ProRegem 2018

Project Title:

Dissecting the genetic and molecular control of cell proliferation

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Location of research lab/research center:

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Summary: (1000 characters)

Correct organ size is determined by the balance between cell death and proliferation. Perturbation of this delicate balance leads to cancer formation. The Hippo pathway controls both cell death and proliferation, and dysregulation of the pathway leads to aberrant cell growth and neoplasia. The core of the Hippo pathway consists of a kinase cascade, transcription coactivators, and DNA-binding partners.

We, and others, have shown that Mob proteins, components of the Hippo pathway, act as kinase-activating subunits. Interestingly we have observed, that the various Mob proteins function in different cellular pathways. For example, Mob1 is involved in the mitotic exit network and is required for proper cytokinesis, whereas Mob2 is required for proper cell morphology.

Despite implicated roles of deregulated Mobs over cell proliferation, a clear genetic association or unique mutational link to the disease (cancer) is still missing. This project aims to dissect the genetic and molecular role of the yet uncharacterized

Mob genes. To achieve these goals a combined approach of genetics and cell biology techniques will be used.

This project, the continuation of a long standing collaboration between Tavares and Glover labs, ultimately aims to use Drosophila melanogaster and in vitro human cells to study the way Mob proteins, and their interacting proteins, regulate cell proliferation and apoptosis.

Bibliographic references:

Meghini F, Martins T, Tait X, Fujimitsu K, Yamano H, **Glover DM**, Kimata Y. (2016) Targeting of Fzr/Cdh1 for timely activation of the APC/C at the centrosome during mitotic exit. Nat Commun. 2016 Aug 25;7:12607.

Florindo C., Perdigão J., Fesquet D., Schiebel E., Pines J. and **Tavares A.A.** (2012) Human Mob1 proteins are required for cytokinesis by regulating microtubule stability. J. Cell Sci 125: 3085-3090.

Full common reference list in
https://scholar.google.com/citations?user=7Vls5H8AAAAJ&hl=en