Centre for Biosystems Science and Engineering

S E M I N A R

at 04:00 PM on May 02, 2017
Meeting Room, BSSE

Nanoclusters of integrins underlie cell matrix adhesions

Dr. Rishita Changede

Mechanobiology Institute, NUS

Integrin adhesions assemble and mature in response to ligand binding and mechanical factors, but the molecular-level organization has not been known. We find that ~100-nm clusters of ~50 β3-activated integrins form very early adhesions under a wide variety of conditions on RGD surfaces. These adhesions form similarly on fluid and rigid substrates, but most adhesions are transient on rigid substrates. Without talin or actin polymerization, few early adhesions form, and expression of either the talin head or rod domain in talin-depleted cells restores early adhesion formation. Mutation of the integrin binding site in the talin rod decreases cluster size. We suggest that the integrin clusters constitute universal early adhesions and that they are the modular units of cell matrix adhesions. They form in the presence of blebbistatin suggesting that they are formed prior to force sensing. They require the association of activated integrins with cytoplasmic proteins, in particular talin and actin, and cytoskeletal contraction on them causes adhesion maturation for cell motility and growth. Using gold nano-patterning we observe that these clusters grow using unliganded but activated integrins. Ligand geometry determines cluster growth. This indicates that free interns assemble the clusters rapidly around an activated and liganded integrins. These early nascent adhesions have distinct behaviors on compliant and rigid substrates, since the epidermal growth factor receptor is recruited to these clusters only on the rigid substrates, in absence of EGF. EGFR acts as a mechanoenzyme that is required for mechanotransduction within fibroblasts. Taken together our studies show that nascent adhesions form on substrates of vastly varying rigidities. These modular clusters of integrins constitute the basis of cell matrix adhesions that control cell growth, differentiation and death. Many questions remain about how different ligands alter cluster behavior and how clusters behave in different cellular functions.

About the speaker:

Dr. Changede is a senior research fellow at MBI working with Prof. Michael Sheetz. Her primary interest is to understand the design principles that allow the cells and organisms to respond appropriately to their diverse physical (geometry and forces) and chemical (biochemical ligands) environment. During her postdoctoral studies, she developed quantitative super resolution imaging based assays to understand the emergent properties of nascent adhesions. Her Ph.D studies in the laboratory of Prof. Pernille Rorth, were focused on developing biosensors to observe the endogenous signaling of guidance receptors (which guide cell migration) in a live tissue. Subcellular localization of this weak endogenous signal was observed at the leading edge of the cell and it was found to be dynamic in both space and time. Her masters thesis was with Prof. Krishanu Ray at Tata Institute of Fundamental Research, India. She studied the role of dynein dynactin complex in endomembrane assembly.