Title: Centromere Integrity: the Crosstalk between Replication and Heterochromatin Proteins in *S. pombe*

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The centromere is a specialized part of the chromosome required for chromosome segregation. Centromere structure is partly maintained by highly condensed heterochromatin, assembly of which relies on Heterochromatin Protein 1 (HP1/Swi6). In fission yeast, Δ*swi6* cells have defects in chromosome segregation, gene silencing, and genome stability. During each cell cycle, the centromere heterochromatin must be unwrapped for DNA replication and reassembled for chromosome segregation. Its highly repetitive sequences must also be protected from genetic rearrangement. How does the cell preserve the integrity of this important genetic region? In my thesis, I used fission yeast to study how replication and heterochromatin proteins cooperate and maintain centromere integrity.

Evidence from our lab and others has demonstrated that DNA replication proteins interact with Swi6, suggesting a close relationship between DNA synthesis and centromere heterochromatin maintenance. We found replication initiator protein Cdc18/Cdc6 associates with Swi6. A mutation *cdc18-I43A* that reduces this association with Swi6 accelerates replication timing in the centromere. However, loss of Swi6 reduces replication timing. We suggest that recruitment of Swi6 to the centromere origins is important for negative as well as positive control of replication initiation. We have characterized centromere replication timing of other heterochromatin proteins. Finally, our genetic studies suggest that *swi6* mutants are extremely sensitive to defects in replication fork stability, suggesting a close interplay between replication fork assembly and maintenance, and function of centromere heterochromatin.