cg06501109	MAG_cg17096126	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg07912416	MAG_cg17096126	Myelin	0.80	1.97E-07	4.80E-06
DDR1_cg07979747	MAG_cg17096126	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg08673763	MAG_cg17096126	Myelin	0.80	1.85E-07	4.55E-06
DDR1_cg08951271	MAG_cg17096126	Myelin	0.84	1.32E-08	4.19E-07
DDR1_cg11530564	MAG_cg17096126	Myelin	0.82	4.50E-08	1.27E-06
DDR1_cg11676038	MAG_cg17096126	Myelin	0.84	1.22E-08	3.91E-07
DDR1_cg12669395	MAG_cg17096126	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg13329862	MAG_cg17096126	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg13351860	MAG_cg17096126	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg14058861	MAG_cg17096126	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg14790552	MAG_cg17096126	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg15656686	MAG_cg17096126	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg15720085	MAG_cg17096126	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg16111190	MAG_cg17096126	Myelin	0.87	8.88E-10	3.80E-08
DDR1_cg16797094	MAG_cg17096126	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg19591099	MAG_cg17096126	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg21677258	MAG_cg17096126	Myelin	0.82	5.16E-08	1.43E-06
DDR1_cg24636809	MAG_cg17096126	Myelin	0.85	5.50E-09	1.92E-07
DDR1_cg24727290	MAG_cg17096126	Myelin	0.80	1.41E-07	3.54E-06
DDR1_cg25655106	MAG_cg17096126	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg27237814	MAG_cg17096126	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg27593250	MAG_cg17096126	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg05703744	MAG_cg17461485	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg07979747	MAG_cg17461485	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg09810078	MAG_cg17461485	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg12669395	MAG_cg17461485	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg13329862	MAG_cg17461485	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg13351860	MAG_cg17461485	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg15656686	MAG_cg17461485	Myelin	0.75	3.05E-06	5.55E-05
DDR1_cg16111190	MAG_cg17461485	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg17604312	MAG_cg17461485	Myelin	0.78	7.04E-07	1.51E-05
DDR1_cg19215110	MAG_cg17461485	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg20955507	MAG_cg17461485	Myelin	0.75	2.36E-06	4.42E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg27237814	MAG_cg17461485	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg00466425	MAG_cg17469069	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg00934322	MAG_cg17469069	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg01598675	MAG_cg17469069	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg01936707	MAG_cg17469069	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg05703744	MAG_cg17469069	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg06200824	MAG_cg17469069	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg06501109	MAG_cg17469069	Myelin	0.84	1.27E-08	4.04E-07
DDR1_cg07912416	MAG_cg17469069	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg07979747	MAG_cg17469069	Myelin	0.85	4.66E-09	1.65E-07
DDR1_cg08673763	MAG_cg17469069	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg08684361	MAG_cg17469069	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg08951271	MAG_cg17469069	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg09965419	MAG_cg17469069	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg11530564	MAG_cg17469069	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg11676038	MAG_cg17469069	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg12669395	MAG_cg17469069	Myelin	0.91	4.51E-12	4.08E-10
DDR1_cg12847793	MAG_cg17469069	Myelin	0.75	2.59E-06	4.80E-05
DDR1_cg13329862	MAG_cg17469069	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg13351860	MAG_cg17469069	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg13695585	MAG_cg17469069	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg14790552	MAG_cg17469069	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg15656686	MAG_cg17469069	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg16111190	MAG_cg17469069	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg16797094	MAG_cg17469069	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg17176005	MAG_cg17469069	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg17604312	MAG_cg17469069	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg19215110	MAG_cg17469069	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg19591099	MAG_cg17469069	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg21677258	MAG_cg17469069	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg24636809	MAG_cg17469069	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg24727290	MAG_cg17469069	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg25613385	MAG_cg17469069	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg25655106	MAG_cg17469069	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg27237814	MAG_cg17469069	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg27593250	MAG_cg17469069	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg05703744	MAG_cg18155720	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg08673763	MAG_cg18155720	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg08951271	MAG_cg18155720	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg11530564	MAG_cg18155720	Myelin	0.83	2.30E-08	6.90E-07
DDR1_cg12669395	MAG_cg18155720	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg13329862	MAG_cg18155720	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg13351860	MAG_cg18155720	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg13695585	MAG_cg18155720	Myelin	0.82	4.82E-08	1.35E-06
DDR1_cg15656686	MAG_cg18155720	Myelin	0.76	1.72E-06	3.35E-05
DDR1_cg16111190	MAG_cg18155720	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg16797094	MAG_cg18155720	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg17176005	MAG_cg18155720	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg19215110	MAG_cg18155720	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg21677258	MAG_cg18155720	Myelin	0.79	4.19E-07	9.49E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg27237814	MAG_cg18155720	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg00466425	MAG_cg19694850	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg01598675	MAG_cg19694850	Myelin	0.80	2.22E-07	5.35E-06
DDR1_cg01936707	MAG_cg19694850	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg05703744	MAG_cg19694850	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg06200824	MAG_cg19694850	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg07908039	MAG_cg19694850	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg07912416	MAG_cg19694850	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg07979747	MAG_cg19694850	Myelin	0.91	1.50E-11	1.13E-09
DDR1_cg08673763	MAG_cg19694850	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg08684361	MAG_cg19694850	Myelin	0.75	2.91E-06	5.32E-05
DDR1_cg08951271	MAG_cg19694850	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg09965419	MAG_cg19694850	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg11530564	MAG_cg19694850	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg11676038	MAG_cg19694850	Myelin	0.87	1.30E-09	5.30E-08
DDR1_cg12669395	MAG_cg19694850	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg13329862	MAG_cg19694850	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg13351860	MAG_cg19694850	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg13695585	MAG_cg19694850	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg14058861	MAG_cg19694850	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg14790552	MAG_cg19694850	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg15656686	MAG_cg19694850	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg16111190	MAG_cg19694850	Myelin	0.87	1.18E-09	4.87E-08
DDR1_cg16797094	MAG_cg19694850	Myelin	0.86	1.63E-09	6.49E-08
DDR1_cg17176005	MAG_cg19694850	Myelin	0.88	2.64E-10	1.32E-08
DDR1_cg17604312	MAG_cg19694850	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg19215110	MAG_cg19694850	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg21677258	MAG_cg19694850	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg24636809	MAG_cg19694850	Myelin	0.82	5.16E-08	1.43E-06
DDR1_cg24727290	MAG_cg19694850	Myelin	0.80	1.50E-07	3.75E-06
DDR1_cg25655106	MAG_cg19694850	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg27237814	MAG_cg19694850	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg00466425	MAG_cg21305926	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg01598675	MAG_cg21305926	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg01936707	MAG_cg21305926	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg05703744	MAG_cg21305926	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg06200824	MAG_cg21305926	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg06501109	MAG_cg21305926	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg07908039	MAG_cg21305926	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg07912416	MAG_cg21305926	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg07979747	MAG_cg21305926	Myelin	0.87	6.31E-10	2.82E-08
DDR1_cg08673763	MAG_cg21305926	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg08951271	MAG_cg21305926	Myelin	0.88	2.64E-10	1.32E-08
DDR1_cg11530564	MAG_cg21305926	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg11676038	MAG_cg21305926	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg12669395	MAG_cg21305926	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg13329862	MAG_cg21305926	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg13351860	MAG_cg21305926	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg14058861	MAG_cg21305926	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg14790552	MAG_cg21305926	Myelin	0.89	1.29E-10	7.09E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg15656686	MAG_cg21305926	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg15720085	MAG_cg21305926	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg16111190	MAG_cg21305926	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg16797094	MAG_cg21305926	Myelin	0.84	1.53E-08	4.79E-07
DDR1_cg17176005	MAG_cg21305926	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg17604312	MAG_cg21305926	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg18577693	MAG_cg21305926	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg19215110	MAG_cg21305926	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg19591099	MAG_cg21305926	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg21677258	MAG_cg21305926	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg24636809	MAG_cg21305926	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg24727290	MAG_cg21305926	Myelin	0.81	1.24E-07	3.16E-06
DDR1_cg25613385	MAG_cg21305926	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg25655106	MAG_cg21305926	Myelin	0.94	8.42E-14	1.60E-11
DDR1_cg27237814	MAG_cg21305926	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg27593250	MAG_cg21305926	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg00466425	MAG_cg22266001	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg01936707	MAG_cg22266001	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg05703744	MAG_cg22266001	Myelin	0.83	3.66E-08	1.05E-06
DDR1_cg06501109	MAG_cg22266001	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg07908039	MAG_cg22266001	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg07912416	MAG_cg22266001	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg07979747	MAG_cg22266001	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg08673763	MAG_cg22266001	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg08684361	MAG_cg22266001	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg08951271	MAG_cg22266001	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg11530564	MAG_cg22266001	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg11676038	MAG_cg22266001	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg12669395	MAG_cg22266001	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg12847793	MAG_cg22266001	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg13329862	MAG_cg22266001	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg13351860	MAG_cg22266001	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg13695585	MAG_cg22266001	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg14790552	MAG_cg22266001	Myelin	0.83	2.86E-08	8.38E-07
DDR1_cg15656686	MAG_cg22266001	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg16111190	MAG_cg22266001	Myelin	0.84	1.04E-08	3.40E-07
DDR1_cg16797094	MAG_cg22266001	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg17176005	MAG_cg22266001	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg19215110	MAG_cg22266001	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg21677258	MAG_cg22266001	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg24636809	MAG_cg22266001	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg24727290	MAG_cg22266001	Myelin	0.80	2.57E-07	6.12E-06
DDR1_cg25655106	MAG_cg22266001	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg27237814	MAG_cg22266001	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg00466425	MAG_cg27017562	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg01598675	MAG_cg27017562	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg01936707	MAG_cg27017562	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg05703744	MAG_cg27017562	Myelin	0.93	4.26E-13	5.84E-11
DDR1_cg06200824	MAG_cg27017562	Myelin	0.83	2.86E-08	8.38E-07
DDR1_cg06501109	MAG_cg27017562	Myelin	0.85	7.61E-09	2.56E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07908039	MAG_cg27017562	Myelin	0.76	1.72E-06	3.35E-05
DDR1_cg07912416	MAG_cg27017562	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg07979747	MAG_cg27017562	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg08673763	MAG_cg27017562	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg08684361	MAG_cg27017562	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg08951271	MAG_cg27017562	Myelin	0.93	3.24E-13	4.65E-11
DDR1_cg09965419	MAG_cg27017562	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg11530564	MAG_cg27017562	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg11676038	MAG_cg27017562	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg12669395	MAG_cg27017562	Myelin	0.92	1.52E-12	1.66E-10
DDR1_cg13329862	MAG_cg27017562	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg13351860	MAG_cg27017562	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg14058861	MAG_cg27017562	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg14790552	MAG_cg27017562	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg15656686	MAG_cg27017562	Myelin	0.86	1.71E-09	6.76E-08
DDR1_cg15720085	MAG_cg27017562	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg16111190	MAG_cg27017562	Myelin	0.86	2.56E-09	9.63E-08
DDR1_cg16797094	MAG_cg27017562	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg17176005	MAG_cg27017562	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg17604312	MAG_cg27017562	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg18577693	MAG_cg27017562	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg19215110	MAG_cg27017562	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg19591099	MAG_cg27017562	Myelin	0.82	5.71E-08	1.57E-06
DDR1_cg21677258	MAG_cg27017562	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg24636809	MAG_cg27017562	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg24727290	MAG_cg27017562	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg25613385	MAG_cg27017562	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg25655106	MAG_cg27017562	Myelin	0.96	4.44E-16	3.14E-13
DDR1_cg27237814	MAG_cg27017562	Myelin	0.89	1.37E-10	7.45E-09
DDR1_cg27593250	MAG_cg27017562	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg00466425	MBP_cg00187503	Myelin	0.81	8.76E-08	2.31E-06
DDR1_cg00934322	MBP_cg00187503	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg01936707	MBP_cg00187503	Myelin	0.91	1.14E-11	8.99E-10
DDR1_cg05703744	MBP_cg00187503	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg06200824	MBP_cg00187503	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg06501109	MBP_cg00187503	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg07908039	MBP_cg00187503	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg07912416	MBP_cg00187503	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg07979747	MBP_cg00187503	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg08673763	MBP_cg00187503	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg08951271	MBP_cg00187503	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg11530564	MBP_cg00187503	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg11676038	MBP_cg00187503	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg12669395	MBP_cg00187503	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg13329862	MBP_cg00187503	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg13351860	MBP_cg00187503	Myelin	0.86	1.96E-09	7.64E-08
DDR1_cg14790552	MBP_cg00187503	Myelin	0.86	1.87E-09	7.34E-08
DDR1_cg15656686	MBP_cg00187503	Myelin	0.87	1.36E-09	5.52E-08
DDR1_cg16111190	MBP_cg00187503	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg16797094	MBP_cg00187503	Myelin	0.89	7.25E-11	4.36E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg17176005	MBP_cg00187503	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg17604312	MBP_cg00187503	Myelin	0.83	2.30E-08	6.90E-07
DDR1_cg19215110	MBP_cg00187503	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg19591099	MBP_cg00187503	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg21677258	MBP_cg00187503	Myelin	0.89	6.44E-11	3.93E-09
DDR1_cg24636809	MBP_cg00187503	Myelin	0.87	1.18E-09	4.87E-08
DDR1_cg24727290	MBP_cg00187503	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg25613385	MBP_cg00187503	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg25655106	MBP_cg00187503	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg27237814	MBP_cg00187503	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg00466425	MBP_cg00706570	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg01936707	MBP_cg00706570	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg05703744	MBP_cg00706570	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg06501109	MBP_cg00706570	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg07908039	MBP_cg00706570	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg07912416	MBP_cg00706570	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg07979747	MBP_cg00706570	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg08673763	MBP_cg00706570	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg08684361	MBP_cg00706570	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg08951271	MBP_cg00706570	Myelin	0.89	1.37E-10	7.45E-09
DDR1_cg11530564	MBP_cg00706570	Myelin	0.94	6.17E-14	1.26E-11
DDR1_cg11676038	MBP_cg00706570	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg12669395	MBP_cg00706570	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg13329862	MBP_cg00706570	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg13351860	MBP_cg00706570	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg13695585	MBP_cg00706570	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg14790552	MBP_cg00706570	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg15656686	MBP_cg00706570	Myelin	0.85	5.97E-09	2.06E-07
DDR1_cg16111190	MBP_cg00706570	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg16797094	MBP_cg00706570	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg17176005	MBP_cg00706570	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg17604312	MBP_cg00706570	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg18577693	MBP_cg00706570	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg19215110	MBP_cg00706570	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg21677258	MBP_cg00706570	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg24636809	MBP_cg00706570	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg24727290	MBP_cg00706570	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg25613385	MBP_cg00706570	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg25655106	MBP_cg00706570	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg27237814	MBP_cg00706570	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg27593250	MBP_cg00706570	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg00466425	MBP_cg00735329	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg01598675	MBP_cg00735329	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg01936707	MBP_cg00735329	Myelin	0.87	1.30E-09	5.30E-08
DDR1_cg05703744	MBP_cg00735329	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg06200824	MBP_cg00735329	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg06501109	MBP_cg00735329	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg07912416	MBP_cg00735329	Myelin	0.83	2.57E-08	7.60E-07
DDR1_cg07979747	MBP_cg00735329	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg08673763	MBP_cg00735329	Myelin	0.85	4.28E-09	1.53E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

DDR1 CpG	Gene CpG	Cell type marker	ρ[a]	*p*-value	Adj *p*-value[b]
DDR1_cg08684361	MBP_cg00735329	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg08951271	MBP_cg00735329	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg11530564	MBP_cg00735329	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg11676038	MBP_cg00735329	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg12669395	MBP_cg00735329	Myelin	0.90	3.49E-11	2.31E-09
DDR1_cg13329862	MBP_cg00735329	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg13351860	MBP_cg00735329	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg14790552	MBP_cg00735329	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg15656686	MBP_cg00735329	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg16111190	MBP_cg00735329	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg16797094	MBP_cg00735329	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg17176005	MBP_cg00735329	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg17604312	MBP_cg00735329	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg19215110	MBP_cg00735329	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg19591099	MBP_cg00735329	Myelin	0.82	6.31E-08	1.72E-06
DDR1_cg20335906	MBP_cg00735329	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg21677258	MBP_cg00735329	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg24636809	MBP_cg00735329	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg24727290	MBP_cg00735329	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg25655106	MBP_cg00735329	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg27237814	MBP_cg00735329	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg27593250	MBP_cg00735329	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg00466425	MBP_cg00839132	Myelin	0.91	4.51E-12	4.08E-10
DDR1_cg01598675	MBP_cg00839132	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg01936707	MBP_cg00839132	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg05703744	MBP_cg00839132	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg06200824	MBP_cg00839132	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg06501109	MBP_cg00839132	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg07908039	MBP_cg00839132	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg07912416	MBP_cg00839132	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg07979747	MBP_cg00839132	Myelin	0.85	3.77E-09	1.37E-07
DDR1_cg08673763	MBP_cg00839132	Myelin	0.86	1.96E-09	7.64E-08
DDR1_cg08951271	MBP_cg00839132	Myelin	0.93	2.04E-13	3.19E-11
DDR1_cg11530564	MBP_cg00839132	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg11676038	MBP_cg00839132	Myelin	0.93	1.68E-13	2.75E-11
DDR1_cg12669395	MBP_cg00839132	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg12847793	MBP_cg00839132	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg13329862	MBP_cg00839132	Myelin	0.92	1.79E-12	1.90E-10
DDR1_cg13351860	MBP_cg00839132	Myelin	0.92	1.94E-12	2.03E-10
DDR1_cg14790552	MBP_cg00839132	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg15656686	MBP_cg00839132	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg15720085	MBP_cg00839132	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg16111190	MBP_cg00839132	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg16797094	MBP_cg00839132	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg17176005	MBP_cg00839132	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg17604312	MBP_cg00839132	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg18577693	MBP_cg00839132	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg19215110	MBP_cg00839132	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg19591099	MBP_cg00839132	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg20335906	MBP_cg00839132	Myelin	0.79	4.19E-07	9.49E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg21677258	MBP_cg00839132	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg24636809	MBP_cg00839132	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg24727290	MBP_cg00839132	Myelin	0.83	2.30E-08	6.90E-07
DDR1_cg25613385	MBP_cg00839132	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg25655106	MBP_cg00839132	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg25943433	MBP_cg00839132	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg27237814	MBP_cg00839132	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg27593250	MBP_cg00839132	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg01598675	MBP_cg00912518	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg14790552	MBP_cg00912518	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg00466425	MBP_cg01475204	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg01598675	MBP_cg01475204	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg01936707	MBP_cg01475204	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg05703744	MBP_cg01475204	Myelin	0.93	2.24E-13	3.46E-11
DDR1_cg06200824	MBP_cg01475204	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg06501109	MBP_cg01475204	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg07908039	MBP_cg01475204	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg07912416	MBP_cg01475204	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg07979747	MBP_cg01475204	Myelin	0.88	2.37E-10	1.20E-08
DDR1_cg08673763	MBP_cg01475204	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg08684361	MBP_cg01475204	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg08951271	MBP_cg01475204	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg09822812	MBP_cg01475204	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg09965419	MBP_cg01475204	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg11530564	MBP_cg01475204	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg11676038	MBP_cg01475204	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg12669395	MBP_cg01475204	Myelin	0.91	1.14E-11	8.99E-10
DDR1_cg13329862	MBP_cg01475204	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg13351860	MBP_cg01475204	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg13695585	MBP_cg01475204	Myelin	0.79	4.55E-07	1.02E-05
DDR1_cg14790552	MBP_cg01475204	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg15656686	MBP_cg01475204	Myelin	0.89	7.25E-11	4.36E-09
DDR1_cg16111190	MBP_cg01475204	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg16797094	MBP_cg01475204	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg17176005	MBP_cg01475204	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg17604312	MBP_cg01475204	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg18577693	MBP_cg01475204	Myelin	0.76	2.20E-06	4.15E-05
DDR1_cg19215110	MBP_cg01475204	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg19591099	MBP_cg01475204	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg20335906	MBP_cg01475204	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg20955507	MBP_cg01475204	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg21677258	MBP_cg01475204	Myelin	0.93	2.04E-13	3.19E-11
DDR1_cg24636809	MBP_cg01475204	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg24727290	MBP_cg01475204	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg25613385	MBP_cg01475204	Myelin	0.78	5.52E-07	1.22E-05
DDR1_cg25655106	MBP_cg01475204	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg27237814	MBP_cg01475204	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg27593250	MBP_cg01475204	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg00466425	MBP_cg02782187	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg00934322	MBP_cg02782187	Myelin	0.78	6.85E-07	1.48E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg01936707	MBP_cg02782187	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg05703744	MBP_cg02782187	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg06200824	MBP_cg02782187	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg06501109	MBP_cg02782187	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg07908039	MBP_cg02782187	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg07912416	MBP_cg02782187	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg07979747	MBP_cg02782187	Myelin	0.84	9.28E-09	3.06E-07
DDR1_cg08673763	MBP_cg02782187	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg08684361	MBP_cg02782187	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg08951271	MBP_cg02782187	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg09822812	MBP_cg02782187	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg09965419	MBP_cg02782187	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg11530564	MBP_cg02782187	Myelin	0.96	4.44E-16	3.14E-13
DDR1_cg11676038	MBP_cg02782187	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg12669395	MBP_cg02782187	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg12847793	MBP_cg02782187	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg13329862	MBP_cg02782187	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg13351860	MBP_cg02782187	Myelin	0.95	4.88E-15	1.86E-12
DDR1_cg13695585	MBP_cg02782187	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg14058861	MBP_cg02782187	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg14790552	MBP_cg02782187	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg15656686	MBP_cg02782187	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg16111190	MBP_cg02782187	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg16797094	MBP_cg02782187	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg17176005	MBP_cg02782187	Myelin	0.80	2.57E-07	6.12E-06
DDR1_cg17604312	MBP_cg02782187	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg19215110	MBP_cg02782187	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg19591099	MBP_cg02782187	Myelin	0.80	1.85E-07	4.55E-06
DDR1_cg21677258	MBP_cg02782187	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg24636809	MBP_cg02782187	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg24727290	MBP_cg02782187	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg25613385	MBP_cg02782187	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg25655106	MBP_cg02782187	Myelin	0.91	4.51E-12	4.08E-10
DDR1_cg27237814	MBP_cg02782187	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg27593250	MBP_cg02782187	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg00466425	MBP_cg03560685	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg00934322	MBP_cg03560685	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg01936707	MBP_cg03560685	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg05703744	MBP_cg03560685	Myelin	0.88	2.13E-10	1.10E-08
DDR1_cg06200824	MBP_cg03560685	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg06501109	MBP_cg03560685	Myelin	0.84	9.28E-09	3.06E-07
DDR1_cg07912416	MBP_cg03560685	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg07979747	MBP_cg03560685	Myelin	0.85	7.92E-09	2.66E-07
DDR1_cg08673763	MBP_cg03560685	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg08684361	MBP_cg03560685	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg08951271	MBP_cg03560685	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg09965419	MBP_cg03560685	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg11530564	MBP_cg03560685	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg11676038	MBP_cg03560685	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg12669395	MBP_cg03560685	Myelin	0.88	2.37E-10	1.20E-08

