IMCB Invited Speaker

Speaker : **Prof. Martin McMahon**
Efim Guzik Distinguished Professor of Cancer Biology,
University of California San Francisco,
Helen Diller Family Comprehensive Cancer Center, USA

Date : 8 November 2012 (Thursday)

Time : 2:00PM - 3:00PM

Venue : Breakthrough Theatrette, Level 4, Matrix, Biopolis

Host : Dr. Philipp Kaldis

Seminar :

Mechanisms of Oncogene Cooperation in Melanoma and Lung Tumorigenesis

Mutational activation of BRAF is detected in melanoma, lung, thyroid and colorectal cancer. However, expression of mutationally activated $BRAF^{V600E}$ is insufficient to convert normal cells to a fully tumorigenic state. Consequently, cancers expressing mutated $BRAF^{V600E}$ generally display alterations in tumor suppressors and/or other oncogenes such as PTEN, TP53, CDKN2A, PIK3CA, c-MYC or CTNNB1. To explore the mechanisms of oncogene–tumor suppressor cooperation we have designed mouse models of $BRAF^{V600E}$-initiated melanoma, lung and thyroid cancer. In melanocytes, $BRAF^{V600E}$ cooperates with either PTEN silencing or mutational activation of PIK3CA by permitting bypass of oncogene-induced senescence. In addition, once melanomas have formed, $BRAF^{V600E}$ cooperates with PI3'-kinase signaling in the regulation of protein translation. In the lung epithelium, $BRAF^{V600E}$ cooperates with either silencing of TP53 or CDKN2A or mutational activation of PIK3CA, c-MYC or CTNNB1. In these situations, the cooperating lesion also promotes bypass of oncogene-induced senescence and also promotes cell proliferation in the tumor cell.

About the Speaker :

Dr. Martin McMahon was awarded a Ph.D. from King's College, University of London for studies on the mechanism of interferon action conducted with Drs. Ian Kerr and George Stark at the Imperial Cancer Research Fund (London) and Stanford University. In 1985, he joined J. Michael Bishop's laboratory at the University of California, San Francisco as a post-doctoral fellow to study oncogenic protein kinases. In 1991 he moved to the DNAX Research Institute to lead an independent research group working on RAF protein kinases. From 1991-1998, Dr. McMahon pioneered the use of a new class of conditional oncoproteins to dissect the corrupting events that lead normal cells to develop aberrant properties of lethal cancer. In 1998 he was recruited to the faculty of the Cancer Research Institute in the UCSF Helen Diller Family Comprehensive Cancer Center. In 2002 he was appointed the Efim Guzik Distinguished Professor of Cancer Biology. Dr, McMahon is currently co-Director of the Experimental Therapeutics Program and Director for Professional Education in the UCSF Cancer Center.

Dr. McMahon's research program focuses on the mechanisms underlying the development of metastatic melanoma, lung and thyroid cancer. Although these malignancies are derived from distinct cell types, they share a striking number of common genetic alterations especially activating mutations in either KRAS or BRAF. To do this, Dr. McMahon's laboratory works with cultured human cancer-derived cells and with genetically engineered mouse models of human cancer. Such model systems have demonstrated considerable valuein the design and evaluation of new diagnostic, prognostic and therapeutic tools to treat patients with cancer.

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