

IRON-SULPHUR PROTEINS AND GENOME STABILITY

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SUMMARY & MISSION STATEMENT

We use biochemistry and cell biology to understand the causes and consequences of DNA replication stress with a particular focus on DNA replication and repair proteins that bind to an iron-sulphur cluster as a co-factor. Understanding DNA replication stress at the molecular level will contribute to our understanding of cancer-related genome instability and will increase the knowledge that is indispensable for the design of more effective treatments with fewer side effects.

OVERVIEW

We are interested to understand how a cell maintains the integrity of its genome despite being exposed to numerous internal and external factors that can potentially damage DNA. Research on the maintenance of genome stability is not only relevant from a molecular biology point of view, but has also further-reaching impact since genome instability is one of the hallmarks of cancer. In particular, in my research group we focus on the role of small inorganic protein co-factors, so-called iron-sulphur clusters, in the processes of DNA replication and repair. Over the last years, iron-sulphur clusters have turned out to be essential co-factors in multiple nuclear proteins that play a role in the maintenance of genome stability. Given the redox-sensitive nature of iron-sulphur clusters and their potential to generate DNA-damaging reactive oxygen species, their occurrence in genome maintenance proteins is highly counter-intuitive, and so far, the role of iron-sulphur clusters in these proteins has remained poorly understood. Most of the projects in my lab therefore focus on the function of the iron-sulphur cluster in various DNA replication and repair proteins, such as DNA polymerase delta and FANCI, mutations of which are associated with colorectal cancer, and breast and ovarian cancer, respectively.

SELECTED CANCER RELATED PUBLICATIONS

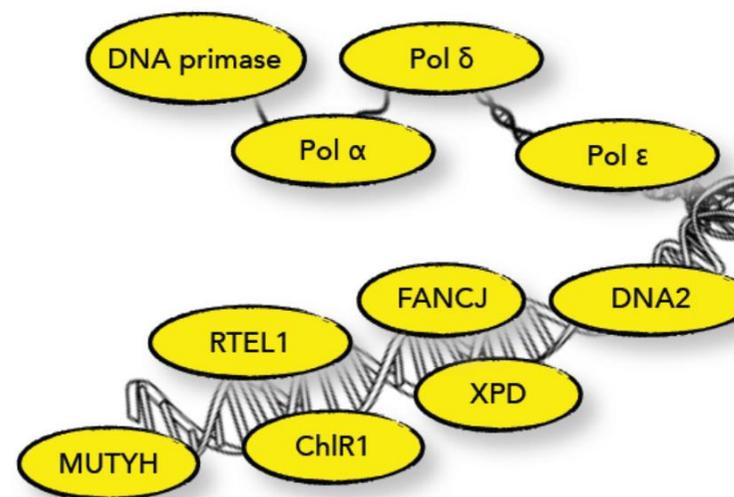
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Iron-sulphur proteins with roles in DNA replication and repair.