FALL 2022

Biochemistry and Molecular Biology Brown Bag Series

Resha Shrestha

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"Genome instability at (CAG) 102 microsatellites in human cells"

Tuesday, November 22, 2022

11:00 AM

135 Oelman Hall

Lab: Michael Leffak, Ph.D.

Boonshoft School of Medicine
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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract:

Genome instability at (CAG) $_{102}$ microsatellites in human cells

Microsatellites are tandem repeats of short nucleotide sequences that are inherently unstable. These repeats can pose obstacles in the ongoing replication process leading to double strand breaks (DSBs). When unrepaired, these breaks can threaten the genomic integrity leading to various neurological and developmental diseases. Such replication-induced breaks are repaired via a highly mutagenic repair mechanism known as break induced replication (BIR). My project specifically focuses on the trinucleotide repeats of CAG units capable of forming hairpin structures which stall the replication fork, eventually causing its collapse. Expansions in CAG repeats have been implicated in Huntington's disease. To study instability caused by this repeat, we are using HeLa cell line with dual fluorescent reporter constructs harboring a repeat of 102 CAG units in the lagging strand template adjacent to a c-myc origin of replication. This will allow us to use flow cytometry, inverse PCR, and sequencing to study the effects of these repeats on replication and chromosomal instability by monitoring subsequent recombination, mutations and translocations generated from the BIR repair mechanism. We will also investigate the role of various replication proteins (STN1, Rad51, Pol h) in such repair, and elucidate the possible roles of these proteins in BIR.