MomentUM

Seminar

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05:00 pm CEST (11:00 am EDT; 8:00 am PDT)

Institut Curie, Amphitheater Hélène Martel-Massignac (BDD), 11 rue Pierre et Marie Curie, Paris
The seminar will also be broadcasted online via Teams*

«Defining the roles of genetic drivers of uveal melanoma with cell-based and Drosophila models»

Uveal melanoma is the most common eye cancer in adults with a set of highly characteristic genetic alterations. We identified mutations in the BAP1 (BRCA1 Associated Protein 1) gene in uveal melanomas with high likelihood of metastasis and recurrent mutations in the splicing factor SF3B1 with less chance of metastasis. Other alterations in this aggressive tumor include early oncogenic changes that are found in all tumor classes as well as characteristic copy number changes. In order to further characterize molecular alterations that drive tumorigenesis and metastasis we have performed long-read single molecule sequencing (SMRT) of DNA from primary UMs with different driver mutations to develop detailed maps of the structural variations (SVs) of the genomes of these tumors, and identified and characterized critical breakpoints, gene fusions and tumor specific isoforms. We have also used an eye organoid model (SEAM) to investigate the consequences of BAP1 loss, and the power of fly genetics to dissect the roles of the different genetic drivers. We have generated and characterized flies with loss of function mutations in the BAP1 ortholog calypso, and generate activating mutations of the GNAQ ortholog GαQ so that the combined effect of loss of calypso and activation of GαQ can be investigated. We have focused on larval eye discs and wing discs that represented well-ordered epithelial monolayers and examined the phenotypic, signaling and epigenomic changes that arise from these mutations. We have also tested drug targets affecting viability of UM lines for the ability to modify the cancer-like phenotypes seen in our one- and two-hit GαQ and calypso fly model. Genetic suppressors of overgrowth, tissue transformation, and metastasis phenotypes represent exciting therapeutic candidates to pursue in future studies. These studies are providing further insights into the roles of alterations leading to UM, and potentially novel targets for treatment.

Invited by: **The Uveal Melanoma Medico-Scientific Program, Institut Curie**
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*Full Teams link: https://teams.microsoft.com/l/meetup-join/19%3ameeting_ZmU4ZWI4MGItNWQzMC00YzcyLTk1ODUtMGQzNWI3Y2NjNTRi%40thread.v2/0?context=%7b%22Tid%22%3a%22183ad437-6002-48ad-8886-c5885ce9be1a%22%2c%22Oid%22%3a%221ed1e97e-4bdf-4145-b23a-9858c31bd9e7%22%7d