Post-doctoral scientist in Cell Cycle Controls :-

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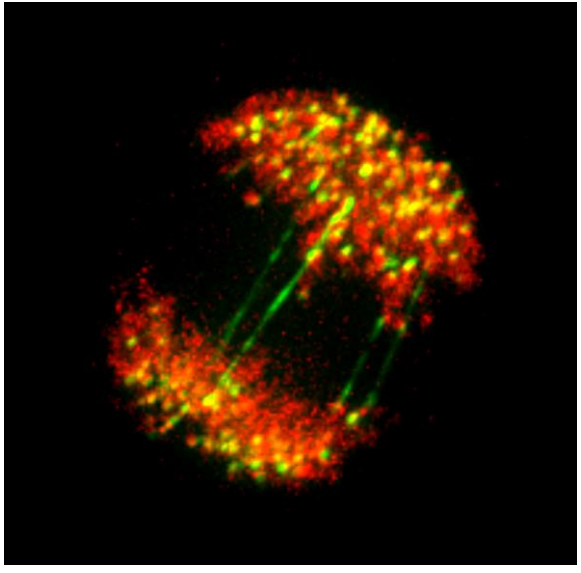

Opportunities are available to investigate the control of chromosome segregation by DNA Topoisomerase II (Topo II) in yeast and human cell models. Chromosome segregation errors result in aneuploidy, which causes birth defects and cancer. This project will characterize a mechanism that controls anaphase initiation when Topo II activity is insufficient for accurate chromosome segregation. This cell cycle control is triggered by stalled Topo II strand passage reactions, where the enzyme becomes trapped on DNA in a Closed Clamp structural conformation. Activation requires two distinct modules within the catalytically inert C-terminal domain of Topo II: (i) A cluster of SUMOylation sites, and (ii) The Chromatin Tether domain of Topo II, which interacts with methylated nucleosomes. The central molecular model is that stalled strand passage leads to C-terminal domain SUMOylation that functions as a signal-generating scaffold to halt cell cycle progression in metaphase. The results of these studies will impact opportunities for translational research through the identification of potential therapeutic targets. The project will synergize with ongoing high-throughput screens that aim to identify novel mitosis inhibitors.