Centre for Biosystems Science and Engineering

S E M I N A R

at 11:00 AM on March 01, 2017

Meeting Room, BSSE

May the force be with you: Piezo modulates protrusion switching in migrating Dictyostelium cells

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Cells can adapt how they move to suit their physical environment. In tissue-like environments, mechanical resistance is greater than under buffer, and cells often move using pressure-driven projections such as blebs, rather than pseudopods. This becomes especially important in the context of development or during tumour invasion. However, very little is known about the effect of purely mechanical cues in protrusion switching. Additionally, underlying mechanosensing pathways governing this plasticity of cell migration are yet to be decipehered.

In the first part of the talk, the author will discuss about the 'cell squasher' which was designed to apply a defined uniaxial compressive load to an agarose overlay underneath which cells migrate. This allowed pressure alone to be varied, and with it the mechanical resistance to movement, while keeping the substratum and overlay constant. A pressure of 100 Pa was sufficient to switch Dictyostelium cells from moving predominantly with pseudopods to bleb-driven migration. This switch was almost instantaneous and sustained so long as the load is applied, but reversed when it was removed. This switch to bleb-driven migration is further accompanied by appreciable cell shape changes and reduction in cellular volume, suggesting that compressive stress alone can act as a governing variable in a cell's response to its environment.

Next, the author will describe a novel mechanosensing pathway utilised by cells to perceive mechanical resistance. Potential mechanosensing mutants were screened for defective response to the load and it was found that the mutants in the Piezo stretch-operated channel were almost blind to increased load. The response to the load depends on external calcium and is accompanied by a sustained increase in cytosolic calcium, which is dependent on Piezo. Myosin-II is recruited to the cell cortex of cells under load, potentially increasing contractility, and this again is abolished in Piezo mutants.

Thus, the mechanical resistance to movement is sensed by cells using the Piezo channel, which opens under load, allowing calcium into the cell and stimulating cortical contractility allowing cells to switch to bleb-based migration.

About the speaker:

Dr. Nishit Srivastava is currently an Investigator Scientist at MRC-LMB, Cambridge. Nishit recently finished his PhD from Cambridge working with Dr. Alexandre Kabla, Department of Engineering and Dr. Robert Kay, MRC-LMB. He was Dr. Manmohan Singh Scholar at St. John's College, Cambridge. Previously, he did a MS in material science from JNCASR working on differentiation of Embryonic stem cells on electroactive polymers. Nishit's current research focus is on studying cell migration in microfludic channels and deciphering the role of nucleus in migration of cells through narrow constrictions.