# FALL 2022

## Biochemistry and Molecular Biology Brown Bag Series

# Sankhadip Bhadra

**Ph.D. Student**

***"Role of TTT complex in regulating DNA replication checkpoint in fission yeast"***

**Tuesday, November 1, 2022**

**11:00 AM**

135 Oelman Hall

**Lab: Yong-jie Xu, M.D., Ph.D.**

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

## Abstract:

**DNA replication can be perturbed by many agents such as hydroxyurea that depletes dNTPs and DNA damaging agents such as methyl methanesulfonate that damage DNA templates. These agents stall replication forks, causing replication stress. If undetected, stalled forks collapse, causing mutations or cell death. In response to the stress, the cell activates the replication checkpoint controlled by the protein kinases ATR and ATM. ATR and ATM are members of the phosphatidylinositol-3-kinase (PI3K) family and their maturation and stability are regulated by TTT (Tel2-Tti1-Tti2) protein complex. The TTT complex regulates the maturation and stability of the PI3K kinases by monitoring their proper binding and assembly. The current model demonstrates the upstream regulation of Rad3 (ATR) by the TTT complex. Recent studies in our lab have identified a *tel2* mutation *tel2-C307Y* that eliminates Rad3 (ATR ortholog)-mediated replication checkpoint signaling in the fission yeast *Schizosaccharomyces pombe.* Surprisingly, although the Rad3-mediated replication checkpoint signaling is eliminated by the mutation, the Rad3-mediated signaling in the DNA damage checkpoint pathway is only moderately reduced, suggesting that in addition to Rad3 maturation, Tel2 may contribute to the replication checkpoint via a previously unknown mechanism in fission yeast. To better understand the checkpoint mechanisms, we are taking a genetic approach to analyze the functions of Tti1, the largest component of the TTT complex. Our preliminary data show that it is likely that new separation- of-function mutants of *tti1* in the DNA replication checkpoint and the DNA damage response have been identified which suggests that the TTT complex might also regulate the downstream checkpoint signaling pathway.**