# FALL 2021

## Biochemistry and Molecular Biology Brown Bag Series

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## "Microsatellite instability initiates Gross Chromosomal Rearrangement and High Frequency Mutagenesis"

**Tuesday, October 5, 2021**

**11:00 AM**

**135 Oelman Hall**

**Lab: Dr. Michael Leffak, Ph.D.**

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**http://www.med.wright.edu/bmb**

## Abstract

### Microsatellite instability initiates Gross Chromosomal Rearrangement and High Frequency Mutagenesis

Microsatellite sequences are repetitive motifs in the genome which are about 1-6 nucleotides long. They make up for 3% of the genome and have an elevated mutation frequency compared to non-microsatellite loci. These sequences are known to form several types of non-B DNA structures like hairpins, G-quadruplex, triplex, etc. which lead to problems during replication, and transcription. As a result, the sequences can undergo expansion or contraction, and is thus responsible for 40 neurodegenerative and neuromuscular diseases. There is rising evidence of these sequences causing translocations, ultimately leading to cancer. This suggested that microsatellite sequences are responsible not just for expansions, but also double strand breaks (DSBs). To study this possibility, we generated a novel, dual fluorescent reporter system and incorporated two independent microsatellites-$(CTG)_{100}$ and (Purine/Pyrimidine-$(Pu/Py)_{88}$. We induced the cells to low levels of replication stress and observed that the $(CTG)_{100}$ microsatellite undergoes DSBs under multiple forms of replication stress and is highly mutagenic. Our study using the $(Pu/Py)_{88}$ microsatellite concluded that they too undergo DSBs. The NGS analysis for the $(Pu/Py)_{88}$ study showed that it is causing genomic instability through gross chromosomal rearrangement and high frequency mutagenesis.