Nucleotide excision repair: from molecular mechanisms to patient phenotypes

Apelt, K.

Stellingen

Behorend bij het proefschrift getiteld

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from molecular mechanisms to patient phenotypes

1 For the damage recognition in nucleosomes the core NER factors are assisted by several post-translational modifiers that finetune the repair (thesis chapter 1).

2 An XPC-PARP axis links the chromatin remodeller ALC1 to GGR (thesis chapter 2).

3 ALC1's catalytic activity, as well as its PAR-binding activity are both required for efficient GGR (thesis chapter 2).

4 Whereas scientific findings in mouse models are often considered to apply to humans, this does not always hold true. Contrary to findings in mice, human HMGN1 and HMGN2 proteins are not involved in transcription-coupled repair (TC-NER) (thesis chapter 3).

5 The ERCC1 point mutation R156W shows dramatically reduced protein levels of ERCC1 and XPF, causing weakened interactions with NER and ICL repair proteins, resulting in diminished recruitment to DNA damage. This leads to a mild repair defect in interstrand crosslink repair and a severe repair defect in NER (thesis chapter 5).

6 Cell culture-based characterization of repair proteins only gives an indication of the complexity of the patient phenotype. Revealing the true role of ERCC1 R156W in patients requires the analysis of the protein during the development and maintenance of specific organs.

7 Mapping clinical variants can provide more insights into the different protein functions. Bearing this in mind, clinical variants can help fundamental science to get a better understanding of the affected protein.

8 Mutation in the central domain or DNA-binding domain of ERCC1 cause distinct phenotypes in patients.

9 Collaborating with patient organizations increases the impact of scientific findings by addressing the patients' needs in the clinical practice.

10 Outstanding research starts at the end of the comfort zone. That is the moment where we embark upon a journey of inspiration and creativity.

11 To bring inventions from the lab into the real-world, we need to be more eager to combine our forces.