The regulation of DNA polymerase eta and its effects on genome stability

DNA replication is a highly accurate and processive process but it is particularly susceptible to DNA damage. If not repaired in a timely manner, DNA damage can lead to the introduction of mutations, block the replication forks and ultimately may cause cell death. At the organism level, these defects can lead to the onset of tumours, neurodegenerative diseases and immunodeficiencies.
Our research is focused on the study of a cellular pathway called PRR (Post Replication Repair) that is able to bypass DNA damage to the double helix during DNA replication, ensuring its completion. In particular, we focus on the study of DNA polymerase eta, a polymerase that is part of this important damage tolerance mechanism. The absence of pol eta is the molecular basis of a rare genetic disease called Xeroderma Pigmentosum Variant, whose patients are extremely susceptible to the onset of skin tumours. Our work focuses on the characterization of pol eta regulation, investigating how it is modulated by interactions with a complex network of proteins in vivo. We also study how pol eta is controlled by post-translational modifications (Ubiquitination, phosphorylation and SUMOylation), in the context of DNA repair systems and the control of the cell cycle. We address these issues through a multidisciplinary approach ranging from cell biology to biochemistry in human cell lines, in order to understand how pol eta can help the maintenance of genome stability and can function as a barrier against the onset of cancer.