

James & Esther King Biomedical Research Program

Kanai, Masayuki

Molecular Oncology

H. Lee Moffitt Cancer Center & Research Institute

2009 Program

New Investigator (3-year project)

Project Title: Molecular Dissection of the RockII-dependent Regulation of Centrosome Duplication

Project Summary: Aneuploidy (chromosome loss and/or gain), which plays a critical role in carcinogenesis with multiple genetic alterations, is commonly found in cancer cells. Chromosome loss/gain occurs as the consequence of chromosome segregation errors during cell division, in which the organelle called centrosome plays a critical role: two centrosomes direct the accurate separation of duplicated chromosomes. Thus, the presence of more than two centrosomes (centrosome amplification) increases the frequencies of chromosome segregation errors, leading to aneuploidy. Indeed, centrosome amplification is frequently observed in cancer cells. Centrosomes duplicate once before cell division, and centrosome amplification is primarily caused by uncontrolled duplication of centrosomes. Thus, it is important to understand how centrosome duplication is controlled, and how loss of the control results in centrosome amplification. We have recently identified the protein named ROCK II. This protein plays a key role to initiate centrosome duplication, and aberrant activity of it leads to centrosome amplification. In this grant, we will investigate how ROCK II controls centrosome duplication and how ROCK II is controlled by other cancer-associated proteins for the initiation of centrosome duplication. Since centrosome duplication may be a superior target for cancer prevention/therapy, the findings from this grant will provide valuable information toward the development of such a protocol.