Prof. Dr. George Garinis

Nucleotide Excision Repair: in Development and Disease

The links between defects in DNA repair and age-related diseases, including cancer are well established. However, little is known about the functional links between DNA repair factors, DNA damage signaling and mammalian development. The latter has recently attracted keen scientific interest for two major reasons: i) because of the growing appreciation of a link between DNA repair deficiencies and severe developmental defects in patients and ii) because of the increasing evidence that events governing the earliest stages of an organism's existence are now known to affect disease onset at later stages in life. Using an innovative in vivo biotinylation tagging knock-in approach in mice, along with animals defective in NER and mouse strains that allow the parental genes to be distinguished, we discussed recent data highlighting a functional link between nucleotide excision repair (NER), chromatin architecture and the developmental silencing of imprinted genes during mammalian development. On the basis of these observations, I have shown that ERCC1-XPF cooperates with CTCF and the cohesin subunits to facilitate the developmental silencing of imprinted genes and that persistent DNA damage signaling triggers chromatin changes that affect gene expression programs associated with NER developmental disorders.

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