FALL 2021

Biochemistry and Molecular Biology Brown Bag Series

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M.S. Students

"DNA Replication Fork Instability at the PKD1 Microsatellite"

Tuesday, October 26, 2021

11:00 AM

135 Oelman Hall

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract

DNA Replication Fork Instability at the PKD1 Microsatellite

Microsatellites are short, repeated sequences of DNA that can disrupt genome integrity by forming non-Watson-Crick structures leading to DNA double strand breaks during replication. When these breaks occur, mutagenic repair processes can be used by the cell that lead to various diseases. For our research, we integrated an 88-base pair mirror repeat sequence (intron 21 of the Polycystic Kidney Disease (PKD1) locus), containing one purine-rich and one pyrimidine-rich strand into HeLa cells modified to detect genomic instability via a dual-fluorescent reporter system. This mirror repeat is known to form secondary structures that slow DNA replication fork progression depending on replication polarity. To study this orientation dependence, we made two HeLa cell lines with either the purine-rich (TTR cell line) or the pyrimidine-rich (TTF) sequence in the lagging strand template of the replication fork. The cells were subjected to drug treatment that stabilized these secondary structures creating a replication barrier. Our results show that the replication polarity associated with fork stalling also leads to replication-dependent DNA double strand breaks.