# 43rd SDBC Meeting

**Date of next meeting**: 18 October 2012 (Thursday)

**Venue:** Auditorium, Temasek Life Sciences Laboratory, 1 Research Link, NUS

**Time:** 5.00pm - 7.00pm

**Prof. Thomas Schilling**
*Professor, Developmental & Cell Biology*
*University of California, Irvine, CA, USA*

**Seminar Title:** Thrombospondin-4 Drives Matrix Assembly at Myotendinous Junctions

Development of a functional musculoskeletal system requires that muscle cells attach at their ends through tendons. Muscle attachments rely on Integrin (Itg) and Dystrophin (Dys) - dependent adhesion and defects in human Itg/Dys ligands in the extracellular matrix (ECM) such as Laminin (Lam) are associated with muscular dystrophy. Lam, collagen and other ECM proteins form complex fibrillar networks at myotendinous junctions (MTJs) to bear the forces of muscle contractions, but how these structures are assembled and maintained remains unclear. I will discuss our evidence in zebrafish that the Itg ligand Thrombospondin-4 (Thbs4) is essential for ECM assembly and muscle attachment at MTJs. Myoblasts initially secrete their own Thbs4 to promote attachment, but downregulate it upon differentiation, at which point Thbs4b production becomes localized to tenocytes as MTJs mature. Depletion of Thbs4 causes muscles to detach upon contraction, and local secretion of Thbs4 in genetic mosaics can rescue these defects. Furthermore, Thbs4 is required to localize Lam and activate Itg signaling at MTJs. Thus, our results reveal a novel role for Thbs4 as a regulator of muscle attachment, and as a critical scaffold for assembly of other ECM components. Thbs proteins may initiate ECM assembly in other contexts where they are required, particularly those that involve high levels of Itg signaling, and understanding the functions of Thbs4 may provide novel strategies to treat muscular dystrophies

**Dr. Fumio Motegi**
*Principal Investigator & NRF Fellow*
*Temasek Life Sciences Laboratory, Singapore*

**Seminar Title:** Breaking symmetry: Polarization of the C. elegans zygote

A hallmark of polarized cells is the segregation of the PAR polarity regulators into asymmetric domains at the cell cortex. Antagonistic interactions involving two conserved kinases, atypical protein kinase C (aPKC) and PAR-1, have been implicated in polarity maintenance, but the mechanisms that initiate the formation of asymmetric PAR domains are not understood. Here, we describe one pathway used by the sperm-donated centrosome to polarize the PAR proteins in Caenorhabditis elegans zygotes. Before polarization, cortical aPKC excludes PAR-1 kinase and its binding partner PAR-2 by phosphorylation. During symmetry breaking, microtubules nucleated by the centrosome locally protect PAR-2 from phosphorylation by aPKC, allowing PAR-2 and PAR-1 to access the cortex nearest the centrosome. Cortical PAR-1 phosphorylates PAR-3, causing the PAR-3/aPKC complex to leave the cortex. Our findings illustrate how microtubules, independent of actin dynamics, stimulate the self-organization of PAR proteins by providing local protection against a global barrier imposed by aPKC.

*All are welcome.*