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg12847793	MBP_cg03560685	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg13329862	MBP_cg03560685	Myelin	0.92	2.45E-12	2.47E-10
DDR1_cg13351860	MBP_cg03560685	Myelin	0.94	1.87E-14	5.00E-12
DDR1_cg13695585	MBP_cg03560685	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg14790552	MBP_cg03560685	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg15656686	MBP_cg03560685	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg16111190	MBP_cg03560685	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg16797094	MBP_cg03560685	Myelin	0.93	4.26E-13	5.84E-11
DDR1_cg17176005	MBP_cg03560685	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg17604312	MBP_cg03560685	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg19215110	MBP_cg03560685	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg19591099	MBP_cg03560685	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg21677258	MBP_cg03560685	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg24636809	MBP_cg03560685	Myelin	0.87	6.96E-10	3.06E-08
DDR1_cg24727290	MBP_cg03560685	Myelin	0.87	1.30E-09	5.30E-08
DDR1_cg25613385	MBP_cg03560685	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg25655106	MBP_cg03560685	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg27237814	MBP_cg03560685	Myelin	0.86	1.96E-09	7.64E-08
DDR1_cg27593250	MBP_cg03560685	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg00466425	MBP_cg06410824	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg01598675	MBP_cg06410824	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg01936707	MBP_cg06410824	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg05703744	MBP_cg06410824	Myelin	0.89	6.44E-11	3.93E-09
DDR1_cg06200824	MBP_cg06410824	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg06501109	MBP_cg06410824	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg07912416	MBP_cg06410824	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg07979747	MBP_cg06410824	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg08673763	MBP_cg06410824	Myelin	0.86	1.87E-09	7.34E-08
DDR1_cg08951271	MBP_cg06410824	Myelin	0.93	2.04E-13	3.19E-11
DDR1_cg11530564	MBP_cg06410824	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg11676038	MBP_cg06410824	Myelin	0.93	2.24E-13	3.46E-11
DDR1_cg12669395	MBP_cg06410824	Myelin	0.91	6.49E-12	5.56E-10
DDR1_cg13329862	MBP_cg06410824	Myelin	0.94	2.09E-14	5.43E-12
DDR1_cg13351860	MBP_cg06410824	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg14058861	MBP_cg06410824	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg14790552	MBP_cg06410824	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg15656686	MBP_cg06410824	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg15720085	MBP_cg06410824	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg16111190	MBP_cg06410824	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg16797094	MBP_cg06410824	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg17176005	MBP_cg06410824	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg18577693	MBP_cg06410824	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg19215110	MBP_cg06410824	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg19591099	MBP_cg06410824	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg21677258	MBP_cg06410824	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg24566261	MBP_cg06410824	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg24636809	MBP_cg06410824	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg24727290	MBP_cg06410824	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg25655106	MBP_cg06410824	Myelin	0.88	2.37E-10	1.20E-08
DDR1_cg27237814	MBP_cg06410824	Myelin	0.90	2.71E-11	1.85E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg27593250	MBP_cg06410824	Myelin	0.82	6.31E-08	1.72E-06
DDR1_cg00466425	MBP_cg06543730	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg01936707	MBP_cg06543730	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg05703744	MBP_cg06543730	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg06200824	MBP_cg06543730	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg06501109	MBP_cg06543730	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg07908039	MBP_cg06543730	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg07912416	MBP_cg06543730	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg07979747	MBP_cg06543730	Myelin	0.83	2.06E-08	6.25E-07
DDR1_cg08673763	MBP_cg06543730	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg08684361	MBP_cg06543730	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg08951271	MBP_cg06543730	Myelin	0.85	5.50E-09	1.92E-07
DDR1_cg09965419	MBP_cg06543730	Myelin	0.79	3.63E-07	8.37E-06
DDR1_cg11530564	MBP_cg06543730	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg11676038	MBP_cg06543730	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg12669395	MBP_cg06543730	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg13329862	MBP_cg06543730	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg13351860	MBP_cg06543730	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg13695585	MBP_cg06543730	Myelin	0.77	1.10E-06	2.25E-05
DDR1_cg14790552	MBP_cg06543730	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg15656686	MBP_cg06543730	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg16111190	MBP_cg06543730	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg16797094	MBP_cg06543730	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg17176005	MBP_cg06543730	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg17604312	MBP_cg06543730	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg19215110	MBP_cg06543730	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg21677258	MBP_cg06543730	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg24566261	MBP_cg06543730	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg24636809	MBP_cg06543730	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg24727290	MBP_cg06543730	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg25655106	MBP_cg06543730	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg27237814	MBP_cg06543730	Myelin	0.85	4.66E-09	1.65E-07
DDR1_cg27593250	MBP_cg06543730	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg00466425	MBP_cg06548292	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg01936707	MBP_cg06548292	Myelin	0.87	8.88E-10	3.80E-08
DDR1_cg05703744	MBP_cg06548292	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg06200824	MBP_cg06548292	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg06501109	MBP_cg06548292	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg07912416	MBP_cg06548292	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg07979747	MBP_cg06548292	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg08673763	MBP_cg06548292	Myelin	0.89	1.22E-10	6.76E-09
DDR1_cg08951271	MBP_cg06548292	Myelin	0.89	1.22E-10	6.76E-09
DDR1_cg09822812	MBP_cg06548292	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg09965419	MBP_cg06548292	Myelin	0.77	9.90E-07	2.05E-05
DDR1_cg11530564	MBP_cg06548292	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg11676038	MBP_cg06548292	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg12669395	MBP_cg06548292	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg13329862	MBP_cg06548292	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg13351860	MBP_cg06548292	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg14058861	MBP_cg06548292	Myelin	0.83	3.41E-08	9.84E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg14790552	MBP_cg06548292	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg15656686	MBP_cg06548292	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg16111190	MBP_cg06548292	Myelin	0.85	6.22E-09	2.14E-07
DDR1_cg16797094	MBP_cg06548292	Myelin	0.83	2.66E-08	7.86E-07
DDR1_cg17176005	MBP_cg06548292	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg17604312	MBP_cg06548292	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg19215110	MBP_cg06548292	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg19591099	MBP_cg06548292	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg21677258	MBP_cg06548292	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg24636809	MBP_cg06548292	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg24727290	MBP_cg06548292	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg25655106	MBP_cg06548292	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg27237814	MBP_cg06548292	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg27593250	MBP_cg06548292	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg00466425	MBP_cg06773488	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg00934322	MBP_cg06773488	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg01936707	MBP_cg06773488	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg05703744	MBP_cg06773488	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg06501109	MBP_cg06773488	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg07912416	MBP_cg06773488	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg08673763	MBP_cg06773488	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg08951271	MBP_cg06773488	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg09822812	MBP_cg06773488	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg09965419	MBP_cg06773488	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg11530564	MBP_cg06773488	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg11676038	MBP_cg06773488	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg12669395	MBP_cg06773488	Myelin	0.87	1.13E-09	4.68E-08
DDR1_cg12847793	MBP_cg06773488	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg13329862	MBP_cg06773488	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg13351860	MBP_cg06773488	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg13695585	MBP_cg06773488	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg14790552	MBP_cg06773488	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg15656686	MBP_cg06773488	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg16111190	MBP_cg06773488	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg16797094	MBP_cg06773488	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg17604312	MBP_cg06773488	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg19215110	MBP_cg06773488	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg19591099	MBP_cg06773488	Myelin	0.78	7.04E-07	1.51E-05
DDR1_cg21677258	MBP_cg06773488	Myelin	0.83	1.99E-08	6.05E-07
DDR1_cg24636809	MBP_cg06773488	Myelin	0.83	1.78E-08	5.48E-07
DDR1_cg24727290	MBP_cg06773488	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg25655106	MBP_cg06773488	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg27237814	MBP_cg06773488	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg00466425	MBP_cg07184627	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg01598675	MBP_cg07184627	Myelin	0.76	1.64E-06	3.21E-05
DDR1_cg01936707	MBP_cg07184627	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg05703744	MBP_cg07184627	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg06200824	MBP_cg07184627	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg07908039	MBP_cg07184627	Myelin	0.78	6.49E-07	1.41E-05
DDR1_cg07912416	MBP_cg07184627	Myelin	0.84	1.32E-08	4.19E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07979747	MBP_cg07184627	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg08673763	MBP_cg07184627	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg08951271	MBP_cg07184627	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg09810078	MBP_cg07184627	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg11530564	MBP_cg07184627	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg11676038	MBP_cg07184627	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg12669395	MBP_cg07184627	Myelin	0.81	8.48E-08	2.24E-06
DDR1_cg12847793	MBP_cg07184627	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg13329862	MBP_cg07184627	Myelin	0.86	1.49E-09	5.99E-08
DDR1_cg13351860	MBP_cg07184627	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg13695585	MBP_cg07184627	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg14790552	MBP_cg07184627	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg15656686	MBP_cg07184627	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg16111190	MBP_cg07184627	Myelin	0.85	5.06E-09	1.78E-07
DDR1_cg16797094	MBP_cg07184627	Myelin	0.82	7.20E-08	1.94E-06
DDR1_cg17176005	MBP_cg07184627	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg18577693	MBP_cg07184627	Myelin	0.81	1.24E-07	3.16E-06
DDR1_cg19215110	MBP_cg07184627	Myelin	0.80	1.50E-07	3.75E-06
DDR1_cg21677258	MBP_cg07184627	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg23222808	MBP_cg07184627	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg24566261	MBP_cg07184627	Myelin	0.77	8.47E-07	1.78E-05
DDR1_cg24636809	MBP_cg07184627	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg24727290	MBP_cg07184627	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg25251478	MBP_cg07184627	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg25613385	MBP_cg07184627	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg25655106	MBP_cg07184627	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg27237814	MBP_cg07184627	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg27593250	MBP_cg07184627	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg00466425	MBP_cg07611666	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg00934322	MBP_cg07611666	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg01936707	MBP_cg07611666	Myelin	0.91	1.14E-11	8.99E-10
DDR1_cg05703744	MBP_cg07611666	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg06200824	MBP_cg07611666	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg06501109	MBP_cg07611666	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg07908039	MBP_cg07611666	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg07912416	MBP_cg07611666	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg07979747	MBP_cg07611666	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg08673763	MBP_cg07611666	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg08684361	MBP_cg07611666	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg08951271	MBP_cg07611666	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg09965419	MBP_cg07611666	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg11530564	MBP_cg07611666	Myelin	0.93	1.39E-13	2.37E-11
DDR1_cg11676038	MBP_cg07611666	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg12669395	MBP_cg07611666	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg12847793	MBP_cg07611666	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg13329862	MBP_cg07611666	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg13351860	MBP_cg07611666	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg13660719	MBP_cg07611666	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg13695585	MBP_cg07611666	Myelin	0.77	1.10E-06	2.25E-05
DDR1_cg14790552	MBP_cg07611666	Myelin	0.82	4.50E-08	1.27E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg15656686	MBP_cg07611666	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg16111190	MBP_cg07611666	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg16797094	MBP_cg07611666	Myelin	0.94	4.51E-14	9.90E-12
DDR1_cg17176005	MBP_cg07611666	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg17604312	MBP_cg07611666	Myelin	0.83	2.47E-08	7.36E-07
DDR1_cg19215110	MBP_cg07611666	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg19591099	MBP_cg07611666	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg21677258	MBP_cg07611666	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg23222808	MBP_cg07611666	Myelin	0.76	2.20E-06	4.15E-05
DDR1_cg24636809	MBP_cg07611666	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg24727290	MBP_cg07611666	Myelin	0.86	1.49E-09	5.99E-08
DDR1_cg25613385	MBP_cg07611666	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg25655106	MBP_cg07611666	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg27237814	MBP_cg07611666	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg27593250	MBP_cg07611666	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg00466425	MBP_cg08093733	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg01598675	MBP_cg08093733	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg01936707	MBP_cg08093733	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg05703744	MBP_cg08093733	Myelin	0.84	1.32E-08	4.19E-07
DDR1_cg06200824	MBP_cg08093733	Myelin	0.77	1.18E-06	2.41E-05
DDR1_cg06501109	MBP_cg08093733	Myelin	0.82	4.50E-08	1.27E-06
DDR1_cg07912416	MBP_cg08093733	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg07979747	MBP_cg08093733	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg08673763	MBP_cg08093733	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg08951271	MBP_cg08093733	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg11530564	MBP_cg08093733	Myelin	0.85	4.66E-09	1.65E-07
DDR1_cg11676038	MBP_cg08093733	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg12669395	MBP_cg08093733	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg12847793	MBP_cg08093733	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg13329862	MBP_cg08093733	Myelin	0.93	2.70E-13	4.02E-11
DDR1_cg13351860	MBP_cg08093733	Myelin	0.87	1.13E-09	4.68E-08
DDR1_cg14058861	MBP_cg08093733	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg14790552	MBP_cg08093733	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg15656686	MBP_cg08093733	Myelin	0.85	5.97E-09	2.06E-07
DDR1_cg16111190	MBP_cg08093733	Myelin	0.83	2.47E-08	7.36E-07
DDR1_cg16797094	MBP_cg08093733	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg17176005	MBP_cg08093733	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg17604312	MBP_cg08093733	Myelin	0.82	4.06E-08	1.15E-06
DDR1_cg19215110	MBP_cg08093733	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg19591099	MBP_cg08093733	Myelin	0.79	3.85E-07	8.81E-06
DDR1_cg21677258	MBP_cg08093733	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg24636809	MBP_cg08093733	Myelin	0.87	1.36E-09	5.52E-08
DDR1_cg24727290	MBP_cg08093733	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg25655106	MBP_cg08093733	Myelin	0.94	1.31E-14	3.81E-12
DDR1_cg27237814	MBP_cg08093733	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg27593250	MBP_cg08093733	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg00466425	MBP_cg08176598	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg01598675	MBP_cg08176598	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg01936707	MBP_cg08176598	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg05703744	MBP_cg08176598	Myelin	0.93	6.06E-13	7.80E-11

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg06200824	MBP_cg08176598	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg06501109	MBP_cg08176598	Myelin	0.81	7.69E-08	2.05E-06
DDR1_cg07908039	MBP_cg08176598	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg07912416	MBP_cg08176598	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg07979747	MBP_cg08176598	Myelin	0.92	2.45E-12	2.47E-10
DDR1_cg08673763	MBP_cg08176598	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg08684361	MBP_cg08176598	Myelin	0.76	2.20E-06	4.15E-05
DDR1_cg08951271	MBP_cg08176598	Myelin	0.94	2.33E-14	5.92E-12
DDR1_cg09965419	MBP_cg08176598	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg11530564	MBP_cg08176598	Myelin	0.93	3.24E-13	4.65E-11
DDR1_cg11676038	MBP_cg08176598	Myelin	0.94	9.33E-14	1.74E-11
DDR1_cg12669395	MBP_cg08176598	Myelin	0.95	3.33E-15	1.40E-12
DDR1_cg13329862	MBP_cg08176598	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg13351860	MBP_cg08176598	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg14058861	MBP_cg08176598	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg14790552	MBP_cg08176598	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg15656686	MBP_cg08176598	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg15720085	MBP_cg08176598	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg16111190	MBP_cg08176598	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg16797094	MBP_cg08176598	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg17176005	MBP_cg08176598	Myelin	0.84	1.53E-08	4.79E-07
DDR1_cg17604312	MBP_cg08176598	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg18577693	MBP_cg08176598	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg19215110	MBP_cg08176598	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg19591099	MBP_cg08176598	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg21677258	MBP_cg08176598	Myelin	0.94	1.47E-14	4.13E-12
DDR1_cg24636809	MBP_cg08176598	Myelin	0.93	3.89E-13	5.41E-11
DDR1_cg24727290	MBP_cg08176598	Myelin	0.87	1.18E-09	4.87E-08
DDR1_cg25613385	MBP_cg08176598	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg25655106	MBP_cg08176598	Myelin	0.94	2.93E-14	7.05E-12
DDR1_cg27237814	MBP_cg08176598	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg27593250	MBP_cg08176598	Myelin	0.77	1.13E-06	2.30E-05
DDR1_cg00466425	MBP_cg08936202	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg01936707	MBP_cg08936202	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg05703744	MBP_cg08936202	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg06200824	MBP_cg08936202	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg06501109	MBP_cg08936202	Myelin	0.83	2.47E-08	7.36E-07
DDR1_cg07908039	MBP_cg08936202	Myelin	0.78	7.04E-07	1.51E-05
DDR1_cg07912416	MBP_cg08936202	Myelin	0.84	9.28E-09	3.06E-07
DDR1_cg07979747	MBP_cg08936202	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg08673763	MBP_cg08936202	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg08951271	MBP_cg08936202	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg09965419	MBP_cg08936202	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg11530564	MBP_cg08936202	Myelin	0.95	3.11E-15	1.36E-12
DDR1_cg11676038	MBP_cg08936202	Myelin	0.94	2.93E-14	7.05E-12
DDR1_cg12669395	MBP_cg08936202	Myelin	0.94	1.87E-14	5.00E-12
DDR1_cg12847793	MBP_cg08936202	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg13329862	MBP_cg08936202	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg13351860	MBP_cg08936202	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg13695585	MBP_cg08936202	Myelin	0.78	6.49E-07	1.41E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg14790552	MBP_cg08936202	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg15656686	MBP_cg08936202	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg16111190	MBP_cg08936202	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg16797094	MBP_cg08936202	Myelin	0.92	1.94E-12	2.03E-10
DDR1_cg17176005	MBP_cg08936202	Myelin	0.80	1.97E-07	4.80E-06
DDR1_cg17604312	MBP_cg08936202	Myelin	0.85	4.66E-09	1.65E-07
DDR1_cg19215110	MBP_cg08936202	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg19591099	MBP_cg08936202	Myelin	0.82	6.31E-08	1.72E-06
DDR1_cg21677258	MBP_cg08936202	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg24566261	MBP_cg08936202	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg24636809	MBP_cg08936202	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg24727290	MBP_cg08936202	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg25613385	MBP_cg08936202	Myelin	0.77	1.10E-06	2.25E-05
DDR1_cg25655106	MBP_cg08936202	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg27237814	MBP_cg08936202	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg27593250	MBP_cg08936202	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg00466425	MBP_cg11195910	Myelin	0.86	1.63E-09	6.49E-08
DDR1_cg00934322	MBP_cg11195910	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg01936707	MBP_cg11195910	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg05703744	MBP_cg11195910	Myelin	0.93	1.39E-13	2.37E-11
DDR1_cg06501109	MBP_cg11195910	Myelin	0.81	8.76E-08	2.31E-06
DDR1_cg07908039	MBP_cg11195910	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg07912416	MBP_cg11195910	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg07979747	MBP_cg11195910	Myelin	0.81	8.76E-08	2.31E-06
DDR1_cg08673763	MBP_cg11195910	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg08951271	MBP_cg11195910	Myelin	0.89	6.44E-11	3.93E-09
DDR1_cg09965419	MBP_cg11195910	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg11530564	MBP_cg11195910	Myelin	0.95	1.15E-14	3.44E-12
DDR1_cg11676038	MBP_cg11195910	Myelin	0.90	3.95E-11	2.57E-09
DDR1_cg12669395	MBP_cg11195910	Myelin	0.92	1.79E-12	1.90E-10
DDR1_cg13329862	MBP_cg11195910	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg13351860	MBP_cg11195910	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg13695585	MBP_cg11195910	Myelin	0.76	1.64E-06	3.21E-05
DDR1_cg14790552	MBP_cg11195910	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg15656686	MBP_cg11195910	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg16111190	MBP_cg11195910	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg16797094	MBP_cg11195910	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg17176005	MBP_cg11195910	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg17604312	MBP_cg11195910	Myelin	0.82	6.74E-08	1.82E-06
DDR1_cg19215110	MBP_cg11195910	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg19591099	MBP_cg11195910	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg21677258	MBP_cg11195910	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg24636809	MBP_cg11195910	Myelin	0.86	1.63E-09	6.49E-08
DDR1_cg24727290	MBP_cg11195910	Myelin	0.82	5.16E-08	1.43E-06
DDR1_cg25655106	MBP_cg11195910	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg27237814	MBP_cg11195910	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg27593250	MBP_cg11195910	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg07908039	MBP_cg12979350	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg08673763	MBP_cg12979350	Myelin	0.80	2.57E-07	6.12E-06
DDR1_cg13329862	MBP_cg12979350	Myelin	0.77	9.16E-07	1.91E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg16111190	MBP_cg12979350	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg17604312	MBP_cg12979350	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg19215110	MBP_cg12979350	Myelin	0.83	2.66E-08	7.86E-07
DDR1_cg24727290	MBP_cg12979350	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg00466425	MBP_cg13141061	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg01936707	MBP_cg13141061	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg05703744	MBP_cg13141061	Myelin	0.90	2.88E-11	1.96E-09
DDR1_cg06200824	MBP_cg13141061	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg06501109	MBP_cg13141061	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg07912416	MBP_cg13141061	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg07979747	MBP_cg13141061	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg08673763	MBP_cg13141061	Myelin	0.88	2.37E-10	1.20E-08
DDR1_cg08684361	MBP_cg13141061	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg08951271	MBP_cg13141061	Myelin	0.94	1.64E-14	4.50E-12
DDR1_cg09965419	MBP_cg13141061	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg11530564	MBP_cg13141061	Myelin	0.95	1.15E-14	3.44E-12
DDR1_cg11676038	MBP_cg13141061	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg12669395	MBP_cg13141061	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg12847793	MBP_cg13141061	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg13329862	MBP_cg13141061	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg13351860	MBP_cg13141061	Myelin	0.95	3.77E-15	1.53E-12
DDR1_cg13695585	MBP_cg13141061	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg14790552	MBP_cg13141061	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg15656686	MBP_cg13141061	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg15720085	MBP_cg13141061	Myelin	0.75	2.59E-06	4.80E-05
DDR1_cg16111190	MBP_cg13141061	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg16797094	MBP_cg13141061	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg17176005	MBP_cg13141061	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg17604312	MBP_cg13141061	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg18577693	MBP_cg13141061	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg19215110	MBP_cg13141061	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg19591099	MBP_cg13141061	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg21677258	MBP_cg13141061	Myelin	0.93	1.53E-13	2.55E-11
DDR1_cg24636809	MBP_cg13141061	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg24727290	MBP_cg13141061	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg25613385	MBP_cg13141061	Myelin	0.80	1.41E-07	3.54E-06
DDR1_cg25655106	MBP_cg13141061	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg27237814	MBP_cg13141061	Myelin	0.89	6.44E-11	3.93E-09
DDR1_cg27593250	MBP_cg13141061	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg00466425	MBP_cg13375905	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg01936707	MBP_cg13375905	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg05703744	MBP_cg13375905	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg07979747	MBP_cg13375905	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg08951271	MBP_cg13375905	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg11530564	MBP_cg13375905	Myelin	0.80	1.45E-07	3.64E-06
DDR1_cg11676038	MBP_cg13375905	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg12669395	MBP_cg13375905	Myelin	0.82	5.71E-08	1.57E-06
DDR1_cg13329862	MBP_cg13375905	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg13351860	MBP_cg13375905	Myelin	0.82	6.31E-08	1.72E-06
DDR1_cg15656686	MBP_cg13375905	Myelin	0.79	4.19E-07	9.49E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg16111190	MBP_cg13375905	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg16797094	MBP_cg13375905	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg21677258	MBP_cg13375905	Myelin	0.76	1.64E-06	3.21E-05
DDR1_cg24636809	MBP_cg13375905	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg25655106	MBP_cg13375905	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg27237814	MBP_cg13375905	Myelin	0.75	2.91E-06	5.32E-05
DDR1_cg00466425	MBP_cg13442966	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg00934322	MBP_cg13442966	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg01936707	MBP_cg13442966	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg05703744	MBP_cg13442966	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg06200824	MBP_cg13442966	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg06501109	MBP_cg13442966	Myelin	0.85	6.22E-09	2.14E-07
DDR1_cg07912416	MBP_cg13442966	Myelin	0.86	1.96E-09	7.64E-08
DDR1_cg07979747	MBP_cg13442966	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg08673763	MBP_cg13442966	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg08684361	MBP_cg13442966	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg08951271	MBP_cg13442966	Myelin	0.92	2.27E-12	2.31E-10
DDR1_cg09822812	MBP_cg13442966	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg09965419	MBP_cg13442966	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg11530564	MBP_cg13442966	Myelin	0.93	1.26E-13	2.20E-11
DDR1_cg11676038	MBP_cg13442966	Myelin	0.93	3.55E-13	5.01E-11
DDR1_cg12669395	MBP_cg13442966	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg12847793	MBP_cg13442966	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg13329862	MBP_cg13442966	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg13351860	MBP_cg13442966	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg14058861	MBP_cg13442966	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg14790552	MBP_cg13442966	Myelin	0.84	1.04E-08	3.40E-07
DDR1_cg15656686	MBP_cg13442966	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg16111190	MBP_cg13442966	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg16797094	MBP_cg13442966	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg17176005	MBP_cg13442966	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg17604312	MBP_cg13442966	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg19215110	MBP_cg13442966	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg19591099	MBP_cg13442966	Myelin	0.82	7.20E-08	1.94E-06
DDR1_cg21677258	MBP_cg13442966	Myelin	0.90	3.95E-11	2.57E-09
DDR1_cg24636809	MBP_cg13442966	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg24727290	MBP_cg13442966	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg25613385	MBP_cg13442966	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg25655106	MBP_cg13442966	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg27237814	MBP_cg13442966	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg27593250	MBP_cg13442966	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg00466425	MBP_cg13515395	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg01598675	MBP_cg13515395	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg01936707	MBP_cg13515395	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg05703744	MBP_cg13515395	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg06501109	MBP_cg13515395	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg07912416	MBP_cg13515395	Myelin	0.83	3.41E-08	9.84E-07
DDR1_cg07979747	MBP_cg13515395	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg08673763	MBP_cg13515395	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg08684361	MBP_cg13515395	Myelin	0.75	2.98E-06	5.43E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg08951271	MBP_cg13515395	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg11530564	MBP_cg13515395	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg11676038	MBP_cg13515395	Myelin	0.84	1.53E-08	4.79E-07
DDR1_cg12669395	MBP_cg13515395	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg13329862	MBP_cg13515395	Myelin	0.86	3.46E-09	1.27E-07
DDR1_cg13351860	MBP_cg13515395	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg13695585	MBP_cg13515395	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg14790552	MBP_cg13515395	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg15656686	MBP_cg13515395	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg16111190	MBP_cg13515395	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg16797094	MBP_cg13515395	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg17176005	MBP_cg13515395	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg21677258	MBP_cg13515395	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg24636809	MBP_cg13515395	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg24727290	MBP_cg13515395	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg25613385	MBP_cg13515395	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg25655106	MBP_cg13515395	Myelin	0.82	5.16E-08	1.43E-06
DDR1_cg27237814	MBP_cg13515395	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg00466425	MBP_cg13807269	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg00934322	MBP_cg13807269	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg01598675	MBP_cg13807269	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg01936707	MBP_cg13807269	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg05703744	MBP_cg13807269	Myelin	0.95	5.77E-15	2.11E-12
DDR1_cg06200824	MBP_cg13807269	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg06501109	MBP_cg13807269	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg07912416	MBP_cg13807269	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg07979747	MBP_cg13807269	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg08673763	MBP_cg13807269	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg08951271	MBP_cg13807269	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg09965419	MBP_cg13807269	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg11530564	MBP_cg13807269	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg11676038	MBP_cg13807269	Myelin	0.95	1.11E-15	6.40E-13
DDR1_cg12669395	MBP_cg13807269	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg12847793	MBP_cg13807269	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg13329862	MBP_cg13807269	Myelin	0.94	4.51E-14	9.90E-12
DDR1_cg13351860	MBP_cg13807269	Myelin	0.92	1.65E-12	1.78E-10
DDR1_cg14058861	MBP_cg13807269	Myelin	0.78	6.49E-07	1.41E-05
DDR1_cg14790552	MBP_cg13807269	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg15656686	MBP_cg13807269	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg16111190	MBP_cg13807269	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg16797094	MBP_cg13807269	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg17176005	MBP_cg13807269	Myelin	0.83	2.96E-08	8.66E-07
DDR1_cg17604312	MBP_cg13807269	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg19215110	MBP_cg13807269	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg19591099	MBP_cg13807269	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg21677258	MBP_cg13807269	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg24566261	MBP_cg13807269	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg24636809	MBP_cg13807269	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg24727290	MBP_cg13807269	Myelin	0.85	4.66E-09	1.65E-07
DDR1_cg25613385	MBP_cg13807269	Myelin	0.76	2.14E-06	4.06E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg25655106	MBP_cg13807269	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg27237814	MBP_cg13807269	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg27593250	MBP_cg13807269	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg00466425	MBP_cg14078587	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg00934322	MBP_cg14078587	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg01936707	MBP_cg14078587	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg05703744	MBP_cg14078587	Myelin	0.94	2.93E-14	7.05E-12
DDR1_cg06200824	MBP_cg14078587	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg06501109	MBP_cg14078587	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg07912416	MBP_cg14078587	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg07979747	MBP_cg14078587	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg08673763	MBP_cg14078587	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg08951271	MBP_cg14078587	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg09965419	MBP_cg14078587	Myelin	0.78	6.85E-07	1.48E-05
DDR1_cg11530564	MBP_cg14078587	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg11676038	MBP_cg14078587	Myelin	0.93	1.14E-13	2.04E-11
DDR1_cg12669395	MBP_cg14078587	Myelin	0.94	2.09E-14	5.43E-12
DDR1_cg12847793	MBP_cg14078587	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg13329862	MBP_cg14078587	Myelin	0.93	3.89E-13	5.41E-11
DDR1_cg13351860	MBP_cg14078587	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg14058861	MBP_cg14078587	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg14790552	MBP_cg14078587	Myelin	0.85	7.61E-09	2.56E-07
DDR1_cg15656686	MBP_cg14078587	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg16111190	MBP_cg14078587	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg16797094	MBP_cg14078587	Myelin	0.89	7.25E-11	4.36E-09
DDR1_cg17176005	MBP_cg14078587	Myelin	0.79	4.55E-07	1.02E-05
DDR1_cg17604312	MBP_cg14078587	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg19215110	MBP_cg14078587	Myelin	0.80	2.35E-07	5.65E-06
DDR1_cg19591099	MBP_cg14078587	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg21677258	MBP_cg14078587	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg24636809	MBP_cg14078587	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg24727290	MBP_cg14078587	Myelin	0.85	7.92E-09	2.66E-07
DDR1_cg25655106	MBP_cg14078587	Myelin	0.90	3.49E-11	2.31E-09
DDR1_cg27237814	MBP_cg14078587	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg27593250	MBP_cg14078587	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg00466425	MBP_cg14298244	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg01936707	MBP_cg14298244	Myelin	0.83	1.99E-08	6.05E-07
DDR1_cg05703744	MBP_cg14298244	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg06501109	MBP_cg14298244	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg07912416	MBP_cg14298244	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg07979747	MBP_cg14298244	Myelin	0.81	8.21E-08	2.18E-06
DDR1_cg08673763	MBP_cg14298244	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg08951271	MBP_cg14298244	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg09822812	MBP_cg14298244	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg09965419	MBP_cg14298244	Myelin	0.78	6.49E-07	1.41E-05
DDR1_cg11530564	MBP_cg14298244	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg11676038	MBP_cg14298244	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg12669395	MBP_cg14298244	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg12847793	MBP_cg14298244	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg13329862	MBP_cg14298244	Myelin	0.93	1.26E-13	2.20E-11

