Description of Funded Research Projects
1st Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers

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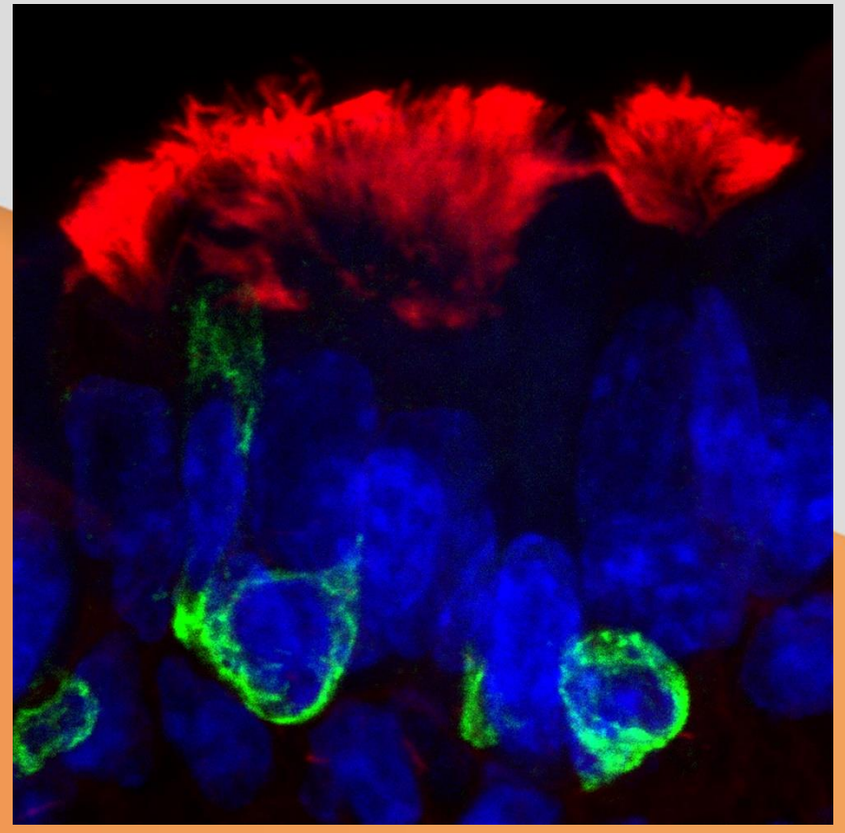
Research Project Title:

From Two to Many: Geminin Family Members Control Centriole Amplification, Cilia Formation and Pathology

Principal Investigator:
Marina Arbi



Popular Title:
Novel proteins contributing to genome stability and cell fate acquisition

Scientific Field:
Life Sciences

Host Institution:
University of Patras

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Maintenance of correct centriole/centrosome numbers is essential for genome stability. The centrosome duplication cycle must occur in concert with the chromosome cycle. Aberrations both in the genome content and in centrosome numbers can lead to genomic inconsistency. However, such aberrations can also be part of the normal life-cycle of specific cell types. Multiciliated cells best exemplify the deviation from a normal centriole cycle, as they exit the cell cycle and generate hundreds of centrioles per cell, breaking the spatiotemporal rules of generation of only one new centriole next to the parental centriole, in each cell cycle.

Recent findings suggest that a novel group of proteins, named Geminin superfamily, control this cell fate decision. In this study, we aim to elucidate how Geminin family members contribute to the normal centriole cycle and how they define, at the right time, a cell fate where multiple rounds of centriole duplication take place. We will combine diverse experimental approaches to study the role of Geminin family proteins in centriole duplication during the cell cycle using cancer and normal cell lines, with biochemical studies for the characterization of the complexes that mediate their functions and studies with genetically modified mice and ex-vivo differentiation systems to study multiciliogenesis. The most upstream pathway that controls the generation of multiciliated cells remains enigmatic and the identification of novel proteins that control this balance will shed light on the pathogenetic mechanisms at the heart of human diseases, caused by defects in centrosome and cilia formation, such as malignant transformation, ciliopathies, respiratory tract abnormalities and microcephaly.

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Project Impact on Society

This study will help us to understand the mechanisms that ensure once-per-cell cycle centriole duplication and how this control is abrogated for the generation of multiple centrioles during multiciliogenesis. The most upstream pathway that controls the generation of multiciliated cells remains enigmatic. The identification of novel proteins that control this balance will shed light on the pathogenetic mechanisms at the heart of human diseases, caused by defects in centrosome and cilia.

Aberrations in the centrosome cycle can lead to aneuploidy and thus to cancer development, as well as in human diseases including chronic obstructive pulmonary disease, hyperplasia-metaplasia of the airway epithelium, hereditary mucociliary clearance disorders and hydrocephalus. Thus, the genetically modified mice that we will use in this study can constitute mouse models for the human diseases related to defects in the function of the multiciliated cells. This study is of outmost importance for the clarification of the pathogenetic mechanisms and the therapeutic approaches of these human diseases.

To me, H.F.R.I. funding would mean...

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The HFRI grant for postdoctoral researchers constitutes one of the most remarkable actions in order to highlight the scientific potential, the innovation and the excellence of Greek Scientists. Moreover, it is very important that this grant gives us the opportunity to design and organize a scientific project. In parallel, being the Scientific Coordinators of our projects and through the formation and guidance of small research groups we are developing management skills. Overall, HFRI’s grant is an opportunity to pursue additional training and research towards an academic career.

The Principal Investigator,
Marina Arbi

Funding

Amount: **180,000 €**

Duration: **36 months**

Foundation: **H.F.R.I.**

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Hellenic Foundation for Research & Innovation

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