NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Seminar Announcement

Cooperation of competitive endogenous RNAs and BRAF in cancer

Date: 01 September 2015 Tuesday

Time: 2:00pm to 3:00pm

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

Host: Asst/Prof Melissa Jane Fullwood

Speaker: Dr. Florian Karreth
Meyer Cancer Center,
Weill Cornell Medical College, USA



Abstract

Competitive endogenous RNAs (ceRNAs) are transcripts that compete for a pool of shared miRNAs, thereby regulating each other's expression. Virtually any transcript containing miRNA binding sites can function as a ceRNA, and ceRNA activity has been demonstrated in vitro for mRNAs, long non-coding RNAs, circular RNAs, and pseudogenes. Using a forward genetic screen in a melanoma mouse model we identified and characterized several mRNAs that regulate the tumor suppressor PTEN as ceRNAs. To study ceRNA crosstalk in vivo more directly, we created a mouse model overexpressing the BRAF pseudogene, BRAFps. BRAFps transgenic mice develop B-cell lymphomas, and we show that BRAFps functions as a ceRNA that sequesters miRNAs from its parental gene BRAF. The ceRNA function of BRAFps is conserved in human cells, indicating that deregulation of this pseudogene may promote cancer in humans. In this seminar, I will present our findings regarding the coding-independent activity of RNAs through miRNA competition and discuss the potential role of this mechanism in the development of cancer.

Dr. Florian Karreth performed his graduate work in Prof. David Tuveson's lab at the Abramson Family Cancer Research Institute of the University of Pennsylvania and the CRUK Cambridge Research Institute, where he interrogated the function of RAF proteins in melanoma and lung cancer development. This work earned Dr. Karreth a Ph.D. degree from the University of Vienna. Dr. Karreth then joined Prof. Pier Paolo Pandolfi's group at the Beth Israel Deaconess Medical Center of Harvard Medical School to study a novel class of RNA molecules, termed competitive endogenous RNAs (ceRNAs). Dr. Karreth showed that both mRNAs and pseudogenes can promote cancer development as ceRNAs through a microRNA competition mechanism. This groundbreaking work was published in two articles in Cell in 2011 and 2015. Dr. Karreth has published numerous highly cited articles in the field of cancer research. In addition, he received a prestigious fellowship from the Boehringer Ingelheim Fonds and was elected as a Future Leader in Translational Cancer Research by the AACR in 2010. Dr. Karreth's work received funding from the DOD, the ACS, and the NCI.