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13351860	MBP_cg14298244	Myelin	0.94	9.33E-14	1.74E-11
DDR1_cg13695585	MBP_cg14298244	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg14058861	MBP_cg14298244	Myelin	0.78	7.42E-07	1.59E-05
DDR1_cg14790552	MBP_cg14298244	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg15656686	MBP_cg14298244	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg16111190	MBP_cg14298244	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg16797094	MBP_cg14298244	Myelin	0.91	6.49E-12	5.56E-10
DDR1_cg17176005	MBP_cg14298244	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg17604312	MBP_cg14298244	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg19215110	MBP_cg14298244	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg19591099	MBP_cg14298244	Myelin	0.78	7.42E-07	1.59E-05
DDR1_cg21677258	MBP_cg14298244	Myelin	0.89	1.22E-10	6.76E-09
DDR1_cg24636809	MBP_cg14298244	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg24727290	MBP_cg14298244	Myelin	0.87	6.31E-10	2.82E-08
DDR1_cg25613385	MBP_cg14298244	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg25655106	MBP_cg14298244	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg27237814	MBP_cg14298244	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg27593250	MBP_cg14298244	Myelin	0.76	1.72E-06	3.35E-05
DDR1_cg01598675	MBP_cg14918582	Myelin	0.80	1.69E-07	4.19E-06
DDR1_cg07908039	MBP_cg14918582	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg07979747	MBP_cg14918582	Myelin	0.77	9.65E-07	2.00E-05
DDR1_cg08673763	MBP_cg14918582	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg08951271	MBP_cg14918582	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg09822812	MBP_cg14918582	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg11530564	MBP_cg14918582	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg11676038	MBP_cg14918582	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg12669395	MBP_cg14918582	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg13329862	MBP_cg14918582	Myelin	0.77	1.18E-06	2.41E-05
DDR1_cg13351860	MBP_cg14918582	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg13695585	MBP_cg14918582	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg14790552	MBP_cg14918582	Myelin	0.80	1.41E-07	3.54E-06
DDR1_cg17604312	MBP_cg14918582	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg19215110	MBP_cg14918582	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg21677258	MBP_cg14918582	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg25655106	MBP_cg14918582	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg27237814	MBP_cg14918582	Myelin	0.77	9.16E-07	1.91E-05
DDR1_cg00466425	MBP_cg14946295	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg00934322	MBP_cg14946295	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg01936707	MBP_cg14946295	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg05703744	MBP_cg14946295	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg06200824	MBP_cg14946295	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg06501109	MBP_cg14946295	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg07908039	MBP_cg14946295	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg07912416	MBP_cg14946295	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg07979747	MBP_cg14946295	Myelin	0.86	2.56E-09	9.63E-08
DDR1_cg08673763	MBP_cg14946295	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg08951271	MBP_cg14946295	Myelin	0.92	1.79E-12	1.90E-10
DDR1_cg09965419	MBP_cg14946295	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg11530564	MBP_cg14946295	Myelin	0.95	6.22E-15	2.20E-12
DDR1_cg11676038	MBP_cg14946295	Myelin	0.95	6.22E-15	2.20E-12

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg12669395	MBP_cg14946295	Myelin	0.93	1.39E-13	2.37E-11
DDR1_cg13329862	MBP_cg14946295	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg13351860	MBP_cg14946295	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg13695585	MBP_cg14946295	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg14058861	MBP_cg14946295	Myelin	0.80	1.69E-07	4.19E-06
DDR1_cg14790552	MBP_cg14946295	Myelin	0.90	3.95E-11	2.57E-09
DDR1_cg15656686	MBP_cg14946295	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg16111190	MBP_cg14946295	Myelin	0.89	1.37E-10	7.45E-09
DDR1_cg16797094	MBP_cg14946295	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg17176005	MBP_cg14946295	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg17604312	MBP_cg14946295	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg18577693	MBP_cg14946295	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg19215110	MBP_cg14946295	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg19591099	MBP_cg14946295	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg21677258	MBP_cg14946295	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg24566261	MBP_cg14946295	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg24636809	MBP_cg14946295	Myelin	0.90	3.95E-11	2.57E-09
DDR1_cg24727290	MBP_cg14946295	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg25613385	MBP_cg14946295	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg25655106	MBP_cg14946295	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg27237814	MBP_cg14946295	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg27593250	MBP_cg14946295	Myelin	0.82	4.35E-08	1.23E-06
DDR1_cg00466425	MBP_cg15224291	Myelin	0.90	2.88E-11	1.96E-09
DDR1_cg01598675	MBP_cg15224291	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg01936707	MBP_cg15224291	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg05703744	MBP_cg15224291	Myelin	0.92	1.94E-12	2.03E-10
DDR1_cg06200824	MBP_cg15224291	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg06501109	MBP_cg15224291	Myelin	0.80	1.45E-07	3.64E-06
DDR1_cg07908039	MBP_cg15224291	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg07912416	MBP_cg15224291	Myelin	0.86	3.46E-09	1.27E-07
DDR1_cg07979747	MBP_cg15224291	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg08673763	MBP_cg15224291	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg08951271	MBP_cg15224291	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg11530564	MBP_cg15224291	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg11676038	MBP_cg15224291	Myelin	0.95	3.33E-15	1.40E-12
DDR1_cg12669395	MBP_cg15224291	Myelin	0.93	1.85E-13	2.96E-11
DDR1_cg12847793	MBP_cg15224291	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg13329862	MBP_cg15224291	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg13351860	MBP_cg15224291	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg14058861	MBP_cg15224291	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg14790552	MBP_cg15224291	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg15656686	MBP_cg15224291	Myelin	0.83	2.47E-08	7.36E-07
DDR1_cg16111190	MBP_cg15224291	Myelin	0.87	1.13E-09	4.68E-08
DDR1_cg16797094	MBP_cg15224291	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg17176005	MBP_cg15224291	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg17604312	MBP_cg15224291	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg19215110	MBP_cg15224291	Myelin	0.83	2.30E-08	6.90E-07
DDR1_cg19591099	MBP_cg15224291	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg21677258	MBP_cg15224291	Myelin	0.89	7.25E-11	4.36E-09
DDR1_cg24636809	MBP_cg15224291	Myelin	0.90	3.71E-11	2.44E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg24727290	MBP_cg15224291	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg25655106	MBP_cg15224291	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg27237814	MBP_cg15224291	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg27593250	MBP_cg15224291	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg00466425	MBP_cg15352683	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg01936707	MBP_cg15352683	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg05703744	MBP_cg15352683	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg06200824	MBP_cg15352683	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg07908039	MBP_cg15352683	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg07912416	MBP_cg15352683	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg07979747	MBP_cg15352683	Myelin	0.83	2.66E-08	7.86E-07
DDR1_cg08673763	MBP_cg15352683	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg08951271	MBP_cg15352683	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg11530564	MBP_cg15352683	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg11676038	MBP_cg15352683	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg12669395	MBP_cg15352683	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg12847793	MBP_cg15352683	Myelin	0.80	1.50E-07	3.75E-06
DDR1_cg13329862	MBP_cg15352683	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg13351860	MBP_cg15352683	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg14790552	MBP_cg15352683	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg15656686	MBP_cg15352683	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg16111190	MBP_cg15352683	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg16797094	MBP_cg15352683	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg17176005	MBP_cg15352683	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg17604312	MBP_cg15352683	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg19215110	MBP_cg15352683	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg19591099	MBP_cg15352683	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg21677258	MBP_cg15352683	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg24636809	MBP_cg15352683	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg24727290	MBP_cg15352683	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg25655106	MBP_cg15352683	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg27237814	MBP_cg15352683	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg27593250	MBP_cg15352683	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg00466425	MBP_cg15391531	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg01936707	MBP_cg15391531	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg05703744	MBP_cg15391531	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg06200824	MBP_cg15391531	Myelin	0.81	9.96E-08	2.59E-06
DDR1_cg06501109	MBP_cg15391531	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg07908039	MBP_cg15391531	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg07912416	MBP_cg15391531	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg07979747	MBP_cg15391531	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg08673763	MBP_cg15391531	Myelin	0.87	9.31E-10	3.96E-08
DDR1_cg08951271	MBP_cg15391531	Myelin	0.94	1.64E-14	4.50E-12
DDR1_cg09822812	MBP_cg15391531	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg09965419	MBP_cg15391531	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg11530564	MBP_cg15391531	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg11676038	MBP_cg15391531	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg12669395	MBP_cg15391531	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg12847793	MBP_cg15391531	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg13329862	MBP_cg15391531	Myelin	0.92	7.84E-13	9.64E-11

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13351860	MBP_cg15391531	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg13695585	MBP_cg15391531	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg14058861	MBP_cg15391531	Myelin	0.80	1.69E-07	4.19E-06
DDR1_cg14790552	MBP_cg15391531	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg15656686	MBP_cg15391531	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg15720085	MBP_cg15391531	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg16111190	MBP_cg15391531	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg16797094	MBP_cg15391531	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg17176005	MBP_cg15391531	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg17604312	MBP_cg15391531	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg18577693	MBP_cg15391531	Myelin	0.81	1.03E-07	2.67E-06
DDR1_cg19215110	MBP_cg15391531	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg19591099	MBP_cg15391531	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg21677258	MBP_cg15391531	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg23222808	MBP_cg15391531	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg24566261	MBP_cg15391531	Myelin	0.77	1.18E-06	2.41E-05
DDR1_cg24636809	MBP_cg15391531	Myelin	0.90	3.49E-11	2.31E-09
DDR1_cg24727290	MBP_cg15391531	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg25613385	MBP_cg15391531	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg25655106	MBP_cg15391531	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg27237814	MBP_cg15391531	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg27593250	MBP_cg15391531	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg00466425	MBP_cg15495463	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg00934322	MBP_cg15495463	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg01598675	MBP_cg15495463	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg01936707	MBP_cg15495463	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg05703744	MBP_cg15495463	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg06200824	MBP_cg15495463	Myelin	0.79	3.63E-07	8.37E-06
DDR1_cg06501109	MBP_cg15495463	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg07908039	MBP_cg15495463	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg07912416	MBP_cg15495463	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg07979747	MBP_cg15495463	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg08673763	MBP_cg15495463	Myelin	0.88	2.13E-10	1.10E-08
DDR1_cg08951271	MBP_cg15495463	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg09965419	MBP_cg15495463	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg11530564	MBP_cg15495463	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg11676038	MBP_cg15495463	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg12669395	MBP_cg15495463	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg12847793	MBP_cg15495463	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg13329862	MBP_cg15495463	Myelin	0.94	5.55E-14	1.16E-11
DDR1_cg13351860	MBP_cg15495463	Myelin	0.93	2.46E-13	3.73E-11
DDR1_cg13695585	MBP_cg15495463	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg14058861	MBP_cg15495463	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg14790552	MBP_cg15495463	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg15656686	MBP_cg15495463	Myelin	0.89	1.22E-10	6.76E-09
DDR1_cg16111190	MBP_cg15495463	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg16797094	MBP_cg15495463	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg17176005	MBP_cg15495463	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg17604312	MBP_cg15495463	Myelin	0.78	6.85E-07	1.48E-05
DDR1_cg19215110	MBP_cg15495463	Myelin	0.77	1.15E-06	2.36E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg19591099	MBP_cg15495463	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg21677258	MBP_cg15495463	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg24566261	MBP_cg15495463	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg24636809	MBP_cg15495463	Myelin	0.87	7.68E-10	3.34E-08
DDR1_cg24727290	MBP_cg15495463	Myelin	0.85	5.97E-09	2.06E-07
DDR1_cg25655106	MBP_cg15495463	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg27237814	MBP_cg15495463	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg27593250	MBP_cg15495463	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg07979747	MBP_cg15783427	Myelin	0.78	7.04E-07	1.51E-05
DDR1_cg08951271	MBP_cg15783427	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg14790552	MBP_cg15783427	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg17176005	MBP_cg15783427	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg25655106	MBP_cg15783427	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg27237814	MBP_cg15783427	Myelin	0.77	9.90E-07	2.05E-05
DDR1_cg24303888	MBP_cg15935527	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg00466425	MBP_cg16305018	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg00934322	MBP_cg16305018	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg05703744	MBP_cg16305018	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg07912416	MBP_cg16305018	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg07979747	MBP_cg16305018	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg08673763	MBP_cg16305018	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg08951271	MBP_cg16305018	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg09822812	MBP_cg16305018	Myelin	0.82	7.20E-08	1.94E-06
DDR1_cg09965419	MBP_cg16305018	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg11530564	MBP_cg16305018	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg11676038	MBP_cg16305018	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg12669395	MBP_cg16305018	Myelin	0.82	6.74E-08	1.82E-06
DDR1_cg12847793	MBP_cg16305018	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg13329862	MBP_cg16305018	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg13351860	MBP_cg16305018	Myelin	0.91	4.51E-12	4.08E-10
DDR1_cg13695585	MBP_cg16305018	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg14790552	MBP_cg16305018	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg15656686	MBP_cg16305018	Myelin	0.84	1.04E-08	3.40E-07
DDR1_cg16111190	MBP_cg16305018	Myelin	0.78	6.49E-07	1.41E-05
DDR1_cg16797094	MBP_cg16305018	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg17176005	MBP_cg16305018	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg19215110	MBP_cg16305018	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg20955507	MBP_cg16305018	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg21677258	MBP_cg16305018	Myelin	0.82	4.20E-08	1.19E-06
DDR1_cg24636809	MBP_cg16305018	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg24727290	MBP_cg16305018	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg25251478	MBP_cg16305018	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg25607383	MBP_cg16305018	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg25655106	MBP_cg16305018	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg27237814	MBP_cg16305018	Myelin	0.86	2.56E-09	9.63E-08
DDR1_cg27593250	MBP_cg16305018	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg00466425	MBP_cg16575175	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg01936707	MBP_cg16575175	Myelin	0.93	1.26E-13	2.20E-11
DDR1_cg05703744	MBP_cg16575175	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg06200824	MBP_cg16575175	Myelin	0.79	3.74E-07	8.58E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg06501109	MBP_cg16575175	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg07908039	MBP_cg16575175	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg07912416	MBP_cg16575175	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg07979747	MBP_cg16575175	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg08673763	MBP_cg16575175	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg08684361	MBP_cg16575175	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg08951271	MBP_cg16575175	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg09965419	MBP_cg16575175	Myelin	0.75	2.91E-06	5.32E-05
DDR1_cg11530564	MBP_cg16575175	Myelin	0.94	5.02E-14	1.08E-11
DDR1_cg11676038	MBP_cg16575175	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg12669395	MBP_cg16575175	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg13329862	MBP_cg16575175	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg13351860	MBP_cg16575175	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg14790552	MBP_cg16575175	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg15656686	MBP_cg16575175	Myelin	0.87	1.36E-09	5.52E-08
DDR1_cg16111190	MBP_cg16575175	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg16797094	MBP_cg16575175	Myelin	0.92	1.52E-12	1.66E-10
DDR1_cg17176005	MBP_cg16575175	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg17604312	MBP_cg16575175	Myelin	0.81	8.76E-08	2.31E-06
DDR1_cg19215110	MBP_cg16575175	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg19591099	MBP_cg16575175	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg21677258	MBP_cg16575175	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg24636809	MBP_cg16575175	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg24727290	MBP_cg16575175	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg25613385	MBP_cg16575175	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg25655106	MBP_cg16575175	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg27237814	MBP_cg16575175	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg27593250	MBP_cg16575175	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg00466425	MBP_cg16762684	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg01936707	MBP_cg16762684	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg06200824	MBP_cg16762684	Myelin	0.76	2.20E-06	4.15E-05
DDR1_cg07912416	MBP_cg16762684	Myelin	0.80	2.22E-07	5.35E-06
DDR1_cg12847793	MBP_cg16762684	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg13329862	MBP_cg16762684	Myelin	0.83	2.86E-08	8.38E-07
DDR1_cg13351860	MBP_cg16762684	Myelin	0.81	1.03E-07	2.67E-06
DDR1_cg16111190	MBP_cg16762684	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg16797094	MBP_cg16762684	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg23222808	MBP_cg16762684	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg24566261	MBP_cg16762684	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg27237814	MBP_cg16762684	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg00466425	MBP_cg17061340	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg00934322	MBP_cg17061340	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg01936707	MBP_cg17061340	Myelin	0.83	1.99E-08	6.05E-07
DDR1_cg05703744	MBP_cg17061340	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg06200824	MBP_cg17061340	Myelin	0.77	1.10E-06	2.25E-05
DDR1_cg06501109	MBP_cg17061340	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg07908039	MBP_cg17061340	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg07912416	MBP_cg17061340	Myelin	0.83	2.66E-08	7.86E-07
DDR1_cg07979747	MBP_cg17061340	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg08673763	MBP_cg17061340	Myelin	0.89	1.15E-10	6.43E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg08951271	MBP_cg17061340	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg09822812	MBP_cg17061340	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg09965419	MBP_cg17061340	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg11530564	MBP_cg17061340	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg11676038	MBP_cg17061340	Myelin	0.85	4.47E-09	1.59E-07
DDR1_cg12669395	MBP_cg17061340	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg13329862	MBP_cg17061340	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg13351860	MBP_cg17061340	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg13695585	MBP_cg17061340	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg14058861	MBP_cg17061340	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg14790552	MBP_cg17061340	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg15656686	MBP_cg17061340	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg15720085	MBP_cg17061340	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg16111190	MBP_cg17061340	Myelin	0.85	7.61E-09	2.56E-07
DDR1_cg16797094	MBP_cg17061340	Myelin	0.84	1.32E-08	4.19E-07
DDR1_cg17176005	MBP_cg17061340	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg17604312	MBP_cg17061340	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg18577693	MBP_cg17061340	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg19591099	MBP_cg17061340	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg21677258	MBP_cg17061340	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg24566261	MBP_cg17061340	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg24636809	MBP_cg17061340	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg24727290	MBP_cg17061340	Myelin	0.85	7.92E-09	2.66E-07
DDR1_cg25655106	MBP_cg17061340	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg27237814	MBP_cg17061340	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg27593250	MBP_cg17061340	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg24517175	MBP_cg17212129	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg00466425	MBP_cg18892054	Myelin	0.90	3.49E-11	2.31E-09
DDR1_cg01598675	MBP_cg18892054	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg01936707	MBP_cg18892054	Myelin	0.88	2.37E-10	1.20E-08
DDR1_cg05703744	MBP_cg18892054	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg06200824	MBP_cg18892054	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg06501109	MBP_cg18892054	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg07908039	MBP_cg18892054	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg07912416	MBP_cg18892054	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg07979747	MBP_cg18892054	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg08673763	MBP_cg18892054	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg08684361	MBP_cg18892054	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg08951271	MBP_cg18892054	Myelin	0.94	4.51E-14	9.90E-12
DDR1_cg09822812	MBP_cg18892054	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg09965419	MBP_cg18892054	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg11530564	MBP_cg18892054	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg11676038	MBP_cg18892054	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg12669395	MBP_cg18892054	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg12847793	MBP_cg18892054	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg13329862	MBP_cg18892054	Myelin	0.94	6.84E-14	1.37E-11
DDR1_cg13351860	MBP_cg18892054	Myelin	0.95	1.15E-14	3.44E-12
DDR1_cg13695585	MBP_cg18892054	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg14058861	MBP_cg18892054	Myelin	0.78	5.67E-07	1.25E-05
DDR1_cg14790552	MBP_cg18892054	Myelin	0.86	1.87E-09	7.34E-08

