

Research on Nucleotide Excision Repair earns George Garinis an ERC Consolidator Grant

George Garinis, a Professor at the Department of Biology, University of Crete and an affiliated group leader at the Foundation for Research and Technology - Hellas (FORTH), has recently been awarded the prestigious European Research Council (ERC) Consolidator Grant for his research proposal titled "Dissecting the Functional Role of Nucleotide Excision Repair in Mammals-DeFiNER."

ERC Consolidator grants are highly competitive and allow exceptional, mid-career research leaders in any field of science, engineering and scholarship to pursue frontier research of their choice. The aim is to encourage risk-taking and interdisciplinarity, and support pioneering frontier research projects. The research proposal must be a product of pioneering frontier research. Funding for each selected proposal can reach a maximum of 2.7 million Euros for up to 5 years. This is an exceptionally high level of funding for individual researches, even by international standards.

"DNA damage accumulates with age and DNA repair defects cause the onset of degenerative changes similar to those seen in natural aging. Nucleotide excision repair (NER) is a major DNA repair pathway that cells employ to counteract DNA damage. However, defects in NER lead, in addition to cancer and aging, to developmental abnormalities whose clinical heterogeneity and varying severity cannot be explained by the DNA-repair defect alone." said George Garinis. "Indeed, we now know that, in addition to DNA repair, NER factors function in nuclear receptor signaling, stem cell reprogramming, and postnatal mammalian growth. This begs the question, though, of how NER prioritizes between such diverse functions?" he added.

Using a unique series of sophisticated mouse models and high-throughput approaches, George Garinis and his research team will attempt to gain mechanistic insights into NER, DNA damage-driven aging and age-related diseases, including cancer.

"The objectives of DeFiNER are manifold. We will focus on identifying the NER-associated protein complexes and assess their functional role in murine development; it will be equally important to define the NER-bound genomic targets and assess their physiological role in cell fate or to examine the functional interplay of NER complexes and underlying gene networks upon DNA damage. A follow up work will be to assess the functional role of NER in the three-dimensional (3D) organization of the genome" he explained.

"We hope that our research strategy will achieve a major breakthrough with an impact beyond the research domain of NER; it will allow us to explore the functional links between DNA repair mechanisms, the process of RNA synthesis and the chromatin architecture. Understanding these connections will provide us with insights into how genome maintenance pathways are connected to developmental defects and disease mechanisms *in vivo*, including aging and cancer." he concluded.

George Garinis heads the Genome (In)stability and Mammalian Physiology lab at the Institute of Molecular Biology and Biotechnology, in Heraklion, Crete, Greece. He earned his Ph.D. degree at the University of Athens, studying molecular mechanisms that lead to lung cancer in humans, and received training in mouse models carrying defects in NER at Erasmus Medical Center, Rotterdam, the Netherlands.

His research focuses on i. elucidating the functional links between genome instability and pathways associated with longevity, aging and age-related pathology, ii. evaluating the impact of progeroid mutations on tumor development, iii dissecting the functional interplay between impaired genome maintenance and tissue-specific progeria and iv. the development of advanced bioinformatics approaches to integrate functional genomics data with biological endpoints in cancer and aging.

George Garinis is a European Molecular Biology Organization (EMBO) Young Investigator.

More information on the research activities of the lab is available at:

<http://www.imbb.forth.gr/imbb-people/index.php/en/garinis-laboratory>