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Selected Publication

Li, X.C. and Tye, B.K. (2011) Ploidy Dictates Repair Pathway Choice under DNA Replication Stress. *Genetics*. 187: 1031-40

Research Aims and Interests

My group has been using multi-prong approaches to study the functions of the MCM complex during replication initiation and replication elongation. Using a genetic approach, we examined the effect of the *mcm4*^{Chaos3} allele that causes cancer susceptibility in mice has on replication fidelity in yeast. We found that *mcm4*^{Chaos3} homozygous diploids accumulate all sorts of mutations from point mutations to large chromosomal rearrangements. This faulty CMG helicase under replication stress becomes a rampant mutations generating machine that can be exploited as a yeast cancer model. Of particular interest, this phenotype of the yeast mutant is ploidy specific, affecting only diploid cells, suggesting that it could be used as a possible model for studying cell type specific cancers. Subsequent analyses showed that the different cell types use different repair pathways to correct similar types of DNA damage. This dichotomous response appears to be due to a difference in histone gene dose in the two cell types. We are also analyzing the functions of the MCM complex at different stages of the replication cycle through structural studies using state of the art Cryo EM.