Open Ph.D. projects

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Title of the research topic: Analyzes of the replication of the stable secondary stucture containig DNA tracks

Description of the research topic: There is a huge number of special DNA sequences present in the human genome that can form stable secondary structures in single-stranded forms and behave as replication blockades. In our proposal, we plan to concentrate on two different blocking structures. One of them is the G quadruplex (G4), and the other is the trinucleotide repeat (TNR), which forms a stable loop structure. The accurate replication of these sequences is both a challenge and a necessity for the cell because G4 structures have various essential functions such as ensuring the stability of the ends of the chromosomes (telomeres), replication initiation, gene expression regulation by transcription and translation repression, and determination of chromosome condensation. Additionally, TNR repeat expansion is responsible for about 40 different neurodegenerative diseases and, theoretically, the loss of G4 structures may lead to oncogene activation and carcinogenesis as the promoter and 5' UTR regions of oncogenes are rich in potentially G4-forming sequences. Therefore, our major goal is to understand how the action of replicative DNA polymerases leads to these failures. DNA polymerases alone cannot cope with the challenge of replicating blocking sequences, therefore, the contribution of several other proteins is needed. Although several contributors have been identified, it is still not clear how they affect the biochemical activity of DNA polymerases. Therefore, we will reconstitute in vitro a replication model of these structures and analyze how the different contributor proteins modify the biochemical activity of DNA polymerases enabling correct replication of the G4 and TNR sequences.