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg15656686	MBP_cg18892054	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg15720085	MBP_cg18892054	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg16111190	MBP_cg18892054	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg16797094	MBP_cg18892054	Myelin	0.92	1.79E-12	1.90E-10
DDR1_cg17176005	MBP_cg18892054	Myelin	0.85	5.50E-09	1.92E-07
DDR1_cg17604312	MBP_cg18892054	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg18577693	MBP_cg18892054	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg19215110	MBP_cg18892054	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg19591099	MBP_cg18892054	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg21677258	MBP_cg18892054	Myelin	0.94	8.42E-14	1.60E-11
DDR1_cg23222808	MBP_cg18892054	Myelin	0.77	1.15E-06	2.36E-05
DDR1_cg24566261	MBP_cg18892054	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg24636809	MBP_cg18892054	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg24727290	MBP_cg18892054	Myelin	0.89	1.22E-10	6.76E-09
DDR1_cg25613385	MBP_cg18892054	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg25655106	MBP_cg18892054	Myelin	0.92	1.52E-12	1.66E-10
DDR1_cg27237814	MBP_cg18892054	Myelin	0.93	1.39E-13	2.37E-11
DDR1_cg27593250	MBP_cg18892054	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg00466425	MBP_cg19178876	Myelin	0.84	1.53E-08	4.79E-07
DDR1_cg01936707	MBP_cg19178876	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg05703744	MBP_cg19178876	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg06501109	MBP_cg19178876	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg07908039	MBP_cg19178876	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg07912416	MBP_cg19178876	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg07979747	MBP_cg19178876	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg08673763	MBP_cg19178876	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg08951271	MBP_cg19178876	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg09965419	MBP_cg19178876	Myelin	0.81	1.03E-07	2.67E-06
DDR1_cg11530564	MBP_cg19178876	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg11676038	MBP_cg19178876	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg12669395	MBP_cg19178876	Myelin	0.86	1.87E-09	7.34E-08
DDR1_cg12847793	MBP_cg19178876	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg13329862	MBP_cg19178876	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg13351860	MBP_cg19178876	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg13695585	MBP_cg19178876	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg14790552	MBP_cg19178876	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg15656686	MBP_cg19178876	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg16111190	MBP_cg19178876	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg16797094	MBP_cg19178876	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg17176005	MBP_cg19178876	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg17604312	MBP_cg19178876	Myelin	0.76	1.64E-06	3.21E-05
DDR1_cg19215110	MBP_cg19178876	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg19591099	MBP_cg19178876	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg21677258	MBP_cg19178876	Myelin	0.83	3.66E-08	1.05E-06
DDR1_cg24566261	MBP_cg19178876	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg24636809	MBP_cg19178876	Myelin	0.81	9.65E-08	2.52E-06
DDR1_cg24727290	MBP_cg19178876	Myelin	0.84	1.22E-08	3.91E-07
DDR1_cg25655106	MBP_cg19178876	Myelin	0.83	3.41E-08	9.84E-07
DDR1_cg27237814	MBP_cg19178876	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg00466425	MBP_cg19480682	Myelin	0.86	2.67E-09	1.00E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg01598675	MBP_cg19480682	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg01936707	MBP_cg19480682	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg05703744	MBP_cg19480682	Myelin	0.89	7.25E-11	4.36E-09
DDR1_cg06200824	MBP_cg19480682	Myelin	0.82	4.82E-08	1.35E-06
DDR1_cg06501109	MBP_cg19480682	Myelin	0.75	2.91E-06	5.32E-05
DDR1_cg07908039	MBP_cg19480682	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg07912416	MBP_cg19480682	Myelin	0.90	5.71E-11	3.53E-09
DDR1_cg07979747	MBP_cg19480682	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg08673763	MBP_cg19480682	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg08951271	MBP_cg19480682	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg11530564	MBP_cg19480682	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg11676038	MBP_cg19480682	Myelin	0.93	1.68E-13	2.75E-11
DDR1_cg12669395	MBP_cg19480682	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg13329862	MBP_cg19480682	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg13351860	MBP_cg19480682	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg13695585	MBP_cg19480682	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg14058861	MBP_cg19480682	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg14790552	MBP_cg19480682	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg15656686	MBP_cg19480682	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg16111190	MBP_cg19480682	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg16797094	MBP_cg19480682	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg17176005	MBP_cg19480682	Myelin	0.83	2.47E-08	7.36E-07
DDR1_cg17604312	MBP_cg19480682	Myelin	0.79	3.63E-07	8.37E-06
DDR1_cg18577693	MBP_cg19480682	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg19215110	MBP_cg19480682	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg19591099	MBP_cg19480682	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg21677258	MBP_cg19480682	Myelin	0.94	6.17E-14	1.26E-11
DDR1_cg24566261	MBP_cg19480682	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg24636809	MBP_cg19480682	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg24727290	MBP_cg19480682	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg25613385	MBP_cg19480682	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg25655106	MBP_cg19480682	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg27237814	MBP_cg19480682	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg27593250	MBP_cg19480682	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg00466425	MBP_cg20074021	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg01936707	MBP_cg20074021	Myelin	0.81	8.48E-08	2.24E-06
DDR1_cg05703744	MBP_cg20074021	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg07912416	MBP_cg20074021	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg08673763	MBP_cg20074021	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg08684361	MBP_cg20074021	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg08951271	MBP_cg20074021	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg11530564	MBP_cg20074021	Myelin	0.83	1.99E-08	6.05E-07
DDR1_cg11676038	MBP_cg20074021	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg12669395	MBP_cg20074021	Myelin	0.77	9.90E-07	2.05E-05
DDR1_cg12847793	MBP_cg20074021	Myelin	0.80	1.59E-07	3.97E-06
DDR1_cg13329862	MBP_cg20074021	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg13351860	MBP_cg20074021	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg13660719	MBP_cg20074021	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg15656686	MBP_cg20074021	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg16111190	MBP_cg20074021	Myelin	0.81	1.28E-07	3.25E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg16797094	MBP_cg20074021	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg17604312	MBP_cg20074021	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg19215110	MBP_cg20074021	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg21677258	MBP_cg20074021	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg23222808	MBP_cg20074021	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg24636809	MBP_cg20074021	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg24727290	MBP_cg20074021	Myelin	0.83	3.66E-08	1.05E-06
DDR1_cg25655106	MBP_cg20074021	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg27237814	MBP_cg20074021	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg00466425	MBP_cg21107579	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg00934322	MBP_cg21107579	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg01936707	MBP_cg21107579	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg05703744	MBP_cg21107579	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg06200824	MBP_cg21107579	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg06501109	MBP_cg21107579	Myelin	0.83	3.18E-08	9.22E-07
DDR1_cg07908039	MBP_cg21107579	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg07912416	MBP_cg21107579	Myelin	0.88	1.91E-10	9.98E-09
DDR1_cg07979747	MBP_cg21107579	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg08673763	MBP_cg21107579	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg08951271	MBP_cg21107579	Myelin	0.94	9.33E-14	1.74E-11
DDR1_cg09965419	MBP_cg21107579	Myelin	0.77	1.13E-06	2.30E-05
DDR1_cg11530564	MBP_cg21107579	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg11676038	MBP_cg21107579	Myelin	0.96	4.44E-16	3.14E-13
DDR1_cg12669395	MBP_cg21107579	Myelin	0.93	1.85E-13	2.96E-11
DDR1_cg12847793	MBP_cg21107579	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg13329862	MBP_cg21107579	Myelin	0.93	2.04E-13	3.19E-11
DDR1_cg13351860	MBP_cg21107579	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg14058861	MBP_cg21107579	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg14790552	MBP_cg21107579	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg15656686	MBP_cg21107579	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg16111190	MBP_cg21107579	Myelin	0.87	8.88E-10	3.80E-08
DDR1_cg16797094	MBP_cg21107579	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg17176005	MBP_cg21107579	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg17604312	MBP_cg21107579	Myelin	0.81	1.03E-07	2.67E-06
DDR1_cg18577693	MBP_cg21107579	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg19215110	MBP_cg21107579	Myelin	0.80	1.45E-07	3.64E-06
DDR1_cg19591099	MBP_cg21107579	Myelin	0.84	1.27E-08	4.04E-07
DDR1_cg21677258	MBP_cg21107579	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg24636809	MBP_cg21107579	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg24727290	MBP_cg21107579	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg25613385	MBP_cg21107579	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg25655106	MBP_cg21107579	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg27237814	MBP_cg21107579	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg27593250	MBP_cg21107579	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg00466425	MBP_cg21322241	Myelin	0.92	2.45E-12	2.47E-10
DDR1_cg01598675	MBP_cg21322241	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg01936707	MBP_cg21322241	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg05703744	MBP_cg21322241	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg06200824	MBP_cg21322241	Myelin	0.84	1.65E-08	5.13E-07
DDR1_cg06501109	MBP_cg21322241	Myelin	0.83	3.18E-08	9.22E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07912416	MBP_cg21322241	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg07979747	MBP_cg21322241	Myelin	0.87	1.24E-09	5.08E-08
DDR1_cg08673763	MBP_cg21322241	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg08951271	MBP_cg21322241	Myelin	0.93	1.68E-13	2.75E-11
DDR1_cg09965419	MBP_cg21322241	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg11530564	MBP_cg21322241	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg11676038	MBP_cg21322241	Myelin	0.95	2.22E-15	1.05E-12
DDR1_cg12669395	MBP_cg21322241	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg12847793	MBP_cg21322241	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg13329862	MBP_cg21322241	Myelin	0.95	1.02E-14	3.15E-12
DDR1_cg13351860	MBP_cg21322241	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg14058861	MBP_cg21322241	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg14790552	MBP_cg21322241	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg15656686	MBP_cg21322241	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg15720085	MBP_cg21322241	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg16111190	MBP_cg21322241	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg16797094	MBP_cg21322241	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg17176005	MBP_cg21322241	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg17604312	MBP_cg21322241	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg18577693	MBP_cg21322241	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg19215110	MBP_cg21322241	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg19591099	MBP_cg21322241	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg21677258	MBP_cg21322241	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg24566261	MBP_cg21322241	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg24636809	MBP_cg21322241	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg24727290	MBP_cg21322241	Myelin	0.87	1.36E-09	5.52E-08
DDR1_cg25613385	MBP_cg21322241	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg25655106	MBP_cg21322241	Myelin	0.93	1.39E-13	2.37E-11
DDR1_cg27237814	MBP_cg21322241	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg27593250	MBP_cg21322241	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg01936707	MBP_cg22168512	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg05703744	MBP_cg22168512	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg07912416	MBP_cg22168512	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg07979747	MBP_cg22168512	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg08673763	MBP_cg22168512	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg08684361	MBP_cg22168512	Myelin	0.84	1.22E-08	3.91E-07
DDR1_cg08951271	MBP_cg22168512	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg09965419	MBP_cg22168512	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg11530564	MBP_cg22168512	Myelin	0.85	7.61E-09	2.56E-07
DDR1_cg12669395	MBP_cg22168512	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg13329862	MBP_cg22168512	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg13351860	MBP_cg22168512	Myelin	0.81	1.17E-07	2.99E-06
DDR1_cg15656686	MBP_cg22168512	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg16111190	MBP_cg22168512	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg16797094	MBP_cg22168512	Myelin	0.86	2.91E-09	1.08E-07
DDR1_cg17176005	MBP_cg22168512	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg17604312	MBP_cg22168512	Myelin	0.78	6.49E-07	1.41E-05
DDR1_cg19215110	MBP_cg22168512	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg21677258	MBP_cg22168512	Myelin	0.84	1.17E-08	3.77E-07
DDR1_cg24636809	MBP_cg22168512	Myelin	0.76	1.64E-06	3.21E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg24727290	MBP_cg22168512	Myelin	0.79	4.55E-07	1.02E-05
DDR1_cg25613385	MBP_cg22168512	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg25655106	MBP_cg22168512	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg27237814	MBP_cg22168512	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg00466425	MBP_cg22239325	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg00934322	MBP_cg22239325	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg01936707	MBP_cg22239325	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg05703744	MBP_cg22239325	Myelin	0.90	3.28E-11	2.19E-09
DDR1_cg06200824	MBP_cg22239325	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg06501109	MBP_cg22239325	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg07912416	MBP_cg22239325	Myelin	0.84	1.71E-08	5.30E-07
DDR1_cg07979747	MBP_cg22239325	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg08673763	MBP_cg22239325	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg08951271	MBP_cg22239325	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg09822812	MBP_cg22239325	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg09965419	MBP_cg22239325	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg11530564	MBP_cg22239325	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg11676038	MBP_cg22239325	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg12669395	MBP_cg22239325	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg12847793	MBP_cg22239325	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg13329862	MBP_cg22239325	Myelin	0.93	1.14E-13	2.04E-11
DDR1_cg13351860	MBP_cg22239325	Myelin	0.95	9.33E-15	2.95E-12
DDR1_cg13660719	MBP_cg22239325	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg13695585	MBP_cg22239325	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg14790552	MBP_cg22239325	Myelin	0.86	1.49E-09	5.99E-08
DDR1_cg15656686	MBP_cg22239325	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg16111190	MBP_cg22239325	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg16797094	MBP_cg22239325	Myelin	0.93	3.24E-13	4.65E-11
DDR1_cg17176005	MBP_cg22239325	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg17604312	MBP_cg22239325	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg19215110	MBP_cg22239325	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg19591099	MBP_cg22239325	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg20955507	MBP_cg22239325	Myelin	0.77	1.10E-06	2.25E-05
DDR1_cg21677258	MBP_cg22239325	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg24636809	MBP_cg22239325	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg24727290	MBP_cg22239325	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg25655106	MBP_cg22239325	Myelin	0.88	2.64E-10	1.32E-08
DDR1_cg27237814	MBP_cg22239325	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg27593250	MBP_cg22239325	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg00466425	MBP_cg22391424	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg00934322	MBP_cg22391424	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg01598675	MBP_cg22391424	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg01936707	MBP_cg22391424	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg05703744	MBP_cg22391424	Myelin	0.90	5.71E-11	3.53E-09
DDR1_cg06200824	MBP_cg22391424	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg06501109	MBP_cg22391424	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg07912416	MBP_cg22391424	Myelin	0.81	1.13E-07	2.90E-06
DDR1_cg07979747	MBP_cg22391424	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg08673763	MBP_cg22391424	Myelin	0.86	1.63E-09	6.49E-08
DDR1_cg08951271	MBP_cg22391424	Myelin	0.93	4.65E-13	6.26E-11

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg09965419	MBP_cg22391424	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg11530564	MBP_cg22391424	Myelin	0.91	8.05E-12	6.68E-10
DDR1_cg11676038	MBP_cg22391424	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg12669395	MBP_cg22391424	Myelin	0.93	2.70E-13	4.02E-11
DDR1_cg12847793	MBP_cg22391424	Myelin	0.77	1.04E-06	2.15E-05
DDR1_cg13329862	MBP_cg22391424	Myelin	0.93	1.14E-13	2.04E-11
DDR1_cg13351860	MBP_cg22391424	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg13695585	MBP_cg22391424	Myelin	0.76	1.64E-06	3.21E-05
DDR1_cg14058861	MBP_cg22391424	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg14790552	MBP_cg22391424	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg15656686	MBP_cg22391424	Myelin	0.89	1.09E-10	6.12E-09
DDR1_cg16111190	MBP_cg22391424	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg16797094	MBP_cg22391424	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg17176005	MBP_cg22391424	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg17604312	MBP_cg22391424	Myelin	0.80	2.29E-07	5.50E-06
DDR1_cg19215110	MBP_cg22391424	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg19591099	MBP_cg22391424	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg21677258	MBP_cg22391424	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg24636809	MBP_cg22391424	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg24727290	MBP_cg22391424	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg25655106	MBP_cg22391424	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg27237814	MBP_cg22391424	Myelin	0.91	1.50E-11	1.13E-09
DDR1_cg27593250	MBP_cg22391424	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg00466425	MBP_cg23327011	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg00934322	MBP_cg23327011	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg01936707	MBP_cg23327011	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg05703744	MBP_cg23327011	Myelin	0.93	2.46E-13	3.73E-11
DDR1_cg06200824	MBP_cg23327011	Myelin	0.82	5.71E-08	1.57E-06
DDR1_cg06501109	MBP_cg23327011	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg07908039	MBP_cg23327011	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg07912416	MBP_cg23327011	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg07979747	MBP_cg23327011	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg08673763	MBP_cg23327011	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg08951271	MBP_cg23327011	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg09965419	MBP_cg23327011	Myelin	0.79	4.07E-07	9.25E-06
DDR1_cg11530564	MBP_cg23327011	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg11676038	MBP_cg23327011	Myelin	0.94	1.87E-14	5.00E-12
DDR1_cg12669395	MBP_cg23327011	Myelin	0.94	9.33E-14	1.74E-11
DDR1_cg12847793	MBP_cg23327011	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg13329862	MBP_cg23327011	Myelin	0.94	1.31E-14	3.81E-12
DDR1_cg13351860	MBP_cg23327011	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg14058861	MBP_cg23327011	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg14790552	MBP_cg23327011	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg15656686	MBP_cg23327011	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg16111190	MBP_cg23327011	Myelin	0.89	1.15E-10	6.43E-09
DDR1_cg16797094	MBP_cg23327011	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg17176005	MBP_cg23327011	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg17604312	MBP_cg23327011	Myelin	0.81	8.21E-08	2.18E-06
DDR1_cg19215110	MBP_cg23327011	Myelin	0.82	3.92E-08	1.12E-06
DDR1_cg19591099	MBP_cg23327011	Myelin	0.86	3.32E-09	1.22E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg21677258	MBP_cg23327011	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg24566261	MBP_cg23327011	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg24636809	MBP_cg23327011	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg24727290	MBP_cg23327011	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg25655106	MBP_cg23327011	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg27237814	MBP_cg23327011	Myelin	0.88	1.91E-10	9.98E-09
DDR1_cg27593250	MBP_cg23327011	Myelin	0.80	1.74E-07	4.31E-06
DDR1_cg00466425	MBP_cg23746811	Myelin	0.85	7.61E-09	2.56E-07
DDR1_cg00934322	MBP_cg23746811	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg01936707	MBP_cg23746811	Myelin	0.90	2.88E-11	1.96E-09
DDR1_cg05703744	MBP_cg23746811	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg06501109	MBP_cg23746811	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg07908039	MBP_cg23746811	Myelin	0.81	1.20E-07	3.07E-06
DDR1_cg07912416	MBP_cg23746811	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg07979747	MBP_cg23746811	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg08673763	MBP_cg23746811	Myelin	0.84	8.92E-09	2.96E-07
DDR1_cg08684361	MBP_cg23746811	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg08951271	MBP_cg23746811	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg09822812	MBP_cg23746811	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg09965419	MBP_cg23746811	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg11530564	MBP_cg23746811	Myelin	0.96	4.44E-16	3.14E-13
DDR1_cg11676038	MBP_cg23746811	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg12669395	MBP_cg23746811	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg12847793	MBP_cg23746811	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg13329862	MBP_cg23746811	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg13351860	MBP_cg23746811	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg13695585	MBP_cg23746811	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg14790552	MBP_cg23746811	Myelin	0.87	1.13E-09	4.68E-08
DDR1_cg15656686	MBP_cg23746811	Myelin	0.90	4.47E-11	2.86E-09
DDR1_cg16111190	MBP_cg23746811	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg16797094	MBP_cg23746811	Myelin	0.94	1.87E-14	5.00E-12
DDR1_cg17176005	MBP_cg23746811	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg17604312	MBP_cg23746811	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg19215110	MBP_cg23746811	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg19591099	MBP_cg23746811	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg21677258	MBP_cg23746811	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg24636809	MBP_cg23746811	Myelin	0.87	1.13E-09	4.68E-08
DDR1_cg24727290	MBP_cg23746811	Myelin	0.80	1.45E-07	3.64E-06
DDR1_cg25613385	MBP_cg23746811	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg25655106	MBP_cg23746811	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg27237814	MBP_cg23746811	Myelin	0.90	5.71E-11	3.53E-09
DDR1_cg27593250	MBP_cg23746811	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg00466425	MBP_cg23975646	Myelin	0.88	2.13E-10	1.10E-08
DDR1_cg00934322	MBP_cg23975646	Myelin	0.78	7.42E-07	1.59E-05
DDR1_cg01936707	MBP_cg23975646	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg05703744	MBP_cg23975646	Myelin	0.93	2.24E-13	3.46E-11
DDR1_cg06200824	MBP_cg23975646	Myelin	0.77	1.25E-06	2.52E-05
DDR1_cg06501109	MBP_cg23975646	Myelin	0.84	1.09E-08	3.52E-07
DDR1_cg07908039	MBP_cg23975646	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg07912416	MBP_cg23975646	Myelin	0.85	7.92E-09	2.66E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07979747	MBP_cg23975646	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg08673763	MBP_cg23975646	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg08951271	MBP_cg23975646	Myelin	0.92	1.94E-12	2.03E-10
DDR1_cg09822812	MBP_cg23975646	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg09965419	MBP_cg23975646	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg11530564	MBP_cg23975646	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg11676038	MBP_cg23975646	Myelin	0.93	1.68E-13	2.75E-11
DDR1_cg12669395	MBP_cg23975646	Myelin	0.94	6.84E-14	1.37E-11
DDR1_cg12847793	MBP_cg23975646	Myelin	0.77	1.18E-06	2.41E-05
DDR1_cg13329862	MBP_cg23975646	Myelin	0.93	1.53E-13	2.55E-11
DDR1_cg13351860	MBP_cg23975646	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg13695585	MBP_cg23975646	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg14058861	MBP_cg23975646	Myelin	0.79	4.43E-07	9.98E-06
DDR1_cg14790552	MBP_cg23975646	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg15656686	MBP_cg23975646	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg16111190	MBP_cg23975646	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg16797094	MBP_cg23975646	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg17176005	MBP_cg23975646	Myelin	0.80	1.91E-07	4.67E-06
DDR1_cg17604312	MBP_cg23975646	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg19215110	MBP_cg23975646	Myelin	0.84	1.22E-08	3.91E-07
DDR1_cg19591099	MBP_cg23975646	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg21677258	MBP_cg23975646	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg24636809	MBP_cg23975646	Myelin	0.90	1.60E-11	1.19E-09
DDR1_cg24727290	MBP_cg23975646	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg25613385	MBP_cg23975646	Myelin	0.75	2.47E-06	4.61E-05
DDR1_cg25655106	MBP_cg23975646	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg27237814	MBP_cg23975646	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg27593250	MBP_cg23975646	Myelin	0.79	3.85E-07	8.81E-06
DDR1_cg07912416	MBP_cg24267485	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg00466425	MBP_cg24274653	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg01598675	MBP_cg24274653	Myelin	0.75	3.35E-06	6.02E-05
DDR1_cg01936707	MBP_cg24274653	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg05703744	MBP_cg24274653	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg06200824	MBP_cg24274653	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg06501109	MBP_cg24274653	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg07908039	MBP_cg24274653	Myelin	0.81	1.06E-07	2.74E-06
DDR1_cg07912416	MBP_cg24274653	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg07979747	MBP_cg24274653	Myelin	0.83	3.29E-08	9.53E-07
DDR1_cg08673763	MBP_cg24274653	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg08684361	MBP_cg24274653	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg08951271	MBP_cg24274653	Myelin	0.88	2.64E-10	1.32E-08
DDR1_cg09822812	MBP_cg24274653	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg09965419	MBP_cg24274653	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg11530564	MBP_cg24274653	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg11676038	MBP_cg24274653	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg12669395	MBP_cg24274653	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg12847793	MBP_cg24274653	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg13329862	MBP_cg24274653	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg13351860	MBP_cg24274653	Myelin	0.89	9.72E-11	5.55E-09
DDR1_cg13660719	MBP_cg24274653	Myelin	0.78	7.04E-07	1.51E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13695585	MBP_cg24274653	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg14790552	MBP_cg24274653	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg15656686	MBP_cg24274653	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg16111190	MBP_cg24274653	Myelin	0.80	1.54E-07	3.86E-06
DDR1_cg16797094	MBP_cg24274653	Myelin	0.93	1.26E-13	2.20E-11
DDR1_cg17176005	MBP_cg24274653	Myelin	0.76	1.56E-06	3.07E-05
DDR1_cg17604312	MBP_cg24274653	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg19591099	MBP_cg24274653	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg20335906	MBP_cg24274653	Myelin	0.75	2.25E-06	4.24E-05
DDR1_cg21677258	MBP_cg24274653	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg24566261	MBP_cg24274653	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg24636809	MBP_cg24274653	Myelin	0.85	6.22E-09	2.14E-07
DDR1_cg24727290	MBP_cg24274653	Myelin	0.78	5.52E-07	1.22E-05
DDR1_cg25613385	MBP_cg24274653	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg25655106	MBP_cg24274653	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg27237814	MBP_cg24274653	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg27593250	MBP_cg24274653	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg00466425	MBP_cg25805393	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg00934322	MBP_cg25805393	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg01598675	MBP_cg25805393	Myelin	0.78	7.62E-07	1.62E-05
DDR1_cg01936707	MBP_cg25805393	Myelin	0.90	4.76E-11	3.02E-09
DDR1_cg05703744	MBP_cg25805393	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg06200824	MBP_cg25805393	Myelin	0.82	4.99E-08	1.39E-06
DDR1_cg06501109	MBP_cg25805393	Myelin	0.81	8.21E-08	2.18E-06
DDR1_cg07908039	MBP_cg25805393	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg07912416	MBP_cg25805393	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg07979747	MBP_cg25805393	Myelin	0.86	2.14E-09	8.25E-08
DDR1_cg08673763	MBP_cg25805393	Myelin	0.87	8.06E-10	3.49E-08
DDR1_cg08951271	MBP_cg25805393	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg09965419	MBP_cg25805393	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg11530564	MBP_cg25805393	Myelin	0.93	3.89E-13	5.41E-11
DDR1_cg11676038	MBP_cg25805393	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg12669395	MBP_cg25805393	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg13329862	MBP_cg25805393	Myelin	0.95	1.11E-15	6.40E-13
DDR1_cg13351860	MBP_cg25805393	Myelin	0.93	1.68E-13	2.75E-11
DDR1_cg13695585	MBP_cg25805393	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg14058861	MBP_cg25805393	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg14790552	MBP_cg25805393	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg15656686	MBP_cg25805393	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg15720085	MBP_cg25805393	Myelin	0.77	8.03E-07	1.70E-05
DDR1_cg16111190	MBP_cg25805393	Myelin	0.93	1.53E-13	2.55E-11
DDR1_cg16797094	MBP_cg25805393	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg17176005	MBP_cg25805393	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg17604312	MBP_cg25805393	Myelin	0.79	3.63E-07	8.37E-06
DDR1_cg18577693	MBP_cg25805393	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg19215110	MBP_cg25805393	Myelin	0.82	5.71E-08	1.57E-06
DDR1_cg19591099	MBP_cg25805393	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg21677258	MBP_cg25805393	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg24566261	MBP_cg25805393	Myelin	0.77	9.65E-07	2.00E-05
DDR1_cg24636809	MBP_cg25805393	Myelin	0.89	6.83E-11	4.13E-09

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg24727290	MBP_cg25805393	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg25655106	MBP_cg25805393	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg27237814	MBP_cg25805393	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg27593250	MBP_cg25805393	Myelin	0.81	8.48E-08	2.24E-06
DDR1_cg00466425	MBP_cg26346730	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg01936707	MBP_cg26346730	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg05703744	MBP_cg26346730	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg07912416	MBP_cg26346730	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg07979747	MBP_cg26346730	Myelin	0.76	1.95E-06	3.73E-05
DDR1_cg08684361	MBP_cg26346730	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg08951271	MBP_cg26346730	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg11530564	MBP_cg26346730	Myelin	0.94	5.02E-14	1.08E-11
DDR1_cg11676038	MBP_cg26346730	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg12669395	MBP_cg26346730	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg13329862	MBP_cg26346730	Myelin	0.79	2.81E-07	6.62E-06
DDR1_cg13351860	MBP_cg26346730	Myelin	0.85	6.48E-09	2.22E-07
DDR1_cg14790552	MBP_cg26346730	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg15656686	MBP_cg26346730	Myelin	0.78	7.42E-07	1.59E-05
DDR1_cg16111190	MBP_cg26346730	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg16797094	MBP_cg26346730	Myelin	0.88	3.61E-10	1.73E-08
DDR1_cg21677258	MBP_cg26346730	Myelin	0.83	2.39E-08	7.13E-07
DDR1_cg24636809	MBP_cg26346730	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg24727290	MBP_cg26346730	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg25655106	MBP_cg26346730	Myelin	0.80	2.35E-07	5.65E-06
DDR1_cg27237814	MBP_cg26346730	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg00466425	MBP_cg26838030	Myelin	0.81	8.48E-08	2.24E-06
DDR1_cg01598675	MBP_cg26838030	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg01936707	MBP_cg26838030	Myelin	0.78	7.42E-07	1.59E-05
DDR1_cg05703744	MBP_cg26838030	Myelin	0.78	6.85E-07	1.48E-05
DDR1_cg06501109	MBP_cg26838030	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg07908039	MBP_cg26838030	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg07912416	MBP_cg26838030	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg07979747	MBP_cg26838030	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg08673763	MBP_cg26838030	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg08951271	MBP_cg26838030	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg11530564	MBP_cg26838030	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg11676038	MBP_cg26838030	Myelin	0.83	3.41E-08	9.84E-07
DDR1_cg12669395	MBP_cg26838030	Myelin	0.81	9.34E-08	2.45E-06
DDR1_cg12847793	MBP_cg26838030	Myelin	0.77	1.28E-06	2.58E-05
DDR1_cg13329862	MBP_cg26838030	Myelin	0.87	6.00E-10	2.70E-08
DDR1_cg13351860	MBP_cg26838030	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg13695585	MBP_cg26838030	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg14790552	MBP_cg26838030	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg15656686	MBP_cg26838030	Myelin	0.83	2.86E-08	8.38E-07
DDR1_cg16111190	MBP_cg26838030	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg16797094	MBP_cg26838030	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg17176005	MBP_cg26838030	Myelin	0.76	1.99E-06	3.82E-05
DDR1_cg17604312	MBP_cg26838030	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg18577693	MBP_cg26838030	Myelin	0.75	2.91E-06	5.32E-05
DDR1_cg21677258	MBP_cg26838030	Myelin	0.86	1.49E-09	5.99E-08

