Institute of Medical Biology
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Seminar Announcement

- All Are Welcome -



Speaker : **G.W. Gant Luxton, Ph.D.**
Assistant Professor, Department of Genetics, Cell Biology, and Development, University of Minnesota

Title : ***"LINC Complex Assembly Mechanisms and Mechanotransduction Across the Nuclear Envelope"***

Date : **3 October 2016 (Monday)**
Time : **11:00am – 12:00pm**
Venue : **Creation Theatre, Matrix Level 4**
Host : **Dr Brian Burke**
(Tel: 64070421; Email: brian.burke@imb.a-star.edu.sg)

Abstract:
The direct coupling of the nucleus to the cytoskeleton plays critical roles during several fundamental cellular processes including DNA damage repair, fertilization, mechanotransduction, meiotic pairing of homologous chromosomes, migration, and polarization. The LINC complex is an evolutionarily conserved molecular bridge in the nuclear envelope that is responsible for nuclear-cytoskeletal coupling. The core of the LINC complex is formed by a translumenal interaction between the outer and inner nuclear membrane KASH and SUN proteins, respectively. Recent *in vitro* studies reveal that mammalian SUN2 is a trimer that recruits three KASH proteins. Here, we test the *in vivo* relevance and conservation of SUN protein trimerization using fluorescence fluctuation spectroscopy and brightness analysis. We show that SUN2 trimerizes within the nuclear envelope of living cells and identify structural requirements for this trimerization. We then reveal that the oligomerization of mammalian SUN1 within the nuclear envelope is not limited to a trimer, suggesting that this is not the sole arrangement for all SUN proteins. We then uncover environment-dependent differences in SUN protein oligomerization suggestive of potential mechanisms for the regulation of LINC complex assembly. Finally, we identify the lumenal AAA+ ATPase torsinA as a key regulator of LINC complex assembly and function. These quantitative *in vivo* assays are the first to directly measure the assembly states of nuclear envelope proteins and will provide critical information to advance the mechanistic understanding of regulated LINC complex assembly and consequently LINC complex-dependent mechanotransduction events.

About the Speaker:
As a biology undergraduate at Grinnell College, Iowa, Dr Luxton became fascinated with viruses and their host cell interactions. This led him to pursue doctoral studies at Northwestern University Medical School with Dr. Greg Smith. During this time, he studied how alpha-herpesviruses hijack microtubule motor proteins in neurons to spread throughout an infected nervous system. Later, as a postdoctoral fellow in Gregg Gundersen's laboratory at Columbia University, Dr Luxton contributed key findings on how forces generated by the actin cytoskeleton are transduced by LINC complexes to position the nucleus at the rear of migrating cells. This involves formation of linear LINC complex arrays, which he named transmembrane actin-associated nuclear (TAN) lines.
Research in his lab at the University of Minnesota continues to focus on TAN line-mediated nuclear movement. He has recently identified torsinA, a AAA+ ATPase, as a regulator of TAN line assembly. To define molecular mechanisms of how torsinA controls LINC complex-dependent mechanotransduction, he has engaged in an exciting collaboration with Dr. Joachim Mueller (Department of Physics and Astronomy). Together, they have developed fluorescence fluctuation spectroscopy and brightness analysis to quantify protein-protein interactions in live cells at the single molecule level.
Additional work with Dr. David Thomas (Department of Biochemistry, Biophysics, and Molecular Biology) involves novel FRET-based biosensors in high-throughput screens for small molecules that influence LINC complex and torsinA assembly. These studies may reveal unique therapeutic compounds for treatment of the torsinA-linked neurological disorder, DYT1 dystonia.