

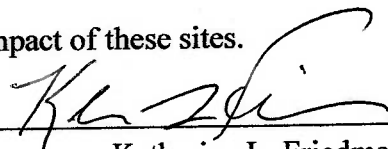
Predicting and characterizing the distribution of sites of repair associated telomere addition in  
*Saccharomyces cerevisiae*

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Dissertation under the direction of Professor Katherine Friedmar

Telomeres, maintained by the enzyme telomerase, are GT-rich, highly repetitive sequences at the ends of most eukaryotic chromosomes. Telomeres protect chromosome ends from degradation and counteract the progressive loss of DNA that is a result of the end replication problem. Telomeres also distinguish the naturally occurring single-stranded DNA (ssDNA) overhangs at the end of the chromosome from the ssDNA that results from a double-strand break (DSB). Rarely, telomerase adds a *de novo* telomere following a DSB, in lieu of other repair mechanisms. The addition of a *de novo* telomere causes a gross chromosomal rearrangement event wherein DNA downstream of the new telomere is lost, but the telomere capping prevents further resection and DNA loss from occurring. Sequences that act as hotspots for *de novo* telomere addition have been termed Sites of Repair-associated Telomere Addition (SiRTAs). In this thesis, I discuss methods used to test whether a sequence is a SiRTA which include a test site to determine whether a sequence is a SiRTA and a high-throughput sequencing method that accurately measures the frequency and specific location of telomere addition within these sequences. With these methods, I identified several SiRTA sequences that were utilized along with computational techniques to develop the first comprehensive map of SiRTAs in the yeast genome. In total we identified 728 putative SiRTAs with an accuracy of ~95%. This map is a novel tool that could be used to study these sources of genomic instability. I discuss ways I have used this map to answer some outstanding questions and I also propose exciting future directions to study the mechanism behind and impact of these sites.

Approved



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Date

5/31/23