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg24566261	MBP_cg26838030	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg24636809	MBP_cg26838030	Myelin	0.79	2.89E-07	6.80E-06
DDR1_cg24727290	MBP_cg26838030	Myelin	0.79	3.85E-07	8.81E-06
DDR1_cg25655106	MBP_cg26838030	Myelin	0.85	7.61E-09	2.56E-07
DDR1_cg27237814	MBP_cg26838030	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg27593250	MBP_cg26838030	Myelin	0.76	1.72E-06	3.35E-05
DDR1_cg00466425	MBP_cg27240008	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg01598675	MBP_cg27240008	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg01936707	MBP_cg27240008	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg05703744	MBP_cg27240008	Myelin	0.91	1.14E-11	8.99E-10
DDR1_cg06200824	MBP_cg27240008	Myelin	0.78	6.85E-07	1.48E-05
DDR1_cg06501109	MBP_cg27240008	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg07912416	MBP_cg27240008	Myelin	0.84	1.47E-08	4.63E-07
DDR1_cg07979747	MBP_cg27240008	Myelin	0.86	3.32E-09	1.22E-07
DDR1_cg08673763	MBP_cg27240008	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg08684361	MBP_cg27240008	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg08951271	MBP_cg27240008	Myelin	0.93	3.24E-13	4.65E-11
DDR1_cg09822812	MBP_cg27240008	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg09965419	MBP_cg27240008	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg11530564	MBP_cg27240008	Myelin	0.90	2.54E-11	1.76E-09
DDR1_cg11676038	MBP_cg27240008	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg12669395	MBP_cg27240008	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg12847793	MBP_cg27240008	Myelin	0.83	3.29E-08	9.53E-07
DDR1_cg13329862	MBP_cg27240008	Myelin	0.95	7.99E-15	2.65E-12
DDR1_cg13351860	MBP_cg27240008	Myelin	0.92	1.41E-12	1.55E-10
DDR1_cg13695585	MBP_cg27240008	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg14790552	MBP_cg27240008	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg15656686	MBP_cg27240008	Myelin	0.89	7.25E-11	4.36E-09
DDR1_cg16111190	MBP_cg27240008	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg16797094	MBP_cg27240008	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg17176005	MBP_cg27240008	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg17604312	MBP_cg27240008	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg19215110	MBP_cg27240008	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg19591099	MBP_cg27240008	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg20955507	MBP_cg27240008	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg21677258	MBP_cg27240008	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg24636809	MBP_cg27240008	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg24727290	MBP_cg27240008	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg25655106	MBP_cg27240008	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg27237814	MBP_cg27240008	Myelin	0.93	3.55E-13	5.01E-11
DDR1_cg27593250	MBP_cg27240008	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg00466425	MBP_cg27328941	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg00934322	MBP_cg27328941	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg01598675	MBP_cg27328941	Myelin	0.75	2.91E-06	5.32E-05
DDR1_cg01936707	MBP_cg27328941	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg05703744	MBP_cg27328941	Myelin	0.88	1.91E-10	9.98E-09
DDR1_cg06200824	MBP_cg27328941	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg06501109	MBP_cg27328941	Myelin	0.83	2.22E-08	6.67E-07
DDR1_cg07908039	MBP_cg27328941	Myelin	0.76	1.45E-06	2.88E-05
DDR1_cg07912416	MBP_cg27328941	Myelin	0.84	8.24E-09	2.76E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07979747	MBP_cg27328941	Myelin	0.85	3.94E-09	1.42E-07
DDR1_cg08673763	MBP_cg27328941	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg08951271	MBP_cg27328941	Myelin	0.95	5.77E-15	2.11E-12
DDR1_cg09965419	MBP_cg27328941	Myelin	0.77	1.07E-06	2.20E-05
DDR1_cg11530564	MBP_cg27328941	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg11676038	MBP_cg27328941	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg12669395	MBP_cg27328941	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg12847793	MBP_cg27328941	Myelin	0.82	5.90E-08	1.62E-06
DDR1_cg13329862	MBP_cg27328941	Myelin	0.95	1.15E-14	3.44E-12
DDR1_cg13351860	MBP_cg27328941	Myelin	0.93	5.55E-13	7.29E-11
DDR1_cg13695585	MBP_cg27328941	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg14058861	MBP_cg27328941	Myelin	0.78	5.83E-07	1.28E-05
DDR1_cg14790552	MBP_cg27328941	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg15656686	MBP_cg27328941	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg16111190	MBP_cg27328941	Myelin	0.88	4.91E-10	2.26E-08
DDR1_cg16797094	MBP_cg27328941	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg17176005	MBP_cg27328941	Myelin	0.83	3.07E-08	8.93E-07
DDR1_cg17604312	MBP_cg27328941	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg18577693	MBP_cg27328941	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg19215110	MBP_cg27328941	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg19591099	MBP_cg27328941	Myelin	0.81	8.21E-08	2.18E-06
DDR1_cg21677258	MBP_cg27328941	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg23222808	MBP_cg27328941	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg24566261	MBP_cg27328941	Myelin	0.78	6.67E-07	1.44E-05
DDR1_cg24636809	MBP_cg27328941	Myelin	0.87	8.46E-10	3.63E-08
DDR1_cg24727290	MBP_cg27328941	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg25613385	MBP_cg27328941	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg25655106	MBP_cg27328941	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg27237814	MBP_cg27328941	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg27593250	MBP_cg27328941	Myelin	0.81	1.10E-07	2.82E-06
DDR1_cg06893977	OLIG1_cg15893431	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg19018599	OLIG2_cg15299832	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg19018599	OLIG2_cg23253569	Myelin	0.81	7.44E-08	1.99E-06
DDR1_cg19894264	OLIG2_cg23253569	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg24303888	OLIG2_cg27357571	Myelin	0.77	9.16E-07	1.91E-05
DDR1_cg08684361	PDGFRA_cg03792767	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg08951271	PDGFRA_cg03792767	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg11530564	PDGFRA_cg03792767	Myelin	0.81	7.95E-08	2.11E-06
DDR1_cg13329862	PDGFRA_cg03792767	Myelin	0.77	1.13E-06	2.30E-05
DDR1_cg13351860	PDGFRA_cg03792767	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg13695585	PDGFRA_cg03792767	Myelin	0.80	1.41E-07	3.54E-06
DDR1_cg15656686	PDGFRA_cg03792767	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg16797094	PDGFRA_cg03792767	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg21677258	PDGFRA_cg03792767	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg25613385	PDGFRA_cg03792767	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg27237814	PDGFRA_cg03792767	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg11530564	PDGFRA_cg03966785	Myelin	0.76	1.52E-06	3.01E-05
DDR1_cg12847793	PDGFRA_cg03966785	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg13351860	PDGFRA_cg03966785	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg08684361	PDGFRA_cg10227863	Myelin	0.75	2.65E-06	4.91E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg08951271	PDGFRA_cg11351886	Myelin	0.77	8.47E-07	1.78E-05
DDR1_cg13329862	PDGFRA_cg11351886	Myelin	0.76	1.72E-06	3.35E-05
DDR1_cg21677258	PDGFRA_cg11351886	Myelin	0.76	1.85E-06	3.58E-05
DDR1_cg11676038	SOX10_cg01586506	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg14790552	SOX10_cg01586506	Myelin	0.77	1.13E-06	2.30E-05
DDR1_cg19215110	SOX10_cg01586506	Myelin	0.79	2.65E-07	6.28E-06
DDR1_cg00466425	SOX10_cg05447556	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg00934322	SOX10_cg05447556	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg01598675	SOX10_cg05447556	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg01936707	SOX10_cg05447556	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg05703744	SOX10_cg05447556	Myelin	0.92	2.27E-12	2.31E-10
DDR1_cg06200824	SOX10_cg05447556	Myelin	0.84	1.13E-08	3.65E-07
DDR1_cg06501109	SOX10_cg05447556	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg07908039	SOX10_cg05447556	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg07912416	SOX10_cg05447556	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg07979747	SOX10_cg05447556	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg08673763	SOX10_cg05447556	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg08684361	SOX10_cg05447556	Myelin	0.76	2.14E-06	4.06E-05
DDR1_cg08951271	SOX10_cg05447556	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg09965419	SOX10_cg05447556	Myelin	0.83	3.53E-08	1.02E-06
DDR1_cg11530564	SOX10_cg05447556	Myelin	0.93	2.24E-13	3.46E-11
DDR1_cg11676038	SOX10_cg05447556	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg12669395	SOX10_cg05447556	Myelin	0.95	9.33E-15	2.95E-12
DDR1_cg12847793	SOX10_cg05447556	Myelin	0.77	8.92E-07	1.87E-05
DDR1_cg13329862	SOX10_cg05447556	Myelin	0.94	1.47E-14	4.13E-12
DDR1_cg13351860	SOX10_cg05447556	Myelin	0.94	3.24E-14	7.65E-12
DDR1_cg14058861	SOX10_cg05447556	Myelin	0.77	8.25E-07	1.74E-05
DDR1_cg14790552	SOX10_cg05447556	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg15656686	SOX10_cg05447556	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg15720085	SOX10_cg05447556	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg16111190	SOX10_cg05447556	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg16797094	SOX10_cg05447556	Myelin	0.92	2.45E-12	2.47E-10
DDR1_cg17176005	SOX10_cg05447556	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg17604312	SOX10_cg05447556	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg18577693	SOX10_cg05447556	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg19215110	SOX10_cg05447556	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg19591099	SOX10_cg05447556	Myelin	0.86	2.45E-09	9.27E-08
DDR1_cg21677258	SOX10_cg05447556	Myelin	0.92	1.19E-12	1.36E-10
DDR1_cg24566261	SOX10_cg05447556	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg24636809	SOX10_cg05447556	Myelin	0.91	1.31E-11	1.01E-09
DDR1_cg24727290	SOX10_cg05447556	Myelin	0.85	5.50E-09	1.92E-07
DDR1_cg25655106	SOX10_cg05447556	Myelin	0.94	1.87E-14	5.00E-12
DDR1_cg27237814	SOX10_cg05447556	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg27593250	SOX10_cg05447556	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg00466425	SOX10_cg05766881	Myelin	0.91	9.26E-12	7.51E-10
DDR1_cg01598675	SOX10_cg05766881	Myelin	0.78	7.83E-07	1.66E-05
DDR1_cg01936707	SOX10_cg05766881	Myelin	0.93	6.06E-13	7.80E-11
DDR1_cg05703744	SOX10_cg05766881	Myelin	0.87	1.02E-09	4.31E-08
DDR1_cg06200824	SOX10_cg05766881	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg06501109	SOX10_cg05766881	Myelin	0.84	9.65E-09	3.17E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07908039	SOX10_cg05766881	Myelin	0.79	3.43E-07	7.95E-06
DDR1_cg07912416	SOX10_cg05766881	Myelin	0.88	4.22E-10	1.99E-08
DDR1_cg07979747	SOX10_cg05766881	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg08673763	SOX10_cg05766881	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg08951271	SOX10_cg05766881	Myelin	0.94	4.51E-14	9.90E-12
DDR1_cg11530564	SOX10_cg05766881	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg11676038	SOX10_cg05766881	Myelin	0.96	4.44E-16	3.14E-13
DDR1_cg12669395	SOX10_cg05766881	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg13329862	SOX10_cg05766881	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg13351860	SOX10_cg05766881	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg14058861	SOX10_cg05766881	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg14790552	SOX10_cg05766881	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg15656686	SOX10_cg05766881	Myelin	0.86	1.71E-09	6.76E-08
DDR1_cg15720085	SOX10_cg05766881	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg16111190	SOX10_cg05766881	Myelin	0.87	1.42E-09	5.75E-08
DDR1_cg16797094	SOX10_cg05766881	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg17176005	SOX10_cg05766881	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg17604312	SOX10_cg05766881	Myelin	0.84	8.24E-09	2.76E-07
DDR1_cg18577693	SOX10_cg05766881	Myelin	0.82	7.20E-08	1.94E-06
DDR1_cg19215110	SOX10_cg05766881	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg19591099	SOX10_cg05766881	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg21677258	SOX10_cg05766881	Myelin	0.93	1.85E-13	2.96E-11
DDR1_cg24636809	SOX10_cg05766881	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg24727290	SOX10_cg05766881	Myelin	0.85	3.77E-09	1.37E-07
DDR1_cg25613385	SOX10_cg05766881	Myelin	0.81	1.36E-07	3.44E-06
DDR1_cg25655106	SOX10_cg05766881	Myelin	0.92	3.09E-12	2.96E-10
DDR1_cg25943433	SOX10_cg05766881	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg27237814	SOX10_cg05766881	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg27593250	SOX10_cg05766881	Myelin	0.83	1.85E-08	5.67E-07
DDR1_cg11676038	SOX10_cg10933281	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg14058861	SOX10_cg10933281	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg19591099	SOX10_cg10933281	Myelin	0.77	9.16E-07	1.91E-05
DDR1_cg00466425	SOX10_cg11864127	Myelin	0.91	6.04E-12	5.23E-10
DDR1_cg01598675	SOX10_cg11864127	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg01936707	SOX10_cg11864127	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg05703744	SOX10_cg11864127	Myelin	0.95	3.11E-15	1.36E-12
DDR1_cg06200824	SOX10_cg11864127	Myelin	0.82	5.16E-08	1.43E-06
DDR1_cg06501109	SOX10_cg11864127	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg07908039	SOX10_cg11864127	Myelin	0.77	9.40E-07	1.96E-05
DDR1_cg07912416	SOX10_cg11864127	Myelin	0.89	8.16E-11	4.81E-09
DDR1_cg07979747	SOX10_cg11864127	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg08673763	SOX10_cg11864127	Myelin	0.91	1.50E-11	1.13E-09
DDR1_cg08684361	SOX10_cg11864127	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg08951271	SOX10_cg11864127	Myelin	0.93	4.26E-13	5.84E-11
DDR1_cg09822812	SOX10_cg11864127	Myelin	0.76	2.09E-06	3.98E-05
DDR1_cg09965419	SOX10_cg11864127	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg11530564	SOX10_cg11864127	Myelin	0.95	1.15E-14	3.44E-12
DDR1_cg11676038	SOX10_cg11864127	Myelin	0.92	3.60E-12	3.37E-10
DDR1_cg12669395	SOX10_cg11864127	Myelin	0.94	6.84E-14	1.37E-11
DDR1_cg12847793	SOX10_cg11864127	Myelin	0.77	8.69E-07	1.83E-05

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13329862	SOX10_cg11864127	Myelin	0.93	6.61E-13	8.36E-11
DDR1_cg13351860	SOX10_cg11864127	Myelin	0.95	4.88E-15	1.86E-12
DDR1_cg13695585	SOX10_cg11864127	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg14058861	SOX10_cg11864127	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg14790552	SOX10_cg11864127	Myelin	0.89	8.65E-11	5.05E-09
DDR1_cg15656686	SOX10_cg11864127	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg15720085	SOX10_cg11864127	Myelin	0.76	1.60E-06	3.14E-05
DDR1_cg16111190	SOX10_cg11864127	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg16797094	SOX10_cg11864127	Myelin	0.93	7.20E-13	8.96E-11
DDR1_cg17176005	SOX10_cg11864127	Myelin	0.85	5.28E-09	1.85E-07
DDR1_cg17604312	SOX10_cg11864127	Myelin	0.89	1.45E-10	7.83E-09
DDR1_cg18577693	SOX10_cg11864127	Myelin	0.75	3.43E-06	6.15E-05
DDR1_cg19215110	SOX10_cg11864127	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg19591099	SOX10_cg11864127	Myelin	0.82	5.34E-08	1.47E-06
DDR1_cg21677258	SOX10_cg11864127	Myelin	0.94	5.55E-14	1.16E-11
DDR1_cg24636809	SOX10_cg11864127	Myelin	0.92	1.30E-12	1.46E-10
DDR1_cg24727290	SOX10_cg11864127	Myelin	0.88	3.43E-10	1.66E-08
DDR1_cg25613385	SOX10_cg11864127	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg25655106	SOX10_cg11864127	Myelin	0.96	2.22E-16	2.02E-13
DDR1_cg27237814	SOX10_cg11864127	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg27593250	SOX10_cg11864127	Myelin	0.80	1.64E-07	4.08E-06
DDR1_cg00466425	SOX10_cg15856662	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg01936707	SOX10_cg15856662	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg05703744	SOX10_cg15856662	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg06200824	SOX10_cg15856662	Myelin	0.75	3.13E-06	5.67E-05
DDR1_cg06501109	SOX10_cg15856662	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg07912416	SOX10_cg15856662	Myelin	0.85	3.77E-09	1.37E-07
DDR1_cg07979747	SOX10_cg15856662	Myelin	0.88	5.17E-10	2.36E-08
DDR1_cg08673763	SOX10_cg15856662	Myelin	0.84	1.22E-08	3.91E-07
DDR1_cg08684361	SOX10_cg15856662	Myelin	0.77	1.34E-06	2.70E-05
DDR1_cg08951271	SOX10_cg15856662	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg09965419	SOX10_cg15856662	Myelin	0.82	4.82E-08	1.35E-06
DDR1_cg11530564	SOX10_cg15856662	Myelin	0.92	2.27E-12	2.31E-10
DDR1_cg11676038	SOX10_cg15856662	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg12669395	SOX10_cg15856662	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg12847793	SOX10_cg15856662	Myelin	0.78	5.08E-07	1.13E-05
DDR1_cg13329862	SOX10_cg15856662	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg13351860	SOX10_cg15856662	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg14790552	SOX10_cg15856662	Myelin	0.81	1.28E-07	3.25E-06
DDR1_cg15656686	SOX10_cg15856662	Myelin	0.84	1.32E-08	4.19E-07
DDR1_cg16111190	SOX10_cg15856662	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg16797094	SOX10_cg15856662	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg17176005	SOX10_cg15856662	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg17604312	SOX10_cg15856662	Myelin	0.78	5.99E-07	1.31E-05
DDR1_cg19591099	SOX10_cg15856662	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg21677258	SOX10_cg15856662	Myelin	0.90	3.71E-11	2.44E-09
DDR1_cg24636809	SOX10_cg15856662	Myelin	0.87	1.07E-09	4.49E-08
DDR1_cg24727290	SOX10_cg15856662	Myelin	0.84	1.32E-08	4.19E-07
DDR1_cg25655106	SOX10_cg15856662	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg27237814	SOX10_cg15856662	Myelin	0.81	8.21E-08	2.18E-06

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg27593250	SOX10_cg15856662	Myelin	0.79	2.97E-07	6.98E-06
DDR1_cg00466425	SOX10_cg19228755	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg00934322	SOX10_cg19228755	Myelin	0.75	2.85E-06	5.22E-05
DDR1_cg01598675	SOX10_cg19228755	Myelin	0.80	2.50E-07	5.95E-06
DDR1_cg01936707	SOX10_cg19228755	Myelin	0.85	4.11E-09	1.48E-07
DDR1_cg05703744	SOX10_cg19228755	Myelin	0.90	2.38E-11	1.66E-09
DDR1_cg06200824	SOX10_cg19228755	Myelin	0.84	1.59E-08	4.96E-07
DDR1_cg06501109	SOX10_cg19228755	Myelin	0.81	1.24E-07	3.16E-06
DDR1_cg07912416	SOX10_cg19228755	Myelin	0.90	2.71E-11	1.85E-09
DDR1_cg07979747	SOX10_cg19228755	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg08673763	SOX10_cg19228755	Myelin	0.88	2.78E-10	1.39E-08
DDR1_cg08684361	SOX10_cg19228755	Myelin	0.78	5.37E-07	1.19E-05
DDR1_cg08951271	SOX10_cg19228755	Myelin	0.88	4.01E-10	1.90E-08
DDR1_cg09965419	SOX10_cg19228755	Myelin	0.82	6.97E-08	1.88E-06
DDR1_cg11530564	SOX10_cg19228755	Myelin	0.90	2.09E-11	1.49E-09
DDR1_cg11676038	SOX10_cg19228755	Myelin	0.90	4.21E-11	2.72E-09
DDR1_cg12669395	SOX10_cg19228755	Myelin	0.88	2.24E-10	1.15E-08
DDR1_cg13329862	SOX10_cg19228755	Myelin	0.91	5.62E-12	4.93E-10
DDR1_cg13351860	SOX10_cg19228755	Myelin	0.91	4.18E-12	3.82E-10
DDR1_cg14790552	SOX10_cg19228755	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg15656686	SOX10_cg19228755	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg16111190	SOX10_cg19228755	Myelin	0.86	3.18E-09	1.17E-07
DDR1_cg16797094	SOX10_cg19228755	Myelin	0.95	7.99E-15	2.65E-12
DDR1_cg17176005	SOX10_cg19228755	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg17604312	SOX10_cg19228755	Myelin	0.82	6.10E-08	1.67E-06
DDR1_cg19215110	SOX10_cg19228755	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg19591099	SOX10_cg19228755	Myelin	0.80	2.42E-07	5.80E-06
DDR1_cg21677258	SOX10_cg19228755	Myelin	0.91	6.49E-12	5.56E-10
DDR1_cg24566261	SOX10_cg19228755	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg24636809	SOX10_cg19228755	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg24727290	SOX10_cg19228755	Myelin	0.83	1.99E-08	6.05E-07
DDR1_cg25613385	SOX10_cg19228755	Myelin	0.80	2.15E-07	5.20E-06
DDR1_cg25655106	SOX10_cg19228755	Myelin	0.91	1.40E-11	1.06E-09
DDR1_cg27237814	SOX10_cg19228755	Myelin	0.91	3.88E-12	3.59E-10
DDR1_cg27593250	SOX10_cg19228755	Myelin	0.77	9.16E-07	1.91E-05
DDR1_cg00466425	SOX10_cg19257200	Myelin	0.92	2.27E-12	2.31E-10
DDR1_cg00934322	SOX10_cg19257200	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg01598675	SOX10_cg19257200	Myelin	0.78	4.81E-07	1.07E-05
DDR1_cg01936707	SOX10_cg19257200	Myelin	0.93	1.14E-13	2.04E-11
DDR1_cg05703744	SOX10_cg19257200	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg06200824	SOX10_cg19257200	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg06501109	SOX10_cg19257200	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg07908039	SOX10_cg19257200	Myelin	0.82	7.20E-08	1.94E-06
DDR1_cg07912416	SOX10_cg19257200	Myelin	0.89	9.17E-11	5.29E-09
DDR1_cg07979747	SOX10_cg19257200	Myelin	0.89	1.22E-10	6.76E-09
DDR1_cg08673763	SOX10_cg19257200	Myelin	0.90	2.23E-11	1.58E-09
DDR1_cg08684361	SOX10_cg19257200	Myelin	0.77	1.22E-06	2.47E-05
DDR1_cg08951271	SOX10_cg19257200	Myelin	0.92	8.54E-13	1.03E-10
DDR1_cg09822812	SOX10_cg19257200	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg09965419	SOX10_cg19257200	Myelin	0.83	1.92E-08	5.86E-07

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg11530564	SOX10_cg19257200	Myelin	0.92	7.84E-13	9.64E-11
DDR1_cg11676038	SOX10_cg19257200	Myelin	0.95	6.22E-15	2.20E-12
DDR1_cg12669395	SOX10_cg19257200	Myelin	0.95	2.66E-15	1.21E-12
DDR1_cg12847793	SOX10_cg19257200	Myelin	0.79	3.15E-07	7.35E-06
DDR1_cg13329862	SOX10_cg19257200	Myelin	0.95	9.33E-15	2.95E-12
DDR1_cg13351860	SOX10_cg19257200	Myelin	0.92	1.79E-12	1.90E-10
DDR1_cg14058861	SOX10_cg19257200	Myelin	0.75	2.30E-06	4.33E-05
DDR1_cg14790552	SOX10_cg19257200	Myelin	0.88	4.67E-10	2.17E-08
DDR1_cg15656686	SOX10_cg19257200	Myelin	0.92	3.34E-12	3.17E-10
DDR1_cg16111190	SOX10_cg19257200	Myelin	0.89	7.69E-11	4.57E-09
DDR1_cg16797094	SOX10_cg19257200	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg17176005	SOX10_cg19257200	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg17604312	SOX10_cg19257200	Myelin	0.87	5.71E-10	2.58E-08
DDR1_cg19215110	SOX10_cg19257200	Myelin	0.82	5.52E-08	1.52E-06
DDR1_cg19591099	SOX10_cg19257200	Myelin	0.86	1.71E-09	6.76E-08
DDR1_cg21677258	SOX10_cg19257200	Myelin	0.93	4.65E-13	6.26E-11
DDR1_cg24566261	SOX10_cg19257200	Myelin	0.76	1.77E-06	3.43E-05
DDR1_cg24636809	SOX10_cg19257200	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg24727290	SOX10_cg19257200	Myelin	0.85	4.28E-09	1.53E-07
DDR1_cg25613385	SOX10_cg19257200	Myelin	0.75	2.98E-06	5.43E-05
DDR1_cg25655106	SOX10_cg19257200	Myelin	0.95	7.99E-15	2.65E-12
DDR1_cg27237814	SOX10_cg19257200	Myelin	0.90	1.71E-11	1.26E-09
DDR1_cg27593250	SOX10_cg19257200	Myelin	0.79	2.73E-07	6.44E-06
DDR1_cg00466425	SOX10_cg20754324	Myelin	0.85	7.31E-09	2.47E-07
DDR1_cg00934322	SOX10_cg20754324	Myelin	0.77	9.65E-07	2.00E-05
DDR1_cg01598675	SOX10_cg20754324	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg01936707	SOX10_cg20754324	Myelin	0.90	5.06E-11	3.18E-09
DDR1_cg05703744	SOX10_cg20754324	Myelin	0.91	1.22E-11	9.52E-10
DDR1_cg06200824	SOX10_cg20754324	Myelin	0.79	3.24E-07	7.55E-06
DDR1_cg06501109	SOX10_cg20754324	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg07908039	SOX10_cg20754324	Myelin	0.82	4.66E-08	1.31E-06
DDR1_cg07912416	SOX10_cg20754324	Myelin	0.89	6.83E-11	4.13E-09
DDR1_cg07979747	SOX10_cg20754324	Myelin	0.86	1.79E-09	7.04E-08
DDR1_cg08673763	SOX10_cg20754324	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg08684361	SOX10_cg20754324	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg08951271	SOX10_cg20754324	Myelin	0.90	5.71E-11	3.53E-09
DDR1_cg09822812	SOX10_cg20754324	Myelin	0.79	3.06E-07	7.17E-06
DDR1_cg09965419	SOX10_cg20754324	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg11530564	SOX10_cg20754324	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg11676038	SOX10_cg20754324	Myelin	0.88	3.09E-10	1.52E-08
DDR1_cg12669395	SOX10_cg20754324	Myelin	0.90	5.37E-11	3.35E-09
DDR1_cg12847793	SOX10_cg20754324	Myelin	0.80	2.09E-07	5.07E-06
DDR1_cg13329862	SOX10_cg20754324	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg13351860	SOX10_cg20754324	Myelin	0.95	7.11E-15	2.44E-12
DDR1_cg13660719	SOX10_cg20754324	Myelin	0.75	2.36E-06	4.42E-05
DDR1_cg13695585	SOX10_cg20754324	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg14790552	SOX10_cg20754324	Myelin	0.87	5.43E-10	2.47E-08
DDR1_cg15656686	SOX10_cg20754324	Myelin	0.92	2.65E-12	2.64E-10
DDR1_cg16111190	SOX10_cg20754324	Myelin	0.89	1.71E-10	9.06E-09
DDR1_cg16797094	SOX10_cg20754324	Myelin	0.94	2.93E-14	7.05E-12

