OBJECTIVES

Our overall research initiative is focused on understanding the molecular mechanism of action and resistance to antitumor drugs that target the microtubule cytoskeleton.

1. Decipher, understand and manipulate the role of microtubule-trafficking in the cell.
    a. To investigate the role of microtubules in the intracellular movement of p53 and HIF-1α.
    b. To investigate the effects of microtubule-targeting drugs on the movement and activity of p53 and HIF-1α.
2. Elucidate the details of the mechanism of action of agents that target the microtubules.
    a. To investigate the proteins and signals involved in the step leading from mitotic arrest to apoptosis.
    b. To investigate and characterize the "new" microtubule targeting agent Laulimalide
3. Understand the timeline of events that takes place during the development of drug resistance to microtubule-targeting agents.
    a. To investigate the genetic differences between cells undergoing drug selection that have a low level of drug resistance and cells that have high levels of drug resistance.
    b. To establish a temporal model for the development of drug resistance
4. Characterize alternate drug regimens that are active in anti-mitotic drug-resistant cells.
    a. To understand the effect on microtubules of farnesyltransferase inhibitors.
    b. To investigate the molecular mechanism underlying the synergy between farnesyltransferase inhibitors and taxanes