Institute of Molecular Biology and Biotechnology
Foundation for Research and Technology-Hellas

PRESS RELEASE

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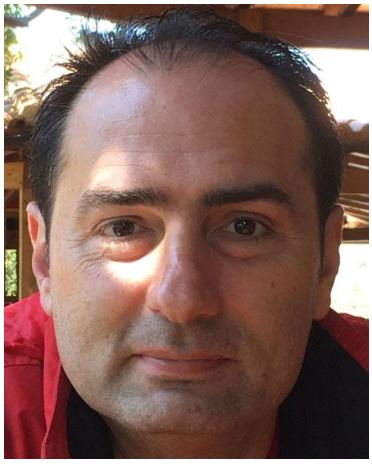
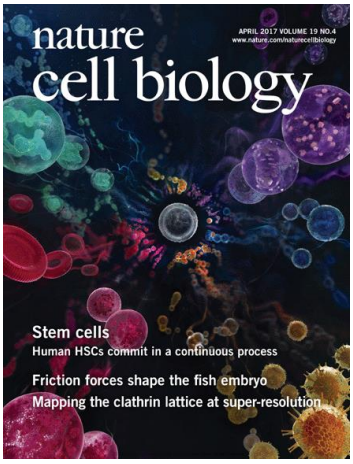
IMBB researchers reveal a novel function for DNA repair proteins during mammalian development





Research carried out at the Institute of Molecular Biology and Biotechnology-FORTH and published today in Nature Cell Biology (http://www.nature.com/ncb/index.html) reveals that DNA repair factors ERCC1 and XPF play a crucial during mammalian development.

Inborn defects in DNA repair mechanisms are associated with cancer, aging but also complex developmental disorders whose causal mechanisms are poorly understood. Using animals carrying specific biotin tag in the DNA repair factor XPF or an inborn mutation in the *Ercc1* gene, the IMBB researchers Georgina Chatzinikolaou and Zivkos Apostolou, working together with the head of the research team Prof. George Garinis, revealed that both XPF and ERCC1 proteins play a crucial role during mammalian development. Importantly, they also find that persistent DNA damage signaling triggers chromatin changes that affect gene expression programs associated with known developmental disorders.

Integrity of the genome is critical for normal cellular function but the DNA is continually challenged by intrinsic and extrinsic genotoxic factors. To counteract DNA damage, cells have evolved DNA repair mechanisms ensuring that the genome remains functionally intact and is faithfully transmitted to progeny. Nucleotide excision repair (NER) is a major DNA repair mechanism that cells employ to remove a wide class of bulky, DNA-distorting lesions from the genome. The importance of NER defects in man is illustrated by rare syndromes that either show increased cancer predisposition or dramatic features of accelerated aging, including depletion of fat depots. However, with the exception of cancer and aging, the links between defects in NER and the rapid onset of developmental defects in humans are not well understood.

Using mice that carry a specific tag in the DNA repair factor XPF and genetically modified animals with an inborn mutation in the *Ercc1* gene, the IMBB researchers provide evidence for a causal link between DNA repair proteins, persistent DNA damage and developmental gene expression programs in mammals.

The findings provide a novel mechanism to explain how inborn mutations in DNA repair genes lead to a wide range of developmental abnormalities in men.

For more information please contact:
Dr. George A. Garinis,
Professor, Dept. of Biology, University of Crete and affiliated group leader at IMBB-FORTH.
http://www.garinislab.gr
(Tel.: +30 2810391246; email: garinis@imbb.forth.gr)