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg17176005	SOX10_cg20754324	Myelin	0.88	2.93E-10	1.45E-08
DDR1_cg17604312	SOX10_cg20754324	Myelin	0.85	4.86E-09	1.71E-07
DDR1_cg19215110	SOX10_cg20754324	Myelin	0.80	2.03E-07	4.93E-06
DDR1_cg19591099	SOX10_cg20754324	Myelin	0.76	1.81E-06	3.50E-05
DDR1_cg20955507	SOX10_cg20754324	Myelin	0.78	7.04E-07	1.51E-05
DDR1_cg21677258	SOX10_cg20754324	Myelin	0.93	5.08E-13	6.78E-11
DDR1_cg24566261	SOX10_cg20754324	Myelin	0.78	5.22E-07	1.16E-05
DDR1_cg24636809	SOX10_cg20754324	Myelin	0.85	5.73E-09	1.99E-07
DDR1_cg24727290	SOX10_cg20754324	Myelin	0.82	4.82E-08	1.35E-06
DDR1_cg25613385	SOX10_cg20754324	Myelin	0.75	2.65E-06	4.91E-05
DDR1_cg25655106	SOX10_cg20754324	Myelin	0.92	2.10E-12	2.17E-10
DDR1_cg27237814	SOX10_cg20754324	Myelin	0.91	8.63E-12	7.11E-10
DDR1_cg27593250	SOX10_cg20754324	Myelin	0.76	1.38E-06	2.76E-05
DDR1_cg00466425	SOX10_cg23109891	Myelin	0.87	1.13E-09	4.68E-08
DDR1_cg00934322	SOX10_cg23109891	Myelin	0.77	8.69E-07	1.83E-05
DDR1_cg01936707	SOX10_cg23109891	Myelin	0.89	1.81E-10	9.50E-09
DDR1_cg05703744	SOX10_cg23109891	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg06200824	SOX10_cg23109891	Myelin	0.76	1.41E-06	2.82E-05
DDR1_cg06501109	SOX10_cg23109891	Myelin	0.85	4.66E-09	1.65E-07
DDR1_cg07912416	SOX10_cg23109891	Myelin	0.80	1.69E-07	4.19E-06
DDR1_cg07979747	SOX10_cg23109891	Myelin	0.75	2.53E-06	4.71E-05
DDR1_cg08673763	SOX10_cg23109891	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg08951271	SOX10_cg23109891	Myelin	0.87	6.96E-10	3.06E-08
DDR1_cg09965419	SOX10_cg23109891	Myelin	0.79	3.74E-07	8.58E-06
DDR1_cg11530564	SOX10_cg23109891	Myelin	0.89	1.29E-10	7.09E-09
DDR1_cg11676038	SOX10_cg23109891	Myelin	0.86	1.56E-09	6.24E-08
DDR1_cg12669395	SOX10_cg23109891	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg13329862	SOX10_cg23109891	Myelin	0.89	6.06E-11	3.72E-09
DDR1_cg13351860	SOX10_cg23109891	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg14058861	SOX10_cg23109891	Myelin	0.78	4.68E-07	1.05E-05
DDR1_cg14790552	SOX10_cg23109891	Myelin	0.84	1.42E-08	4.48E-07
DDR1_cg15656686	SOX10_cg23109891	Myelin	0.84	8.58E-09	2.86E-07
DDR1_cg16111190	SOX10_cg23109891	Myelin	0.87	7.31E-10	3.20E-08
DDR1_cg16797094	SOX10_cg23109891	Myelin	0.88	3.81E-10	1.82E-08
DDR1_cg17604312	SOX10_cg23109891	Myelin	0.79	3.53E-07	8.16E-06
DDR1_cg19215110	SOX10_cg23109891	Myelin	0.75	3.20E-06	5.78E-05
DDR1_cg19591099	SOX10_cg23109891	Myelin	0.82	3.79E-08	1.08E-06
DDR1_cg21677258	SOX10_cg23109891	Myelin	0.86	2.24E-09	8.58E-08
DDR1_cg24636809	SOX10_cg23109891	Myelin	0.84	1.22E-08	3.91E-07
DDR1_cg24727290	SOX10_cg23109891	Myelin	0.84	1.37E-08	4.33E-07
DDR1_cg25655106	SOX10_cg23109891	Myelin	0.89	1.53E-10	8.23E-09
DDR1_cg27237814	SOX10_cg23109891	Myelin	0.84	9.28E-09	3.06E-07
DDR1_cg27593250	SOX10_cg23109891	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg01936707	SOX10_cg24397874	Myelin	0.76	1.49E-06	2.95E-05
DDR1_cg08951271	SOX10_cg24397874	Myelin	0.75	2.72E-06	5.01E-05
DDR1_cg11676038	SOX10_cg24397874	Myelin	0.80	1.80E-07	4.43E-06
DDR1_cg12669395	SOX10_cg24397874	Myelin	0.75	2.59E-06	4.80E-05
DDR1_cg13329862	SOX10_cg24397874	Myelin	0.75	3.51E-06	6.27E-05
DDR1_cg20335906	SOX10_cg24397874	Myelin	0.78	6.15E-07	1.34E-05
DDR1_cg00466425	SOX10_cg25036707	Myelin	0.91	9.26E-12	7.51E-10

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg01936707	SOX10_cg25036707	Myelin	0.91	6.98E-12	5.91E-10
DDR1_cg05703744	SOX10_cg25036707	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg06200824	SOX10_cg25036707	Myelin	0.79	3.34E-07	7.75E-06
DDR1_cg06501109	SOX10_cg25036707	Myelin	0.86	3.04E-09	1.13E-07
DDR1_cg07908039	SOX10_cg25036707	Myelin	0.81	8.21E-08	2.18E-06
DDR1_cg07912416	SOX10_cg25036707	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg07979747	SOX10_cg25036707	Myelin	0.84	1.00E-08	3.29E-07
DDR1_cg08673763	SOX10_cg25036707	Myelin	0.85	3.61E-09	1.32E-07
DDR1_cg08951271	SOX10_cg25036707	Myelin	0.92	1.10E-12	1.27E-10
DDR1_cg09822812	SOX10_cg25036707	Myelin	0.75	3.27E-06	5.90E-05
DDR1_cg09965419	SOX10_cg25036707	Myelin	0.78	4.94E-07	1.10E-05
DDR1_cg11530564	SOX10_cg25036707	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg11676038	SOX10_cg25036707	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg12669395	SOX10_cg25036707	Myelin	0.88	3.26E-10	1.59E-08
DDR1_cg12847793	SOX10_cg25036707	Myelin	0.83	2.14E-08	6.46E-07
DDR1_cg13329862	SOX10_cg25036707	Myelin	0.90	1.95E-11	1.41E-09
DDR1_cg13351860	SOX10_cg25036707	Myelin	0.89	1.62E-10	8.64E-09
DDR1_cg14058861	SOX10_cg25036707	Myelin	0.77	9.16E-07	1.91E-05
DDR1_cg14790552	SOX10_cg25036707	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg15656686	SOX10_cg25036707	Myelin	0.85	6.74E-09	2.30E-07
DDR1_cg16111190	SOX10_cg25036707	Myelin	0.88	4.44E-10	2.07E-08
DDR1_cg16797094	SOX10_cg25036707	Myelin	0.85	7.02E-09	2.39E-07
DDR1_cg17176005	SOX10_cg25036707	Myelin	0.79	3.96E-07	9.02E-06
DDR1_cg17604312	SOX10_cg25036707	Myelin	0.86	2.34E-09	8.92E-08
DDR1_cg18577693	SOX10_cg25036707	Myelin	0.75	2.78E-06	5.11E-05
DDR1_cg19215110	SOX10_cg25036707	Myelin	0.76	2.04E-06	3.90E-05
DDR1_cg19591099	SOX10_cg25036707	Myelin	0.82	6.52E-08	1.77E-06
DDR1_cg21677258	SOX10_cg25036707	Myelin	0.89	1.03E-10	5.83E-09
DDR1_cg24566261	SOX10_cg25036707	Myelin	0.79	4.19E-07	9.49E-06
DDR1_cg24636809	SOX10_cg25036707	Myelin	0.85	3.77E-09	1.37E-07
DDR1_cg24727290	SOX10_cg25036707	Myelin	0.86	2.05E-09	7.94E-08
DDR1_cg25655106	SOX10_cg25036707	Myelin	0.91	9.93E-12	7.98E-10
DDR1_cg27237814	SOX10_cg25036707	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg27593250	SOX10_cg25036707	Myelin	0.81	1.32E-07	3.34E-06
DDR1_cg00466425	SOX10_cg25625951	Myelin	0.89	6.44E-11	3.93E-09
DDR1_cg00934322	SOX10_cg25625951	Myelin	0.77	1.31E-06	2.64E-05
DDR1_cg01936707	SOX10_cg25625951	Myelin	0.95	7.11E-15	2.44E-12
DDR1_cg05703744	SOX10_cg25625951	Myelin	0.93	2.46E-13	3.73E-11
DDR1_cg06200824	SOX10_cg25625951	Myelin	0.88	2.50E-10	1.26E-08
DDR1_cg06501109	SOX10_cg25625951	Myelin	0.83	1.92E-08	5.86E-07
DDR1_cg07908039	SOX10_cg25625951	Myelin	0.80	1.85E-07	4.55E-06
DDR1_cg07912416	SOX10_cg25625951	Myelin	0.91	1.06E-11	8.47E-10
DDR1_cg07979747	SOX10_cg25625951	Myelin	0.88	2.01E-10	1.05E-08
DDR1_cg08673763	SOX10_cg25625951	Myelin	0.87	9.77E-10	4.12E-08
DDR1_cg08684361	SOX10_cg25625951	Myelin	0.77	1.02E-06	2.10E-05
DDR1_cg08951271	SOX10_cg25625951	Myelin	0.90	1.83E-11	1.33E-09
DDR1_cg09965419	SOX10_cg25625951	Myelin	0.81	9.05E-08	2.38E-06
DDR1_cg11530564	SOX10_cg25625951	Myelin	0.94	2.09E-14	5.43E-12
DDR1_cg11676038	SOX10_cg25625951	Myelin	0.94	7.59E-14	1.48E-11
DDR1_cg12669395	SOX10_cg25625951	Myelin	0.95	2.00E-15	9.75E-13

Table S8. Adjusted significant correlation coefficients ≥ 0.75 for individual CpG 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in OC tissues *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13329862	SOX10_cg25625951	Myelin	0.91	7.49E-12	6.29E-10
DDR1_cg13351860	SOX10_cg25625951	Myelin	0.92	2.86E-12	2.79E-10
DDR1_cg14058861	SOX10_cg25625951	Myelin	0.75	2.41E-06	4.52E-05
DDR1_cg14790552	SOX10_cg25625951	Myelin	0.87	6.63E-10	2.93E-08
DDR1_cg15656686	SOX10_cg25625951	Myelin	0.91	5.22E-12	4.64E-10
DDR1_cg15720085	SOX10_cg25625951	Myelin	0.79	4.30E-07	9.73E-06
DDR1_cg16111190	SOX10_cg25625951	Myelin	0.93	2.96E-13	4.31E-11
DDR1_cg16797094	SOX10_cg25625951	Myelin	0.91	6.49E-12	5.56E-10
DDR1_cg17176005	SOX10_cg25625951	Myelin	0.83	2.76E-08	8.11E-07
DDR1_cg17604312	SOX10_cg25625951	Myelin	0.85	3.77E-09	1.37E-07
DDR1_cg18577693	SOX10_cg25625951	Myelin	0.76	1.90E-06	3.66E-05
DDR1_cg19215110	SOX10_cg25625951	Myelin	0.78	6.32E-07	1.37E-05
DDR1_cg19591099	SOX10_cg25625951	Myelin	0.86	2.67E-09	1.00E-07
DDR1_cg21677258	SOX10_cg25625951	Myelin	0.94	1.03E-13	1.89E-11
DDR1_cg24566261	SOX10_cg25625951	Myelin	0.78	7.23E-07	1.55E-05
DDR1_cg24636809	SOX10_cg25625951	Myelin	0.91	4.85E-12	4.35E-10
DDR1_cg24727290	SOX10_cg25625951	Myelin	0.84	9.65E-09	3.17E-07
DDR1_cg25613385	SOX10_cg25625951	Myelin	0.76	1.68E-06	3.28E-05
DDR1_cg25655106	SOX10_cg25625951	Myelin	0.92	9.29E-13	1.11E-10
DDR1_cg27237814	SOX10_cg25625951	Myelin	0.86	2.79E-09	1.04E-07
DDR1_cg27593250	SOX10_cg25625951	Myelin	0.79	2.97E-07	6.98E-06

[a]Spearman correlation coefficient.
[b]Post hoc Benjamini & Hochberg method for multiple testing correction.
Results sorted in alphabetical order by myelin gene name.
Abbreviations: 5-mC: 5-methylcytosine; OC: Oxcipital cortex.

Anexo 4. Artículo 2: Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC

DDR1 CpG	Gene CpG	Cell type marker	ρ[a]	*p*-value	Adj *p*-value[b]
DDR1_cg05703744	CNP_cg01443071	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg11676038	CNP_cg01443071	Myelin	0.92	<2.22E-16	<2.22E-16
DDR1_cg07912416	CNP_cg01443071	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg12316667	CNP_cg01443071	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg06200824	CNP_cg01443071	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg13218242	CNP_cg01443071	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg21677258	CNP_cg01443071	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg19591099	CNP_cg01443071	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg12669395	CNP_cg01443071	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg17604312	CNP_cg01443071	Myelin	0.82	1.00E-13	1.71E-11
DDR1_cg06501109	CNP_cg01443071	Myelin	0.81	1.67E-13	2.70E-11
DDR1_cg07979747	CNP_cg01443071	Myelin	0.79	2.55E-12	3.05E-10
DDR1_cg25655106	CNP_cg01443071	Myelin	0.78	5.61E-12	6.13E-10
DDR1_cg08673763	CNP_cg01443071	Myelin	0.76	4.01E-11	3.55E-09
DDR1_cg01598675	CNP_cg01443071	Myelin	0.75	1.42E-10	1.08E-08
DDR1_cg05703744	CNP_cg02357631	Myelin	0.94	<2.22E-16	<2.22E-16
DDR1_cg11676038	CNP_cg02357631	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg12669395	CNP_cg02357631	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg07912416	CNP_cg02357631	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12316667	CNP_cg02357631	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg19591099	CNP_cg02357631	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	CNP_cg02357631	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg21677258	CNP_cg02357631	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg13218242	CNP_cg02357631	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg17604312	CNP_cg02357631	Myelin	0.83	2.18E-14	4.32E-12
DDR1_cg06501109	CNP_cg02357631	Myelin	0.83	2.62E-14	5.14E-12
DDR1_cg25655106	CNP_cg02357631	Myelin	0.81	1.58E-13	2.57E-11
DDR1_cg07979747	CNP_cg02357631	Myelin	0.81	3.38E-13	5.04E-11
DDR1_cg08673763	CNP_cg02357631	Myelin	0.79	1.55E-12	1.96E-10
DDR1_cg16111190	CNP_cg02357631	Myelin	0.75	6.60E-11	5.47E-09
DDR1_cg27237814	CNP_cg02357631	Myelin	0.75	9.35E-11	7.43E-09
DDR1_cg21677258	CNP_cg04242650	Myelin	0.79	2.54E-12	3.04E-10
DDR1_cg05703744	CNP_cg04242650	Myelin	0.78	9.28E-12	9.68E-10
DDR1_cg06200824	CNP_cg04242650	Myelin	0.76	4.53E-11	3.94E-09
DDR1_cg05703744	CNP_cg09479341	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg11676038	CNP_cg09479341	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg21677258	CNP_cg09479341	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg07912416	CNP_cg09479341	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg06200824	CNP_cg09479341	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg12669395	CNP_cg09479341	Myelin	0.84	3.55E-15	8.58E-13
DDR1_cg19591099	CNP_cg09479341	Myelin	0.82	5.40E-14	9.79E-12
DDR1_cg12316667	CNP_cg09479341	Myelin	0.82	6.04E-14	1.08E-11
DDR1_cg13218242	CNP_cg09479341	Myelin	0.81	1.65E-13	2.66E-11
DDR1_cg08673763	CNP_cg09479341	Myelin	0.77	1.80E-11	1.75E-09

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg21677258	CNP_cg14376548	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg11676038	CNP_cg14376548	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg07912416	CNP_cg14376548	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	CNP_cg14376548	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg12316667	CNP_cg14376548	Myelin	0.85	1.11E-15	3.06E-13
DDR1_cg19591099	CNP_cg14376548	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg13218242	CNP_cg14376548	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg12669395	CNP_cg14376548	Myelin	0.84	1.78E-15	4.58E-13
DDR1_cg06501109	CNP_cg14376548	Myelin	0.81	2.35E-13	3.64E-11
DDR1_cg17604312	CNP_cg14376548	Myelin	0.81	3.28E-13	4.91E-11
DDR1_cg08673763	CNP_cg14376548	Myelin	0.77	2.45E-11	2.31E-09
DDR1_cg01598675	CNP_cg14376548	Myelin	0.76	3.60E-11	3.23E-09
DDR1_cg25655106	CNP_cg14376548	Myelin	0.76	5.93E-11	5.00E-09
DDR1_cg05703744	CNP_cg14826331	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg11676038	CNP_cg14826331	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg12316667	CNP_cg14826331	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg07912416	CNP_cg14826331	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg17604312	CNP_cg14826331	Myelin	0.85	1.11E-15	3.06E-13
DDR1_cg12669395	CNP_cg14826331	Myelin	0.84	2.89E-15	7.16E-13
DDR1_cg06200824	CNP_cg14826331	Myelin	0.84	7.11E-15	1.61E-12
DDR1_cg13218242	CNP_cg14826331	Myelin	0.84	7.55E-15	1.69E-12
DDR1_cg19591099	CNP_cg14826331	Myelin	0.83	1.20E-14	2.55E-12
DDR1_cg21677258	CNP_cg14826331	Myelin	0.83	2.00E-14	4.02E-12
DDR1_cg06501109	CNP_cg14826331	Myelin	0.79	1.54E-12	1.95E-10
DDR1_cg25655106	CNP_cg14826331	Myelin	0.76	5.26E-11	4.50E-09
DDR1_cg07979747	CNP_cg14826331	Myelin	0.75	9.20E-11	7.33E-09
DDR1_cg21677258	CNP_cg16563470	Myelin	0.82	7.59E-14	1.33E-11
DDR1_cg05703744	CNP_cg16563470	Myelin	0.80	1.15E-12	1.51E-10
DDR1_cg07912416	CNP_cg16563470	Myelin	0.76	3.54E-11	3.19E-09
DDR1_cg11676038	CNP_cg16563470	Myelin	0.75	6.90E-11	5.68E-09
DDR1_cg05703744	CNP_cg27435103	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg11676038	CNP_cg27435103	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg21677258	CNP_cg27435103	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg13218242	CNP_cg27435103	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg07912416	CNP_cg27435103	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg12316667	CNP_cg27435103	Myelin	0.84	2.66E-15	6.66E-13
DDR1_cg06200824	CNP_cg27435103	Myelin	0.84	3.77E-15	9.08E-13
DDR1_cg19591099	CNP_cg27435103	Myelin	0.84	4.22E-15	1.00E-12
DDR1_cg12669395	CNP_cg27435103	Myelin	0.81	1.78E-13	2.84E-11
DDR1_cg17604312	CNP_cg27435103	Myelin	0.81	1.95E-13	3.09E-11
DDR1_cg06501109	CNP_cg27435103	Myelin	0.76	2.90E-11	2.68E-09
DDR1_cg19591099	CNP_g23687677	Myelin	0.77	2.41E-11	2.28E-09
DDR1_cg06200824	CSPG4_cg02400942	Myelin	0.82	4.75E-14	8.74E-12
DDR1_cg11676038	CSPG4_cg02400942	Myelin	0.81	2.20E-13	3.43E-11
DDR1_cg05703744	CSPG4_cg02400942	Myelin	0.80	7.03E-13	9.71E-11
DDR1_cg19591099	CSPG4_cg02400942	Myelin	0.79	1.36E-12	1.75E-10
DDR1_cg07912416	CSPG4_cg02400942	Myelin	0.77	1.17E-11	1.19E-09
DDR1_cg15720085	CSPG4_cg02400942	Myelin	0.75	6.80E-11	5.61E-09
DDR1_cg12669395	CSPG4_cg02400942	Myelin	0.75	8.11E-11	6.57E-09

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg13218242	CSPG4_cg03238581	Myelin	0.76	4.46E-11	3.89E-09
DDR1_cg05703744	CSPG4_cg16682872	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg19591099	CSPG4_cg16682872	Myelin	0.82	3.42E-14	6.55E-12
DDR1_cg11676038	CSPG4_cg16682872	Myelin	0.82	5.60E-14	1.01E-11
DDR1_cg07912416	CSPG4_cg16682872	Myelin	0.79	2.25E-12	2.72E-10
DDR1_cg06200824	CSPG4_cg16682872	Myelin	0.78	6.92E-12	7.40E-10
DDR1_cg12316667	CSPG4_cg16682872	Myelin	0.76	2.59E-11	2.42E-09
DDR1_cg12669395	CSPG4_cg16682872	Myelin	0.76	4.61E-11	4.00E-09
DDR1_cg06501109	CSPG4_cg16682872	Myelin	0.75	1.44E-10	1.09E-08
DDR1_cg21677258	CSPG4_cg16682872	Myelin	0.75	1.54E-10	1.15E-08
DDR1_cg06200824	CSPG4_cg21815847	Myelin	0.75	8.21E-11	6.63E-09
DDR1_cg24727290	MAG_cg00162517	Myelin	0.83	2.04E-14	4.09E-12
DDR1_cg02695062	MAG_cg00162517	Myelin	0.81	1.52E-13	2.48E-11
DDR1_cg08951271	MAG_cg00162517	Myelin	0.80	7.77E-13	1.06E-10
DDR1_cg25655106	MAG_cg00162517	Myelin	0.79	2.74E-12	3.26E-10
DDR1_cg13329862	MAG_cg00162517	Myelin	0.77	1.06E-11	1.09E-09
DDR1_cg08673763	MAG_cg00162517	Myelin	0.76	3.16E-11	2.88E-09
DDR1_cg18093866	MAG_cg00162517	Myelin	0.76	4.99E-11	4.30E-09
DDR1_cg07803420	MAG_cg00162517	Myelin	0.76	6.46E-11	5.38E-09
DDR1_cg16111190	MAG_cg00162517	Myelin	0.75	9.69E-11	7.67E-09
DDR1_cg05703744	MAG_cg01349478	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg01349478	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg07912416	MAG_cg01349478	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg19591099	MAG_cg01349478	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg12669395	MAG_cg01349478	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg06200824	MAG_cg01349478	Myelin	0.85	1.55E-15	4.11E-13
DDR1_cg12316667	MAG_cg01349478	Myelin	0.84	1.78E-15	4.58E-13
DDR1_cg21677258	MAG_cg01349478	Myelin	0.83	8.44E-15	1.86E-12
DDR1_cg13218242	MAG_cg01349478	Myelin	0.82	7.06E-14	1.24E-11
DDR1_cg25655106	MAG_cg01349478	Myelin	0.81	3.10E-13	4.67E-11
DDR1_cg08673763	MAG_cg01349478	Myelin	0.80	4.41E-13	6.37E-11
DDR1_cg06501109	MAG_cg01349478	Myelin	0.79	1.57E-12	1.98E-10
DDR1_cg16111190	MAG_cg01349478	Myelin	0.79	2.06E-12	2.52E-10
DDR1_cg17604312	MAG_cg01349478	Myelin	0.79	2.94E-12	3.46E-10
DDR1_cg06200824	MAG_cg05055150	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg05703744	MAG_cg05055150	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg19591099	MAG_cg05055150	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg05055150	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	MAG_cg05055150	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg07912416	MAG_cg05055150	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12316667	MAG_cg05055150	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg25655106	MAG_cg05055150	Myelin	0.83	2.09E-14	4.17E-12
DDR1_cg21677258	MAG_cg05055150	Myelin	0.82	3.69E-14	6.99E-12
DDR1_cg06501109	MAG_cg05055150	Myelin	0.79	2.84E-12	3.36E-10
DDR1_cg15720085	MAG_cg05055150	Myelin	0.78	4.09E-12	4.64E-10
DDR1_cg13218242	MAG_cg05055150	Myelin	0.78	5.91E-12	6.43E-10
DDR1_cg17604312	MAG_cg05055150	Myelin	0.78	7.33E-12	7.80E-10
DDR1_cg16111190	MAG_cg05055150	Myelin	0.77	1.35E-11	1.35E-09
DDR1_cg01598675	MAG_cg05055150	Myelin	0.75	1.28E-10	9.76E-09

