



FALL 2018

**Biochemistry and Molecular Biology
Brown Bag Series**

Rujuta Gadgil

PH.D. Student

***“DNA Breaks at Microsatellite Sequences during
Replication Stress; Analysis by a Novel Flow
Cytometry Assay”***

Tuesday, November 6, 2018

11:00 AM

129 Medical Sciences Building

Lab: Michael Leffak



Boonshoft
School of Medicine
WRIGHT STATE UNIVERSITY



WRIGHT STATE
UNIVERSITY

<http://www.med.wright.edu/bmb>

Rujuta Gadgil

DNA Breaks at Microsatellite Sequences During Replication Stress; Analysis By A Novel Flow Cytometry Assay

Sequences that appear in tandem in the genome and include repetitions of 1-6 nucleotides are known as microsatellite sequences. For the purpose of our study we have focused on trinucleotide repeats (TNRs) since they are prone to form non-B DNA structures and mutations. They also undergo expansions in vivo to cause various inherited neurodegenerative diseases. We hypothesized that the non-B DNA structures formed at these TNRs can cause replication fork stalling and if left unrepaired lead to single or double strand breaks. To study this, a novel two color marker gene assay was devised that can be analyzed by flow cytometry. By inducing replication stress, our results show that TNRs are prone to DNA strand breaks. We have also shown that these breaks are length dependent and polarity dependent. The cells that encounter these breaks are genetically unstable and hence undergo apoptosis. Also, our data showed that the cell undertakes different mechanisms to repair the broken DNA. Finally, we show that some translesion polymerases are essential to maintain genomic stability at these TNR sequences. Our study thus helped to show that the TNRs could be considered as fragile sites that can lead to chromosome breaks under replication stress.