

Description of Funded Research Projects

1<sup>st</sup> Call for H.F.R.I. Research Projects  
to support Post-Doctoral Researchers



**H.F.R.I.**  
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Research Project Title:

**Hippo pathway in genome and  
epigenome maintenance**

**Principal Investigator:**  
**Dafni Eleftheria Pefani**

**Popular Title:**  
**DNA damage and cancer**

**Scientific Field:**  
**Life Sciences**

**Host Institution:**  
**Biomedical Research Foundation**  
**Academy of Athens**



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DNA damage is an ongoing threat to both our ability to faithfully transmit genetic information to our offspring, as well as our own survival. When DNA damage occurs, cells utilize complex signaling networks that mediate cell cycle arrest and repair or trigger senescence or apoptotic pathways in case of extensive, irreparable lesions. These pathways are collectively known as the DNA damage response (DDR), which consists of hierarchically-organized signaling cascades. The activation of the DDR promotes lesion recognition, modification of the surrounding chromatin environment to allow recruitment of the DNA repair machinery and ultimately the repair of the damage.

Recent studies have shown that signaling pathways previously studied in cell growth or metabolism also feed in to the canonical DDR to increase the efficiency of the process. Hippo is a kinase cascade that was originally identified as a developmental pathway; however, several studies have shown that the pathway acts as a tumor suppressor, and inactivation of the cascade is linked to tumor formation and metastatic behavior. Our previous research showed that the pathway is responsive to DDR triggering and inactivation of core components of the signaling results in accumulation of chromosomal aberrations and malignant transformation. However, the molecular details of how the Hippo cascade contributes to protection of genomic stability are still missing. In the proposed research we aim to investigate: 1) The mechanistic details of Hippo activity at the sites of DNA damage, and 2) Hippo pathway inactivation as a biomarker and target for synthetic lethality therapeutic approaches in tumors that lack activity of the cascade.

Overall, the proposed research using state-of-the-art approaches aims to deeply characterize the intersection between the DDR and the Hippo signaling cascaded, study Hippo pathway activation and regulation of downstream events during malignant transformation and explore new therapeutic approaches to target tumors that have lost Hippo activity.

Damage to our genetic material is an ongoing threat to both our ability to faithfully transmit genetic information to our offspring as well as our own survival, leading to cancer transformation. We are exposed every day in a plethora of DNA damage sources such as the ultraviolet (UV) component of sunlight, ionizing radiation and numerous genotoxic chemicals. To cope with this threat cells have developed a series of sophisticated mechanisms that mediate the repair of the DNA lesions and safeguard the integrity of our genome. This research aims to understand the mechanistic details of how cells orchestrate this response in order to achieve cancer free survival and utilize this knowledge for design of novel anticancer therapies.



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Funding from the Hellenic Foundation for Research and Innovation is of fundamental importance for the accomplishment of my research aims. As the grant's starting date coincides with my employment as an Assistant Professor at the Medical School of the National and Kapodistrian University of Athens, it gives me the opportunity to establish my own research team. I believe that this grant will allow me to answer important research questions about the molecular mechanisms that govern cancer biology and with this knowledge contribute to the field of cancer research. I recognize the importance of this initiative, as so far support to young researchers though National funding has been limited, and I hope that the funding scheme will continue to support young scientists.

*The Principal Investigator,  
Dafni Eleftheria Pefani*

## Funding

Amount: **180,000 €**

Duration: **36 months**

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





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## CONTACT

127, Vasilissis Sofias Avenue  
115 21 Athens, Greece  
info@elidek.gr  
www.elidek.gr



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