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Selected Publication

Schalbetter, Stephanie, Mansoubi, Sahar, Chambers, Anna L., Downs, Jessica and Baxter, Jon (2015) Fork rotation and DNA precatenation are restricted during DNA replication to prevent chromosomal instability. *Proc Natl Acad Sci USA*. 112(33):E4565-70

Research Aims and Interests

The Baxter laboratory studies the process of chromosome resolution. During chromosome replication the sister chromatids become entangled. All such entanglements need to be resolved before the chromosomes can be faithfully segregated to the daughter cells during mitosis. In particular we study how the induction of topological stress across the chromosome results in the generation of double stranded intertwines or catenanes during DNA replication. The essential role of Topoisomerase II is to ensure that all of the DNA catenanes generated by DNA replication are resolved before the completion of cell division.

In order to directly visualize the generation of DNA catenation during DNA replication we primarily analyze the DNA topology of yeast plasmids. This allows us to directly assess the extent of DNA catenation and supercoiling tension on a test replicon in vivo. In our latest work we have found that fork rotation and DNA catenation primarily occurs during termination and at stable protein-DNA sites that pause ongoing replication. In addition we have found that this limitation of DNA catenation is achieved through the action of the yeast homologues of Timeless/Tipin, Tof1/Csm3. Tof1/Csm3 appear to limit fork rotation to ensure the excessive pre-catenation does not cause DNA damage on the newly replicated strands.

From this work we are examining how excessive pre-catenation could cause DNA damage in sister-chromatids and how Tof1/Csm3 restricts fork rotation and DNA catenation during DNA replication. Our long term aim is to understand how topological tension and generation of entanglements influences genome stability in both normal and pathological altered cell types.