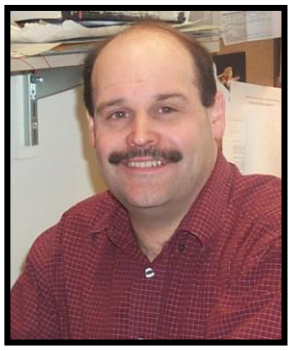
Institute of Medical Biology
A*STAR

Seminar Announcement

- All Are Welcome -



Speaker: **Dr Raymond Birge, PhD**
University of Medicine and Dentistry of New Jersey - New Jersey Medical School

Title: **Signal transduction by the Crk oncogene in breast cancer**

Date : **27 June 2012 (Wednesday)**

Time : **11.00am – 12.00pm**

Venue: **Aspiration Theatrette, Matrix Level 2M, Biopolis**

Host : **Dr Giulia Rancati**
(Tel: 64070805, email: giulia.rancati@imb.a-star.edu.sg)

Abstract of the Seminar:

The SH2 and SH3 domain-containing adaptor proteins Crk, Grb2 and Nck participate in the organized assembly of protein complexes downstream of tyrosine kinases and control a wide range of biological processes in metazoans. Crk can transform primary mammalian cells, and in recent years, over-expression has been shown to positively correlate with metastasis in several human cancer types, including glioblastoma, ovarian cancer, and breast cancer. Consistent with its role as a dominant oncogene, stable knockdown of Crk attenuates invasion and migration of patient derived cancer cell lines. The canonical signaling paradigm involves the Crk SH2 binding to specific phosphotyrosine motifs at focal adhesions and the SH3N binding to polyproline motifs of proteins that regulate Rho GTPase. Using structural biology and biochemistry, we have shown that Crk has an unconventional role in signal transduction through phosphorylation at Y251 and Y239 in the carboxyl-terminal SH3 (SH3C). These phosphorylated motifs recruit novel SH2/PTB containing proteins to initiate non-canonical signaling pathways. Phosphorylated Y251 on Crk promotes Abl kinase transactivation by binding to and displacing the Abl SH2. By generating phospho-specific antibodies specific for pY251 and pY239, we identified that Y251 is rapidly phosphorylated, concommittant with Abl activation, upon induction of the EGFR signaling axis by EGF in primary human breast cancer cells. Further, SH2 domain profiling reveals several new binding partners of pY251 and pY239. Identification of the functional significance of pY251 on the Crk SH3C has provided unique insight into how Crk promotes the aggressive phenotypes of cancer cells.

About the Speaker:

Raymond Birge, PhD., is a Professor of Biochemistry and Head of Laboratory at the University of Medicine and Dentistry of New Jersey (UMDNJ)-New Jersey Medical School in Newark New Jersey. Dr. Birge received his B.S from the University of Connecticut (1984), and a PhD in Biochemical Toxicology, also from the University of Connecticut (1989). He completed his postdoctoral training at The Rockefeller University with Professor Hidesaburo Hanafusa from 1990 to1994 and was promoted to Assistant Professor in the Laboratory of Molecular Oncology at Rockefeller University from 1994 to 1998, acting as head of that same laboratory from 1998-2000. Dr. Birge joined UMDNJ-New Jersey Medical in 2000 and maintains a position of Professor in the Department of Biochemistry and Molecular Biology.

Dr. Birge's research focuses on apoptosis and cancer biology, emphasizing genes and signaling pathways that promote tumor progression and metastasis. He was the founding member (with Richard Lockshin and Zahra Zakeri) of the Cell Death Society and presently serves on the Board of Directors of the International Cell Death Society Dr. Birge serves as a scientific consultant on numerous federal and private grant study sections that includes the National Institutes of Health, National Science Foundation, Department of Defense Congressionally Breast and Prostate Cancer Funding, and the Susan B Komen Foundation. He is currently on the editorial board of The Journal of Biological Chemistry and Cell Signaling and Communication. Dr. Birge has authored over 65 scientific publications and chapters in molecular and cancer biology.