**ROLE OF TEL1-SEN1 INTERACTION IN THE MAINTENANCE OF GENOME STABILITY**

Double-strand DNA breaks (DSBs) are among the most dangerous DNA damage because only one of these unrepaired breaks can cause cell death, while inaccurate repair promotes tumorigenesis. The formation of DSBs leads to the activation of the cell cycle checkpoints, the remodelling of chromatin, and to the transcriptional inhibition of genes located near the breaks. RNA / DNA hybrids (R-loops), caused by the collision between the transcription machinery and the replication forks, are a major source of genetic instability that can trigger DSBs formation. Conversely, DNA-RNA hybrids appear to be formed in response to DSBs at transcriptionally active loci. The disassembly of R-loops by Senataxin, a human helicase, and by its ortholog Sen1 in the yeast *Saccharomyces cerevisiae*, contributes to maintain genome integrity.

Despite their dangerousness, DSBs are also formed in a programmed manner during meiosis by Spo11, a type 2 topoisomerase, in hotspots that are largely determined by epigenetic marks. These programmed DSBs are essential for accurate chromosome segregation and genetic diversity, but require a fine regulation to prevent genetic instability and aneuploidy. The protein kinase Tel1 in Saccharomyces cerevisiae, and its ortholog ATM in humans, play a fundamental role in genome stability maintenance, in particular in response to DSBs. Mutations in ATM are the cause of a rare genetic disease, Ataxia Telangiectasia (AT) which confers neurodegenerative symptoms, infertility, and an increased predisposition to cancers. Phosphorylation targets of Tel1/ATM in response to DSBs are multiple and involved in various DSBs signalling pathways.

Using the yeast Saccharomyces cerevisiae we recently uncovered an interaction between Tel1 and Sen1 during meiosis, indicating a link between Tel1 and R-loops, an area that has remained unexplored so far. The project aims to investigate R-loops formation during meiosis, and their impact on DSB formation and repair. The project will be based on a multidisciplinary approach combining genetics, molecular biology and bioinformatics.