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07803420	MAG_cg05663558	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg08951271	MAG_cg05663558	Myelin	0.82	3.40E-14	6.51E-12
DDR1_cg24727290	MAG_cg05663558	Myelin	0.81	2.25E-13	3.50E-11
DDR1_cg02695062	MAG_cg05663558	Myelin	0.80	1.05E-12	1.39E-10
DDR1_cg25655106	MAG_cg05663558	Myelin	0.79	2.26E-12	2.74E-10
DDR1_cg16111190	MAG_cg05663558	Myelin	0.78	3.82E-12	4.37E-10
DDR1_cg13329862	MAG_cg05663558	Myelin	0.78	5.34E-12	5.88E-10
DDR1_cg08673763	MAG_cg05663558	Myelin	0.77	1.36E-11	1.36E-09
DDR1_cg05703744	MAG_cg08585489	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg08585489	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg19591099	MAG_cg08585489	Myelin	0.92	<2.22E-16	<2.22E-16
DDR1_cg06200824	MAG_cg08585489	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg12669395	MAG_cg08585489	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg12316667	MAG_cg08585489	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg21677258	MAG_cg08585489	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg07912416	MAG_cg08585489	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg25655106	MAG_cg08585489	Myelin	0.84	5.33E-15	1.24E-12
DDR1_cg17604312	MAG_cg08585489	Myelin	0.80	9.41E-13	1.26E-10
DDR1_cg06501109	MAG_cg08585489	Myelin	0.79	1.67E-12	2.09E-10
DDR1_cg13218242	MAG_cg08585489	Myelin	0.79	1.81E-12	2.25E-10
DDR1_cg08673763	MAG_cg08585489	Myelin	0.77	1.39E-11	1.38E-09
DDR1_cg15720085	MAG_cg08585489	Myelin	0.76	2.63E-11	2.45E-09
DDR1_cg16111190	MAG_cg08585489	Myelin	0.75	1.50E-10	1.13E-08
DDR1_cg05703744	MAG_cg10618943	Myelin	0.80	7.21E-13	9.94E-11
DDR1_cg11676038	MAG_cg10618943	Myelin	0.79	2.45E-12	2.95E-10
DDR1_cg12316667	MAG_cg10618943	Myelin	0.78	3.80E-12	4.35E-10
DDR1_cg07912416	MAG_cg10618943	Myelin	0.77	9.76E-12	1.01E-09
DDR1_cg06200824	MAG_cg10618943	Myelin	0.75	8.56E-11	6.88E-09
DDR1_cg05703744	MAG_cg11902728	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg11902728	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg19591099	MAG_cg11902728	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg07912416	MAG_cg11902728	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	MAG_cg11902728	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12316667	MAG_cg11902728	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	MAG_cg11902728	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg13218242	MAG_cg11902728	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg21677258	MAG_cg11902728	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg17604312	MAG_cg11902728	Myelin	0.84	5.33E-15	1.24E-12
DDR1_cg25655106	MAG_cg11902728	Myelin	0.82	1.08E-13	1.83E-11
DDR1_cg06501109	MAG_cg11902728	Myelin	0.81	3.04E-13	4.59E-11
DDR1_cg07979747	MAG_cg11902728	Myelin	0.78	7.59E-12	8.06E-10
DDR1_cg01598675	MAG_cg11902728	Myelin	0.76	4.72E-11	4.09E-09
DDR1_cg05703744	MAG_cg12402033	Myelin	0.92	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg12402033	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg21677258	MAG_cg12402033	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg19591099	MAG_cg12402033	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg06200824	MAG_cg12402033	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12316667	MAG_cg12402033	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12669395	MAG_cg12402033	Myelin	0.87	<2.22E-16	<2.22E-16

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07912416	MAG_cg12402033	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg13218242	MAG_cg12402033	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg06501109	MAG_cg12402033	Myelin	0.79	1.30E-12	1.68E-10
DDR1_cg25655106	MAG_cg12402033	Myelin	0.79	2.99E-12	3.51E-10
DDR1_cg17604312	MAG_cg12402033	Myelin	0.78	4.09E-12	4.64E-10
DDR1_cg08673763	MAG_cg12402033	Myelin	0.78	7.82E-12	8.29E-10
DDR1_cg01598675	MAG_cg12402033	Myelin	0.76	2.98E-11	2.75E-09
DDR1_cg15720085	MAG_cg12402033	Myelin	0.75	7.64E-11	6.23E-09
DDR1_cg25655106	MAG_cg14535518	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	MAG_cg14535518	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg08951271	MAG_cg14535518	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg16111190	MAG_cg14535518	Myelin	0.82	7.06E-14	1.24E-11
DDR1_cg24727290	MAG_cg14535518	Myelin	0.81	1.48E-13	2.42E-11
DDR1_cg12316667	MAG_cg14535518	Myelin	0.80	4.21E-13	6.11E-11
DDR1_cg13329862	MAG_cg14535518	Myelin	0.80	5.17E-13	7.38E-11
DDR1_cg11676038	MAG_cg14535518	Myelin	0.79	1.51E-12	1.92E-10
DDR1_cg27237814	MAG_cg14535518	Myelin	0.79	1.90E-12	2.35E-10
DDR1_cg07803420	MAG_cg14535518	Myelin	0.79	2.23E-12	2.71E-10
DDR1_cg19591099	MAG_cg14535518	Myelin	0.79	2.41E-12	2.90E-10
DDR1_cg08673763	MAG_cg14535518	Myelin	0.78	5.27E-12	5.80E-10
DDR1_cg05703744	MAG_cg14535518	Myelin	0.77	1.30E-11	1.30E-09
DDR1_cg02695062	MAG_cg14535518	Myelin	0.77	2.15E-11	2.05E-09
DDR1_cg17604312	MAG_cg14535518	Myelin	0.75	8.58E-11	6.88E-09
DDR1_cg06200824	MAG_cg14535518	Myelin	0.75	9.83E-11	7.76E-09
DDR1_cg18093866	MAG_cg14535518	Myelin	0.75	1.21E-10	9.32E-09
DDR1_cg06501109	MAG_cg14535518	Myelin	0.75	1.43E-10	1.08E-08
DDR1_cg11676038	MAG_cg15005368	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg05703744	MAG_cg15005368	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg13218242	MAG_cg15005368	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg07912416	MAG_cg15005368	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg12669395	MAG_cg15005368	Myelin	0.84	6.22E-15	1.43E-12
DDR1_cg12316667	MAG_cg15005368	Myelin	0.83	1.11E-14	2.37E-12
DDR1_cg19591099	MAG_cg15005368	Myelin	0.83	1.78E-14	3.63E-12
DDR1_cg21677258	MAG_cg15005368	Myelin	0.80	4.10E-13	5.97E-11
DDR1_cg06200824	MAG_cg15005368	Myelin	0.79	1.32E-12	1.70E-10
DDR1_cg01598675	MAG_cg15005368	Myelin	0.77	1.45E-11	1.44E-09
DDR1_cg25655106	MAG_cg15005368	Myelin	0.76	2.96E-11	2.73E-09
DDR1_cg17604312	MAG_cg15005368	Myelin	0.76	3.01E-11	2.77E-09
DDR1_cg07979747	MAG_cg15005368	Myelin	0.76	3.04E-11	2.79E-09
DDR1_cg25655106	MAG_cg15761414	Myelin	0.79	1.26E-12	1.63E-10
DDR1_cg12316667	MAG_cg15761414	Myelin	0.77	2.34E-11	2.22E-09
DDR1_cg12669395	MAG_cg17096126	Myelin	0.92	<2.22E-16	<2.22E-16
DDR1_cg19591099	MAG_cg17096126	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg17096126	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg12316667	MAG_cg17096126	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg25655106	MAG_cg17096126	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg05703744	MAG_cg17096126	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg06200824	MAG_cg17096126	Myelin	0.83	1.89E-14	3.83E-12
DDR1_cg13218242	MAG_cg17096126	Myelin	0.83	2.26E-14	4.48E-12

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg07912416	MAG_cg17096126	Myelin	0.82	4.29E-14	7.99E-12
DDR1_cg06501109	MAG_cg17096126	Myelin	0.82	4.37E-14	8.14E-12
DDR1_cg17604312	MAG_cg17096126	Myelin	0.82	8.48E-14	1.47E-11
DDR1_cg16111190	MAG_cg17096126	Myelin	0.79	1.58E-12	1.99E-10
DDR1_cg21677258	MAG_cg17096126	Myelin	0.79	1.76E-12	2.19E-10
DDR1_cg08673763	MAG_cg17096126	Myelin	0.78	4.57E-12	5.11E-10
DDR1_cg27237814	MAG_cg17096126	Myelin	0.78	4.84E-12	5.39E-10
DDR1_cg08951271	MAG_cg17096126	Myelin	0.78	5.31E-12	5.84E-10
DDR1_cg24727290	MAG_cg17096126	Myelin	0.76	6.14E-11	5.15E-09
DDR1_cg01598675	MAG_cg17096126	Myelin	0.75	1.13E-10	8.77E-09
DDR1_cg16111190	MAG_cg21305926	Myelin	0.75	8.83E-11	7.06E-09
DDR1_cg11676038	MAG_cg22266001	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg05703744	MAG_cg22266001	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	MAG_cg22266001	Myelin	0.84	3.11E-15	7.61E-13
DDR1_cg17604312	MAG_cg22266001	Myelin	0.83	2.60E-14	5.11E-12
DDR1_cg12316667	MAG_cg22266001	Myelin	0.82	3.64E-14	6.92E-12
DDR1_cg21677258	MAG_cg22266001	Myelin	0.82	6.26E-14	1.11E-11
DDR1_cg07912416	MAG_cg22266001	Myelin	0.82	9.17E-14	1.57E-11
DDR1_cg19591099	MAG_cg22266001	Myelin	0.81	2.75E-13	4.20E-11
DDR1_cg12669395	MAG_cg22266001	Myelin	0.79	1.85E-12	2.29E-10
DDR1_cg13218242	MAG_cg22266001	Myelin	0.79	3.31E-12	3.85E-10
DDR1_cg06501109	MAG_cg22266001	Myelin	0.76	3.38E-11	3.06E-09
DDR1_cg05703744	MAG_cg27017562	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg11676038	MAG_cg27017562	Myelin	0.92	<2.22E-16	<2.22E-16
DDR1_cg19591099	MAG_cg27017562	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg06200824	MAG_cg27017562	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	MAG_cg27017562	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12316667	MAG_cg27017562	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg25655106	MAG_cg27017562	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg07912416	MAG_cg27017562	Myelin	0.84	2.00E-15	5.11E-13
DDR1_cg21677258	MAG_cg27017562	Myelin	0.84	3.55E-15	8.58E-13
DDR1_cg06501109	MAG_cg27017562	Myelin	0.80	6.31E-13	8.81E-11
DDR1_cg13218242	MAG_cg27017562	Myelin	0.80	1.12E-12	1.47E-10
DDR1_cg17604312	MAG_cg27017562	Myelin	0.79	3.24E-12	3.77E-10
DDR1_cg15720085	MAG_cg27017562	Myelin	0.78	4.52E-12	5.07E-10
DDR1_cg08673763	MAG_cg27017562	Myelin	0.77	1.61E-11	1.58E-09
DDR1_cg16111190	MAG_cg27017562	Myelin	0.76	4.23E-11	3.73E-09
DDR1_cg05703744	MBP_cg00735329	Myelin	0.83	2.33E-14	4.61E-12
DDR1_cg12316667	MBP_cg00735329	Myelin	0.81	3.48E-13	5.17E-11
DDR1_cg21677258	MBP_cg00735329	Myelin	0.80	8.52E-13	1.16E-10
DDR1_cg19591099	MBP_cg00735329	Myelin	0.80	8.67E-13	1.18E-10
DDR1_cg12669395	MBP_cg00735329	Myelin	0.80	1.05E-12	1.39E-10
DDR1_cg11676038	MBP_cg00735329	Myelin	0.79	2.02E-12	2.48E-10
DDR1_cg25655106	MBP_cg00735329	Myelin	0.79	2.33E-12	2.81E-10
DDR1_cg07912416	MBP_cg00735329	Myelin	0.76	4.27E-11	3.75E-09
DDR1_cg13218242	MBP_cg00735329	Myelin	0.75	7.53E-11	6.15E-09
DDR1_cg07979747	MBP_cg00735329	Myelin	0.75	1.50E-10	1.13E-08
DDR1_cg05703744	MBP_cg01475204	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg21677258	MBP_cg01475204	Myelin	0.84	5.33E-15	1.24E-12

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg11676038	MBP_cg01475204	Myelin	0.81	2.08E-13	3.28E-11
DDR1_cg13218242	MBP_cg01475204	Myelin	0.79	2.49E-12	2.99E-10
DDR1_cg07912416	MBP_cg01475204	Myelin	0.78	4.45E-12	5.00E-10
DDR1_cg06200824	MBP_cg01475204	Myelin	0.77	9.82E-12	1.02E-09
DDR1_cg12316667	MBP_cg01475204	Myelin	0.77	1.29E-11	1.29E-09
DDR1_cg07979747	MBP_cg01475204	Myelin	0.77	1.51E-11	1.49E-09
DDR1_cg12669395	MBP_cg01475204	Myelin	0.76	4.04E-11	3.57E-09
DDR1_cg11676038	MBP_cg02782187	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg05703744	MBP_cg02782187	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg19591099	MBP_cg02782187	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg12316667	MBP_cg02782187	Myelin	0.84	7.77E-15	1.74E-12
DDR1_cg07912416	MBP_cg02782187	Myelin	0.83	1.89E-14	3.83E-12
DDR1_cg06200824	MBP_cg02782187	Myelin	0.83	2.58E-14	5.07E-12
DDR1_cg21677258	MBP_cg02782187	Myelin	0.82	7.73E-14	1.35E-11
DDR1_cg12669395	MBP_cg02782187	Myelin	0.80	4.04E-13	5.90E-11
DDR1_cg17604312	MBP_cg02782187	Myelin	0.80	4.25E-13	6.16E-11
DDR1_cg13218242	MBP_cg02782187	Myelin	0.78	7.95E-12	8.41E-10
DDR1_cg25655106	MBP_cg02782187	Myelin	0.77	2.36E-11	2.23E-09
DDR1_cg06501109	MBP_cg02782187	Myelin	0.77	2.49E-11	2.34E-09
DDR1_cg05703744	MBP_cg06410824	Myelin	0.75	9.83E-11	7.76E-09
DDR1_cg07912416	MBP_cg06543730	Myelin	0.80	5.21E-13	7.42E-11
DDR1_cg05703744	MBP_cg06543730	Myelin	0.76	3.58E-11	3.22E-09
DDR1_cg11676038	MBP_cg06548292	Myelin	0.83	2.53E-14	4.98E-12
DDR1_cg12316667	MBP_cg06548292	Myelin	0.82	4.51E-14	8.36E-12
DDR1_cg19591099	MBP_cg06548292	Myelin	0.77	1.34E-11	1.34E-09
DDR1_cg12669395	MBP_cg06548292	Myelin	0.77	1.49E-11	1.47E-09
DDR1_cg06200824	MBP_cg06548292	Myelin	0.76	6.46E-11	5.38E-09
DDR1_cg12669395	MBP_cg06773488	Myelin	0.80	8.70E-13	1.18E-10
DDR1_cg05703744	MBP_cg06773488	Myelin	0.76	3.81E-11	3.40E-09
DDR1_cg16111190	MBP_cg06773488	Myelin	0.75	1.15E-10	8.93E-09
DDR1_cg12316667	MBP_cg08176598	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg08176598	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	MBP_cg08176598	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg19591099	MBP_cg08176598	Myelin	0.85	1.11E-15	3.06E-13
DDR1_cg17604312	MBP_cg08176598	Myelin	0.84	2.00E-15	5.11E-13
DDR1_cg05703744	MBP_cg08176598	Myelin	0.84	3.11E-15	7.61E-13
DDR1_cg25655106	MBP_cg08176598	Myelin	0.82	6.93E-14	1.22E-11
DDR1_cg06501109	MBP_cg08176598	Myelin	0.80	8.75E-13	1.18E-10
DDR1_cg06200824	MBP_cg08176598	Myelin	0.76	3.35E-11	3.04E-09
DDR1_cg25655106	MBP_cg08936202	Myelin	0.79	2.81E-12	3.34E-10
DDR1_cg21677258	MBP_cg08936202	Myelin	0.78	4.23E-12	4.78E-10
DDR1_cg07912416	MBP_cg08936202	Myelin	0.77	1.24E-11	1.25E-09
DDR1_cg13218242	MBP_cg08936202	Myelin	0.77	1.70E-11	1.66E-09
DDR1_cg08673763	MBP_cg08936202	Myelin	0.77	1.75E-11	1.71E-09
DDR1_cg05703744	MBP_cg08936202	Myelin	0.77	2.10E-11	2.01E-09
DDR1_cg12669395	MBP_cg08936202	Myelin	0.76	3.06E-11	2.80E-09
DDR1_cg19591099	MBP_cg08936202	Myelin	0.75	7.47E-11	6.12E-09
DDR1_cg12316667	MBP_cg08936202	Myelin	0.75	1.30E-10	9.91E-09
DDR1_cg12669395	MBP_cg10542482	Myelin	-0.75	1.24E-10	9.52E-09

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg11676038	MBP_cg10542482	Myelin	-0.75	9.37E-11	7.45E-09
DDR1_cg24727290	MBP_cg10542482	Myelin	-0.75	8.21E-11	6.63E-09
DDR1_cg08951271	MBP_cg10542482	Myelin	-0.76	6.46E-11	5.38E-09
DDR1_cg19591099	MBP_cg10542482	Myelin	-0.76	3.90E-11	3.46E-09
DDR1_cg05703744	MBP_cg10542482	Myelin	-0.78	5.53E-12	6.06E-10
DDR1_cg25655106	MBP_cg10542482	Myelin	-0.79	1.95E-12	2.41E-10
DDR1_cg12316667	MBP_cg10542482	Myelin	-0.82	1.09E-13	1.84E-11
DDR1_cg05703744	MBP_cg11195910	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg11195910	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg07912416	MBP_cg11195910	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg12316667	MBP_cg11195910	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg12669395	MBP_cg11195910	Myelin	0.84	3.11E-15	7.61E-13
DDR1_cg06200824	MBP_cg11195910	Myelin	0.84	5.33E-15	1.24E-12
DDR1_cg19591099	MBP_cg11195910	Myelin	0.82	9.99E-14	1.70E-11
DDR1_cg21677258	MBP_cg11195910	Myelin	0.81	1.23E-13	2.05E-11
DDR1_cg13218242	MBP_cg11195910	Myelin	0.81	2.01E-13	3.17E-11
DDR1_cg17604312	MBP_cg11195910	Myelin	0.78	4.03E-12	4.58E-10
DDR1_cg25655106	MBP_cg11195910	Myelin	0.77	1.35E-11	1.35E-09
DDR1_cg27237814	MBP_cg11195910	Myelin	0.75	6.55E-11	5.44E-09
DDR1_cg08673763	MBP_cg11195910	Myelin	0.75	9.22E-11	7.33E-09
DDR1_cg07912416	MBP_cg11772665	Myelin	0.84	3.11E-15	7.61E-13
DDR1_cg21677258	MBP_cg11772665	Myelin	0.81	1.13E-13	1.89E-11
DDR1_cg05703744	MBP_cg11772665	Myelin	0.81	2.17E-13	3.39E-11
DDR1_cg11676038	MBP_cg11772665	Myelin	0.79	2.04E-12	2.50E-10
DDR1_cg13218242	MBP_cg11772665	Myelin	0.76	3.23E-11	2.94E-09
DDR1_cg12316667	MBP_cg11772665	Myelin	0.75	8.96E-11	7.15E-09
DDR1_cg06200824	MBP_cg11772665	Myelin	0.75	9.83E-11	7.76E-09
DDR1_cg21677258	MBP_cg12433779	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg05703744	MBP_cg12433779	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg06200824	MBP_cg12433779	Myelin	0.85	1.78E-15	4.58E-13
DDR1_cg07912416	MBP_cg12433779	Myelin	0.84	2.00E-15	5.11E-13
DDR1_cg11676038	MBP_cg12433779	Myelin	0.81	1.77E-13	2.83E-11
DDR1_cg12316667	MBP_cg12433779	Myelin	0.80	5.22E-13	7.43E-11
DDR1_cg06501109	MBP_cg12433779	Myelin	0.76	4.50E-11	3.92E-09
DDR1_cg19591099	MBP_cg12433779	Myelin	0.76	6.36E-11	5.32E-09
DDR1_cg05703744	MBP_cg13141061	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg13141061	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	MBP_cg13141061	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12316667	MBP_cg13141061	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg07912416	MBP_cg13141061	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg12669395	MBP_cg13141061	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg21677258	MBP_cg13141061	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg19591099	MBP_cg13141061	Myelin	0.84	5.11E-15	1.19E-12
DDR1_cg06501109	MBP_cg13141061	Myelin	0.80	8.36E-13	1.14E-10
DDR1_cg13218242	MBP_cg13141061	Myelin	0.77	1.27E-11	1.27E-09
DDR1_cg17604312	MBP_cg13141061	Myelin	0.77	2.04E-11	1.95E-09
DDR1_cg25655106	MBP_cg13141061	Myelin	0.76	3.35E-11	3.04E-09
DDR1_cg07979747	MBP_cg13141061	Myelin	0.76	6.50E-11	5.41E-09
DDR1_cg05703744	MBP_cg13807269	Myelin	0.90	<2.22E-16	<2.22E-16

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg21677258	MBP_cg13807269	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg07912416	MBP_cg13807269	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg13807269	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg13218242	MBP_cg13807269	Myelin	0.84	4.88E-15	1.15E-12
DDR1_cg12316667	MBP_cg13807269	Myelin	0.83	2.26E-14	4.48E-12
DDR1_cg06200824	MBP_cg13807269	Myelin	0.82	4.24E-14	7.92E-12
DDR1_cg12669395	MBP_cg13807269	Myelin	0.81	2.18E-13	3.41E-11
DDR1_cg07979747	MBP_cg13807269	Myelin	0.80	5.14E-13	7.34E-11
DDR1_cg19591099	MBP_cg13807269	Myelin	0.80	6.29E-13	8.79E-11
DDR1_cg17604312	MBP_cg13807269	Myelin	0.77	2.15E-11	2.05E-09
DDR1_cg06501109	MBP_cg13807269	Myelin	0.75	8.09E-11	6.56E-09
DDR1_cg11676038	MBP_cg14078587	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12316667	MBP_cg14078587	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg19591099	MBP_cg14078587	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg17604312	MBP_cg14078587	Myelin	0.85	6.66E-16	1.96E-13
DDR1_cg05703744	MBP_cg14078587	Myelin	0.85	1.78E-15	4.58E-13
DDR1_cg06200824	MBP_cg14078587	Myelin	0.84	4.88E-15	1.15E-12
DDR1_cg13218242	MBP_cg14078587	Myelin	0.83	1.82E-14	3.71E-12
DDR1_cg07912416	MBP_cg14078587	Myelin	0.83	1.87E-14	3.79E-12
DDR1_cg06501109	MBP_cg14078587	Myelin	0.82	3.91E-14	7.37E-12
DDR1_cg12669395	MBP_cg14078587	Myelin	0.81	2.95E-13	4.48E-11
DDR1_cg25655106	MBP_cg14078587	Myelin	0.80	6.23E-13	8.72E-11
DDR1_cg07979747	MBP_cg14078587	Myelin	0.76	3.75E-11	3.35E-09
DDR1_cg21677258	MBP_cg14078587	Myelin	0.76	4.30E-11	3.78E-09
DDR1_cg05703744	MBP_cg14298244	Myelin	0.75	6.60E-11	5.47E-09
DDR1_cg05703744	MBP_cg14946295	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg14946295	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg06200824	MBP_cg14946295	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg07912416	MBP_cg14946295	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12316667	MBP_cg14946295	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg12669395	MBP_cg14946295	Myelin	0.84	3.55E-15	8.58E-13
DDR1_cg21677258	MBP_cg14946295	Myelin	0.83	9.10E-15	2.00E-12
DDR1_cg19591099	MBP_cg14946295	Myelin	0.82	6.00E-14	1.07E-11
DDR1_cg13218242	MBP_cg14946295	Myelin	0.81	1.67E-13	2.68E-11
DDR1_cg06501109	MBP_cg14946295	Myelin	0.80	1.05E-12	1.39E-10
DDR1_cg17604312	MBP_cg14946295	Myelin	0.80	1.08E-12	1.42E-10
DDR1_cg07979747	MBP_cg14946295	Myelin	0.79	2.56E-12	3.06E-10
DDR1_cg05703744	MBP_cg15495463	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg06200824	MBP_cg15495463	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg07912416	MBP_cg15495463	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg15495463	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg12669395	MBP_cg15495463	Myelin	0.84	4.00E-15	9.53E-13
DDR1_cg12316667	MBP_cg15495463	Myelin	0.83	1.82E-14	3.71E-12
DDR1_cg19591099	MBP_cg15495463	Myelin	0.82	5.17E-14	9.42E-12
DDR1_cg06501109	MBP_cg15495463	Myelin	0.82	9.50E-14	1.62E-11
DDR1_cg21677258	MBP_cg15495463	Myelin	0.81	1.21E-13	2.02E-11
DDR1_cg13218242	MBP_cg15495463	Myelin	0.80	1.11E-12	1.45E-10
DDR1_cg15720085	MBP_cg15495463	Myelin	0.78	5.91E-12	6.43E-10
DDR1_cg25655106	MBP_cg15495463	Myelin	0.75	8.96E-11	7.15E-09

