NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Seminar Announcement

Diverse functions of the ARF-MDM2-p53 tumor suppressive network

Date: 14 September 2015 Monday

Time: 2:30pm to 3:30pm

Venue: SBS Classroom 4 (SBS-01n-24)

Host: A/Prof Koh Cheng Gee

Speaker: Asst/Prof Koji Itahana
Cancer & Stem Cell Biology Program
Duke-NUS Graduate Medical School
Singapore



Abstract

The ARF-MDM2-p53 pathway is known as a critical tumor suppressive pathway, and this pathway must be disrupted in order for cells to become cancerous. It has been long believed that the major tumor suppressive functions of ARF-MDM2-p53 pathway are the induction of cell cycle arrest, senescence and apoptosis. However, recent evidences have challenged this dogma, and it is becoming evident that ARF and p53 have much more diverse functions that are important for tumor suppression. In this seminar, I would like to introduce the novel functions of ARF and p53 respectively which we recently found in my laboratory. It has been known that ARF enhances the SUMOylation of its binding partners; however, the physiological function of ARF-mediated SUMOylation has been unclear due to the lack of a known, associated E3 SUMO ligase. We uncovered TRIM28/KAP1 as a novel ARF-binding protein and E3 SUMO ligase for NPM1/B23. We showed that ARF inhibits centrosome amplification by SUMOylating NPM1 via TRIM28. We also uncovered the first beneficial links between p53 and uric acid metabolism. We identified the uric acid transporter SLC2A9 as a direct p53 target gene and a key downstream effector in the reduction of ROS through the transportation of uric acid as a source of antioxidant. Our studies reveal the potential contribution of these new functions of ARF and p53 in tumor suppression.