University of Cyprus
Department of Biological Sciences

Ph.D. Thesis Defense

Student Presentation

Thursday, 07 May 2020 at 10:00

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.

Myrofora Panagi

"The role of innate immunity and stress signaling pathways in intestinal proliferation, endoreplication and tumorigenesis"

Excessive proliferation and polyploidy have been widely described in cancer cells. Given that both phenomena are driven by misregulations of cell cycle, a thorough understanding of their genetic and molecular links may provide fundamental insights in cancer biology. Primarily, I dissected the phenotypic variation of *Drosophila melanogaster* midgut mitosis using an array of highly inbred wild-type strains and identified a correlation between mitosis and ability to cope with bacterial infection and dysplasia. Our findings indicate that strains exhibiting either high or low mitotic potential can maintain tissue homeostasis. Moreover, when cell renewal capacity is limited, the differentiating cells of lowly mitotic strains undergo DNA replication without division, termed endoreplication, as a means to compensate for cell loss in tissue repair. With reference to oncogenesis, I demonstrate that excessive stem cell mitosis predisposes for dysplasia, which in turn compromises host defense. Collaborating with lab researchers we identified Eiger (Egr) as a mitogen controlling the counterbalance between mitosis and endoreplication. Genetic manipulation of Egr expression and quantification of tissue endoreplication indicates that Egr accelerates mitosis and dysplasia to the expense of endoreplication. Modulating regeneration responses through factors like Egr, could be of high significance in dealing with genetic variation and colorectal cancer (CRC) risk.

CRC is the second leading cause of death in the western world. The complex process of cancer cell invasion into local tissues and concomitant metastasis accounts for ~90% of cancer related deaths. Thus, revealing novel molecular markers deployed by cancer cells in their transition to malignancy is paramount. Using transcriptomic analysis of the *Drosophila* oncogenic hindgut enterocytes, I identified differential expression in genes encoding components of small Rho-GTPases and the Toll (NF-κB-like) immune pathway. Following genetic manipulation of these differentially expressed genes, I demonstrate that both signaling pathways are necessary and sufficient for hindgut enterocyte migration. I propose a mechanism of cross-regulation among small Rho-GTPases and Toll and JNK pathway responses that facilitates actin cytoskeleton alterations and hindgut epithelial-to-mesenchymal transition through the Snail-depended E-cadherin repression. Unlike Rho-GTPases and the Toll signaling pathway, JNK signaling does not suffice to cause cell delamination. Nevertheless, I demonstrate the existence of a cross-talk among Rho, Rac1, Toll and JNK signaling that in addition to cytoskeletal and cell junction rearrangements upregulates MMP1 expression leading to basement membrane degradation and neighboring tissues invasion.