University of Cyprus
Department of Biological Sciences

Ph.D. Thesis Defense

Student Presentation

Monday, 22 June 2020 at 09:00

This seminar will be held through teleconferencing and is not open to the public

It is noted that as a result of the coronavirus COVID-19 pandemic at an international level and within the Republic of Cyprus and in compliance with the instructions of the competent bodies of the Republic of Cyprus, the physical presence of members for meeting purposes in the meeting areas is not feasible.

Anastasiou Ouranio

"Extracellular matrix adhesion independent roles of integrins and FA proteins."

Mechanosensation and Mechanotransduction are the abilities of a cell to sense and respond to mechanical signals by translating them into biochemical pathways. The realization that mechanical forces influence and regulate numerous cell processes has changed our perspective in cell and molecular biology. Integrin-based adhesions and Cadherin-based adhesions are the two major metazoan adhesion systems that facilitate the cell-ECM and cell-cell adhesion respectively. Both systems have been found indispensable for proper embryonic development and loss of protein members of these complexes leads to embryonic lethality and are implicated in disease. The two systems are known to be spatially segregated in both cells and tissues. However numerous studies underline their crosstalk without providing any mechanistic insight of this interaction. Earlier work from our group revealed that a well characterized member of focal adhesions (FAs), FAK is implicated in tissue morphogenesis in Xenopus through the regulation of spindle orientation. Later work suggested that integrin β1 becomes activated through mechanical stimuli in the absence of a ligand at the lateral cortex of mitotic cells. Upon this activation, known FA proteins were shown to be recruited at the mitotic cortex forming the cortical mechanosensory complex (composed of FAK, p130Cas and Src). Here we show that both integrin-based and cadherin-based adhesion drive proper mitotic spindle orientation parallel to the plane of the attachment and promote identical responses to spatial cues provided by adhesion geometry showing that cell substrate interactions simply provide mechanistically cues to the dividing cells which are independent from the molecular nature of adhesion. We also show that integrin activation and the cortical mechanosensory complex are crucial for spindle orientation both on cadherin and fibronectin substrates showing that spindle responses to adhesion topology are a result of force anisotropy on the cell cortex and the role of cortical mechanosensory complex in this process is distinct from its role in cell-ECM adhesion. We move on to show that integrin β1 also becomes activated and clustered at adherens junctions and that this activation is relies on PM tension followed by stabilization through actin trapping within the actomyosin bundles terminating at mature AJs. We go on to show that that integrin β1 activation modulates adherens junction dynamics leading to their disassembly through caveolin based endocytosis. The activation of integrin β1 at AJs leads to the recruitment of FA proteins leading to the formation of hybrid adhesion complexes in which the stoichiometry of FA proteins and the conformation of integrin β1 is distinct from that at focal

adhesions and displays similarities to the cortical mechanosensory complex. Finally, we go on to show that integrin activation at AJs under increased tension not only leads to AJ disassembly but also spatially guides ECM deposition in vitro and in the embryo.