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg01598675	MBP_cg15495463	Myelin	0.75	9.63E-11	7.63E-09
DDR1_cg12316667	MBP_cg16305018	Myelin	0.79	1.90E-12	2.35E-10
DDR1_cg12669395	MBP_cg16305018	Myelin	0.76	3.40E-11	3.08E-09
DDR1_cg05703744	MBP_cg16305018	Myelin	0.76	5.62E-11	4.76E-09
DDR1_cg12316667	MBP_cg18892054	Myelin	0.83	9.33E-15	2.03E-12
DDR1_cg11676038	MBP_cg18892054	Myelin	0.80	3.91E-13	5.73E-11
DDR1_cg19591099	MBP_cg18892054	Myelin	0.80	1.16E-12	1.51E-10
DDR1_cg17604312	MBP_cg18892054	Myelin	0.79	2.91E-12	3.44E-10
DDR1_cg06200824	MBP_cg18892054	Myelin	0.78	3.49E-12	4.03E-10
DDR1_cg05703744	MBP_cg18892054	Myelin	0.78	5.14E-12	5.66E-10
DDR1_cg15720085	MBP_cg18892054	Myelin	0.75	1.56E-10	1.17E-08
DDR1_cg05703744	MBP_cg21107579	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg21107579	Myelin	0.85	6.66E-16	1.96E-13
DDR1_cg07912416	MBP_cg21107579	Myelin	0.84	4.00E-15	9.53E-13
DDR1_cg12669395	MBP_cg21107579	Myelin	0.84	5.11E-15	1.19E-12
DDR1_cg21677258	MBP_cg21107579	Myelin	0.83	1.95E-14	3.95E-12
DDR1_cg12316667	MBP_cg21107579	Myelin	0.82	6.31E-14	1.12E-11
DDR1_cg06200824	MBP_cg21107579	Myelin	0.81	2.48E-13	3.82E-11
DDR1_cg19591099	MBP_cg21107579	Myelin	0.78	3.58E-12	4.12E-10
DDR1_cg16111190	MBP_cg21107579	Myelin	0.76	2.86E-11	2.64E-09
DDR1_cg13218242	MBP_cg21107579	Myelin	0.76	3.16E-11	2.88E-09
DDR1_cg17604312	MBP_cg21107579	Myelin	0.76	4.36E-11	3.82E-09
DDR1_cg07979747	MBP_cg21107579	Myelin	0.75	1.23E-10	9.50E-09
DDR1_cg07912416	MBP_cg22239325	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg05703744	MBP_cg22239325	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg06501109	MBP_cg22239325	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg06200824	MBP_cg22239325	Myelin	0.84	2.22E-15	5.63E-13
DDR1_cg11676038	MBP_cg22239325	Myelin	0.83	8.88E-15	1.95E-12
DDR1_cg21677258	MBP_cg22239325	Myelin	0.83	1.60E-14	3.32E-12
DDR1_cg12316667	MBP_cg22239325	Myelin	0.83	2.75E-14	5.38E-12
DDR1_cg19591099	MBP_cg22239325	Myelin	0.80	6.12E-13	8.57E-11
DDR1_cg13218242	MBP_cg22239325	Myelin	0.80	1.10E-12	1.44E-10
DDR1_cg12669395	MBP_cg22239325	Myelin	0.76	5.49E-11	4.67E-09
DDR1_cg19591099	MBP_cg22258096	Myelin	0.82	5.06E-14	9.23E-12
DDR1_cg05703744	MBP_cg22258096	Myelin	0.82	6.64E-14	1.17E-11
DDR1_cg12669395	MBP_cg22258096	Myelin	0.82	9.37E-14	1.60E-11
DDR1_cg11676038	MBP_cg22258096	Myelin	0.81	1.17E-13	1.96E-11
DDR1_cg12316667	MBP_cg22258096	Myelin	0.76	2.65E-11	2.47E-09
DDR1_cg06200824	MBP_cg22258096	Myelin	0.76	4.33E-11	3.80E-09
DDR1_cg05703744	MBP_cg22391424	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg11676038	MBP_cg22391424	Myelin	0.81	2.49E-13	3.83E-11
DDR1_cg21677258	MBP_cg22391424	Myelin	0.80	1.03E-12	1.37E-10
DDR1_cg12669395	MBP_cg22391424	Myelin	0.79	1.88E-12	2.32E-10
DDR1_cg12316667	MBP_cg22391424	Myelin	0.78	6.06E-12	6.57E-10
DDR1_cg17604312	MBP_cg22391424	Myelin	0.78	6.27E-12	6.77E-10
DDR1_cg07912416	MBP_cg22391424	Myelin	0.76	3.06E-11	2.81E-09
DDR1_cg06200824	MBP_cg22391424	Myelin	0.76	6.18E-11	5.18E-09
DDR1_cg11676038	MBP_cg23327011	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg05703744	MBP_cg23327011	Myelin	0.87	<2.22E-16	<2.22E-16

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg12316667	MBP_cg23327011	Myelin	0.83	9.77E-15	2.12E-12
DDR1_cg19591099	MBP_cg23327011	Myelin	0.83	1.29E-14	2.72E-12
DDR1_cg07912416	MBP_cg23327011	Myelin	0.83	1.62E-14	3.36E-12
DDR1_cg21677258	MBP_cg23327011	Myelin	0.81	2.71E-13	4.13E-11
DDR1_cg06200824	MBP_cg23327011	Myelin	0.80	4.41E-13	6.37E-11
DDR1_cg13218242	MBP_cg23327011	Myelin	0.79	1.28E-12	1.65E-10
DDR1_cg17604312	MBP_cg23327011	Myelin	0.77	1.06E-11	1.09E-09
DDR1_cg12669395	MBP_cg23327011	Myelin	0.77	1.66E-11	1.62E-09
DDR1_cg21677258	MBP_cg23975646	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg05703744	MBP_cg23975646	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	MBP_cg23975646	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg11676038	MBP_cg23975646	Myelin	0.84	3.55E-15	8.58E-13
DDR1_cg07912416	MBP_cg23975646	Myelin	0.83	2.89E-14	5.63E-12
DDR1_cg12316667	MBP_cg23975646	Myelin	0.79	2.21E-12	2.68E-10
DDR1_cg19591099	MBP_cg23975646	Myelin	0.78	4.57E-12	5.11E-10
DDR1_cg13218242	MBP_cg23975646	Myelin	0.76	3.67E-11	3.29E-09
DDR1_cg12669395	MBP_cg23975646	Myelin	0.76	5.80E-11	4.90E-09
DDR1_cg11676038	MBP_cg24274653	Myelin	0.77	1.02E-11	1.05E-09
DDR1_cg12316667	MBP_cg24274653	Myelin	0.76	3.39E-11	3.07E-09
DDR1_cg17604312	MBP_cg24274653	Myelin	0.75	7.80E-11	6.34E-09
DDR1_cg13351860	MBP_cg26457248	Myelin	-0.76	5.53E-11	4.70E-09
DDR1_cg15656686	MBP_cg26457248	Myelin	-0.78	3.67E-12	4.21E-10
DDR1_cg24566261	MBP_cg26457248	Myelin	-0.79	1.55E-12	1.96E-10
DDR1_cg25655106	MBP_cg26457248	Myelin	-0.79	1.35E-12	1.73E-10
DDR1_cg00466425	MBP_cg26457248	Myelin	-0.84	4.00E-15	9.53E-13
DDR1_cg11676038	MBP_cg27328941	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg05703744	MBP_cg27328941	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg07912416	MBP_cg27328941	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg06200824	MBP_cg27328941	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg21677258	MBP_cg27328941	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg19591099	MBP_cg27328941	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg12316667	MBP_cg27328941	Myelin	0.84	2.66E-15	6.66E-13
DDR1_cg12669395	MBP_cg27328941	Myelin	0.83	7.99E-15	1.78E-12
DDR1_cg13218242	MBP_cg27328941	Myelin	0.83	1.31E-14	2.76E-12
DDR1_cg17604312	MBP_cg27328941	Myelin	0.79	1.82E-12	2.26E-10
DDR1_cg25655106	MBP_cg27328941	Myelin	0.78	4.57E-12	5.11E-10
DDR1_cg08673763	MBP_cg27328941	Myelin	0.78	6.01E-12	6.52E-10
DDR1_cg06501109	MBP_cg27328941	Myelin	0.78	8.91E-12	9.33E-10
DDR1_cg07979747	MBP_cg27328941	Myelin	0.77	2.54E-11	2.39E-09
DDR1_cg16111190	MBP_cg27328941	Myelin	0.75	6.55E-11	5.44E-09
DDR1_cg15720085	MBP_cg27328941	Myelin	0.75	8.04E-11	6.52E-09
DDR1_cg08673763	MBP_g23653885	Myelin	-0.75	1.38E-10	1.05E-08
DDR1_cg13218242	MBP_g23653885	Myelin	-0.75	1.38E-10	1.05E-08
DDR1_cg21677258	MBP_g23653885	Myelin	-0.75	8.98E-11	7.16E-09
DDR1_cg24727290	MBP_g23653885	Myelin	-0.76	4.41E-11	3.85E-09
DDR1_cg16111190	MBP_g23653885	Myelin	-0.77	2.26E-11	2.14E-09
DDR1_cg15656686	MBP_g23653885	Myelin	-0.77	1.96E-11	1.89E-09
DDR1_cg06200824	MBP_g23653885	Myelin	-0.78	9.30E-12	9.70E-10
DDR1_cg08951271	MBP_g23653885	Myelin	-0.78	8.37E-12	8.81E-10

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg17604312	MBP_g23653885	Myelin	-0.78	4.52E-12	5.07E-10
DDR1_cg19591099	MBP_g23653885	Myelin	-0.79	1.22E-12	1.58E-10
DDR1_cg06501109	MBP_g23653885	Myelin	-0.81	1.21E-13	2.02E-11
DDR1_cg11676038	MBP_g23653885	Myelin	-0.82	8.62E-14	1.49E-11
DDR1_cg27237814	MBP_g23653885	Myelin	-0.82	8.35E-14	1.44E-11
DDR1_cg00466425	MBP_g23653885	Myelin	-0.82	5.08E-14	9.26E-12
DDR1_cg25655106	MBP_g23653885	Myelin	-0.86	0	0
DDR1_cg05703744	MBP_g23653885	Myelin	-0.87	0	0
DDR1_cg12316667	MBP_g23653885	Myelin	-0.89	0	0
DDR1_cg12669395	MBP_g23653885	Myelin	-0.91	0	0
DDR1_cg07908039	OLIG2_cg17013986	Myelin	-0.75	8.20E-11	6.63E-09
DDR1_cg24566261	OLIG2_cg17013986	Myelin	-0.77	2.17E-11	2.07E-09
DDR1_cg05703744	SOX10_cg05447556	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg11676038	SOX10_cg05447556	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg06200824	SOX10_cg05447556	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12316667	SOX10_cg05447556	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg19591099	SOX10_cg05447556	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg07912416	SOX10_cg05447556	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg21677258	SOX10_cg05447556	Myelin	0.85	1.78E-15	4.58E-13
DDR1_cg12669395	SOX10_cg05447556	Myelin	0.82	6.20E-14	1.10E-11
DDR1_cg13218242	SOX10_cg05447556	Myelin	0.81	3.19E-13	4.80E-11
DDR1_cg17604312	SOX10_cg05447556	Myelin	0.78	3.52E-12	4.06E-10
DDR1_cg06501109	SOX10_cg05447556	Myelin	0.78	5.87E-12	6.39E-10
DDR1_cg19591099	SOX10_cg05766881	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg11676038	SOX10_cg05766881	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg05703744	SOX10_cg05766881	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg06200824	SOX10_cg05766881	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	SOX10_cg05766881	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg21677258	SOX10_cg05766881	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg12316667	SOX10_cg05766881	Myelin	0.85	1.11E-15	3.06E-13
DDR1_cg25655106	SOX10_cg05766881	Myelin	0.78	3.55E-12	4.08E-10
DDR1_cg07912416	SOX10_cg05766881	Myelin	0.78	4.61E-12	5.15E-10
DDR1_cg06501109	SOX10_cg05766881	Myelin	0.78	5.91E-12	6.43E-10
DDR1_cg01598675	SOX10_cg05766881	Myelin	0.76	3.89E-11	3.46E-09
DDR1_cg17604312	SOX10_cg05766881	Myelin	0.76	4.30E-11	3.78E-09
DDR1_cg13218242	SOX10_cg05766881	Myelin	0.75	1.23E-10	9.50E-09
DDR1_cg06200824	SOX10_cg10933281	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg05703744	SOX10_cg10933281	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg11676038	SOX10_cg10933281	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg21677258	SOX10_cg10933281	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg07912416	SOX10_cg10933281	Myelin	0.86	2.22E-16	7.30E-14
DDR1_cg19591099	SOX10_cg10933281	Myelin	0.86	4.44E-16	1.33E-13
DDR1_cg12316667	SOX10_cg10933281	Myelin	0.83	1.11E-14	2.37E-12
DDR1_cg01598675	SOX10_cg10933281	Myelin	0.79	1.45E-12	1.85E-10
DDR1_cg13218242	SOX10_cg10933281	Myelin	0.79	2.37E-12	2.86E-10
DDR1_cg06501109	SOX10_cg10933281	Myelin	0.78	7.94E-12	8.40E-10
DDR1_cg12669395	SOX10_cg10933281	Myelin	0.77	1.02E-11	1.05E-09
DDR1_cg15720085	SOX10_cg10933281	Myelin	0.76	6.13E-11	5.15E-09
DDR1_cg05703744	SOX10_cg11864127	Myelin	0.93	<2.22E-16	<2.22E-16

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg11676038	SOX10_cg11864127	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg21677258	SOX10_cg11864127	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12316667	SOX10_cg11864127	Myelin	0.85	4.44E-16	1.33E-13
DDR1_cg12669395	SOX10_cg11864127	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg07912416	SOX10_cg11864127	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg19591099	SOX10_cg11864127	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg08673763	SOX10_cg11864127	Myelin	0.81	1.30E-13	2.15E-11
DDR1_cg13218242	SOX10_cg11864127	Myelin	0.81	1.75E-13	2.80E-11
DDR1_cg06200824	SOX10_cg11864127	Myelin	0.81	2.34E-13	3.63E-11
DDR1_cg06501109	SOX10_cg11864127	Myelin	0.80	6.06E-13	8.49E-11
DDR1_cg17604312	SOX10_cg11864127	Myelin	0.79	1.30E-12	1.68E-10
DDR1_cg25655106	SOX10_cg11864127	Myelin	0.77	9.90E-12	1.03E-09
DDR1_cg07979747	SOX10_cg11864127	Myelin	0.75	1.36E-10	1.03E-08
DDR1_cg08951271	SOX10_cg11864127	Myelin	0.75	1.58E-10	1.18E-08
DDR1_cg25655106	SOX10_cg15856662	Myelin	0.83	8.22E-15	1.82E-12
DDR1_cg08673763	SOX10_cg15856662	Myelin	0.82	4.75E-14	8.74E-12
DDR1_cg07803420	SOX10_cg15856662	Myelin	0.81	1.82E-13	2.89E-11
DDR1_cg12669395	SOX10_cg15856662	Myelin	0.81	3.54E-13	5.25E-11
DDR1_cg16111190	SOX10_cg15856662	Myelin	0.80	4.58E-13	6.61E-11
DDR1_cg05703744	SOX10_cg15856662	Myelin	0.80	9.85E-13	1.31E-10
DDR1_cg08951271	SOX10_cg15856662	Myelin	0.79	3.28E-12	3.82E-10
DDR1_cg19591099	SOX10_cg15856662	Myelin	0.78	7.15E-12	7.63E-10
DDR1_cg24727290	SOX10_cg15856662	Myelin	0.76	3.11E-11	2.84E-09
DDR1_cg11676038	SOX10_cg15856662	Myelin	0.76	4.51E-11	3.93E-09
DDR1_cg06200824	SOX10_cg15856662	Myelin	0.75	9.49E-11	7.52E-09
DDR1_cg05703744	SOX10_cg19228755	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg11676038	SOX10_cg19228755	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg21677258	SOX10_cg19228755	Myelin	0.85	1.11E-15	3.06E-13
DDR1_cg12316667	SOX10_cg19228755	Myelin	0.84	1.78E-15	4.58E-13
DDR1_cg07912416	SOX10_cg19228755	Myelin	0.84	6.22E-15	1.43E-12
DDR1_cg13218242	SOX10_cg19228755	Myelin	0.81	2.76E-13	4.20E-11
DDR1_cg17604312	SOX10_cg19228755	Myelin	0.80	3.79E-13	5.56E-11
DDR1_cg06200824	SOX10_cg19228755	Myelin	0.80	6.83E-13	9.48E-11
DDR1_cg12669395	SOX10_cg19228755	Myelin	0.79	1.40E-12	1.79E-10
DDR1_cg19591099	SOX10_cg19228755	Myelin	0.79	1.49E-12	1.89E-10
DDR1_cg07979747	SOX10_cg19228755	Myelin	0.75	7.33E-11	6.01E-09
DDR1_cg05703744	SOX10_cg19257200	Myelin	0.93	<2.22E-16	<2.22E-16
DDR1_cg11676038	SOX10_cg19257200	Myelin	0.92	<2.22E-16	<2.22E-16
DDR1_cg21677258	SOX10_cg19257200	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg07912416	SOX10_cg19257200	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12669395	SOX10_cg19257200	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg12316667	SOX10_cg19257200	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg19591099	SOX10_cg19257200	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg06200824	SOX10_cg19257200	Myelin	0.87	<2.22E-16	<2.22E-16
DDR1_cg17604312	SOX10_cg19257200	Myelin	0.84	6.88E-15	1.57E-12
DDR1_cg13218242	SOX10_cg19257200	Myelin	0.82	3.15E-14	6.10E-12
DDR1_cg06501109	SOX10_cg19257200	Myelin	0.80	8.99E-13	1.21E-10
DDR1_cg25655106	SOX10_cg19257200	Myelin	0.77	1.77E-11	1.72E-09
DDR1_cg07979747	SOX10_cg19257200	Myelin	0.77	1.84E-11	1.78E-09

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg01598675	SOX10_cg19257200	Myelin	0.75	7.79E-11	6.34E-09
DDR1_cg08673763	SOX10_cg19257200	Myelin	0.75	9.76E-11	7.72E-09
DDR1_cg05703744	SOX10_cg20754324	Myelin	0.91	<2.22E-16	<2.22E-16
DDR1_cg06200824	SOX10_cg20754324	Myelin	0.90	<2.22E-16	<2.22E-16
DDR1_cg07912416	SOX10_cg20754324	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg12316667	SOX10_cg20754324	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg11676038	SOX10_cg20754324	Myelin	0.88	<2.22E-16	<2.22E-16
DDR1_cg21677258	SOX10_cg20754324	Myelin	0.85	1.55E-15	4.11E-13
DDR1_cg13218242	SOX10_cg20754324	Myelin	0.84	3.11E-15	7.61E-13
DDR1_cg12669395	SOX10_cg20754324	Myelin	0.84	4.88E-15	1.15E-12
DDR1_cg19591099	SOX10_cg20754324	Myelin	0.83	8.88E-15	1.95E-12
DDR1_cg17604312	SOX10_cg20754324	Myelin	0.80	4.71E-13	6.76E-11
DDR1_cg25655106	SOX10_cg20754324	Myelin	0.79	2.47E-12	2.97E-10
DDR1_cg06501109	SOX10_cg20754324	Myelin	0.79	2.89E-12	3.41E-10
DDR1_cg01598675	SOX10_cg20754324	Myelin	0.78	3.88E-12	4.42E-10
DDR1_cg15720085	SOX10_cg20754324	Myelin	0.78	8.56E-12	8.98E-10
DDR1_cg08673763	SOX10_cg20754324	Myelin	0.76	3.35E-11	3.04E-09
DDR1_cg25655106	SOX10_cg23109891	Myelin	0.85	8.88E-16	2.50E-13
DDR1_cg08951271	SOX10_cg23109891	Myelin	0.83	9.33E-15	2.03E-12
DDR1_cg12669395	SOX10_cg23109891	Myelin	0.83	2.18E-14	4.32E-12
DDR1_cg11676038	SOX10_cg23109891	Myelin	0.80	6.42E-13	8.95E-11
DDR1_cg12316667	SOX10_cg23109891	Myelin	0.80	6.77E-13	9.40E-11
DDR1_cg07803420	SOX10_cg23109891	Myelin	0.80	8.28E-13	1.13E-10
DDR1_cg17604312	SOX10_cg23109891	Myelin	0.80	9.67E-13	1.29E-10
DDR1_cg08673763	SOX10_cg23109891	Myelin	0.79	2.99E-12	3.51E-10
DDR1_cg13218242	SOX10_cg23109891	Myelin	0.78	5.05E-12	5.58E-10
DDR1_cg05703744	SOX10_cg23109891	Myelin	0.78	6.06E-12	6.57E-10
DDR1_cg13329862	SOX10_cg23109891	Myelin	0.78	8.42E-12	8.85E-10
DDR1_cg19591099	SOX10_cg23109891	Myelin	0.76	2.69E-11	2.50E-09
DDR1_cg24727290	SOX10_cg23109891	Myelin	0.76	2.99E-11	2.75E-09
DDR1_cg27237814	SOX10_cg23109891	Myelin	0.75	1.46E-10	1.10E-08
DDR1_cg16111190	SOX10_cg23109891	Myelin	0.75	1.53E-10	1.14E-08
DDR1_cg25655106	SOX10_cg25036707	Myelin	0.85	1.33E-15	3.55E-13
DDR1_cg07803420	SOX10_cg25036707	Myelin	0.83	1.13E-14	2.42E-12
DDR1_cg12669395	SOX10_cg25036707	Myelin	0.83	1.82E-14	3.71E-12
DDR1_cg05703744	SOX10_cg25036707	Myelin	0.82	3.22E-14	6.21E-12
DDR1_cg08673763	SOX10_cg25036707	Myelin	0.82	4.20E-14	7.84E-12
DDR1_cg16111190	SOX10_cg25036707	Myelin	0.82	4.57E-14	8.47E-12
DDR1_cg08951271	SOX10_cg25036707	Myelin	0.82	4.80E-14	8.80E-12
DDR1_cg24727290	SOX10_cg25036707	Myelin	0.81	1.57E-13	2.54E-11
DDR1_cg19591099	SOX10_cg25036707	Myelin	0.80	5.37E-13	7.61E-11
DDR1_cg11676038	SOX10_cg25036707	Myelin	0.80	7.04E-13	9.72E-11
DDR1_cg13329862	SOX10_cg25036707	Myelin	0.80	7.42E-13	1.02E-10
DDR1_cg06200824	SOX10_cg25036707	Myelin	0.78	6.11E-12	6.62E-10
DDR1_cg12316667	SOX10_cg25036707	Myelin	0.75	8.27E-11	6.67E-09
DDR1_cg07912416	SOX10_cg25036707	Myelin	0.75	1.03E-10	8.07E-09
DDR1_cg13218242	SOX10_cg25036707	Myelin	0.75	1.31E-10	9.97E-09
DDR1_cg21677258	SOX10_cg25036707	Myelin	0.75	1.46E-10	1.10E-08
DDR1_cg06200824	SOX10_cg25625951	Myelin	0.90	<2.22E-16	<2.22E-16

Table S9. Adjusted significant correlation coefficients ≥ 0.75 for individual CpGs 5-mC levels between *DDR1* 5-mC levels and selected Myelin genes in NeuN+ nuclei from the FC *(Continued)*

***DDR1* CpG**	**Gene CpG**	**Cell type marker**	**ρ[a]**	***p*-value**	**Adj *p*-value[b]**
DDR1_cg11676038	SOX10_cg25625951	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg05703744	SOX10_cg25625951	Myelin	0.89	<2.22E-16	<2.22E-16
DDR1_cg12316667	SOX10_cg25625951	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg19591099	SOX10_cg25625951	Myelin	0.86	<2.22E-16	<2.22E-16
DDR1_cg12669395	SOX10_cg25625951	Myelin	0.85	6.66E-16	1.96E-13
DDR1_cg07912416	SOX10_cg25625951	Myelin	0.84	4.22E-15	1.00E-12
DDR1_cg21677258	SOX10_cg25625951	Myelin	0.81	2.36E-13	3.66E-11
DDR1_cg15720085	SOX10_cg25625951	Myelin	0.76	2.65E-11	2.47E-09
DDR1_cg13218242	SOX10_cg25625951	Myelin	0.76	3.48E-11	3.14E-09
DDR1_cg01598675	SOX10_cg25625951	Myelin	0.76	3.87E-11	3.44E-09
DDR1_cg17604312	SOX10_cg25625951	Myelin	0.76	4.12E-11	3.63E-09
DDR1_cg06501109	SOX10_cg25625951	Myelin	0.75	6.89E-11	5.68E-09
DDR1_cg25655106	SOX10_cg25625951	Myelin	0.75	1.10E-10	8.60E-09

[a]Spearman correlation coefficient.
[b]Post hoc Benjamini & Hochberg method for multiple testing correction.
Results sorted in alphabetical order by myelin gene names.
Abbreviations: 5-mC: 5-methylcytosine; FC: Frontal cortex; NeuN+: Neuronal nuclei.

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