# Fall 2025

## Biochemistry and Molecular Biology Brown Bag Series

## Balveer Singh

## Postdoctoral Researcher

***"Mrc1 Mediated Mechanisms of DNA Replication Checkpoint Signaling and Epigenetic Memory Maintenance"***

**Tuesday, September 9, 2025**

**11:00 AM**

**Location 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

**Eukaryotic DNA replication initiates from multiple origins under strict spatiotemporal control to ensure genome stability. Mrc1 (hClaspin), an essential replication stress protein, functions as the key DNA replication checkpoint (DRC) mediator while also regulating origin activity, epigenetic memory, and fork stabilization through its interaction with Swi1/Tof1 (hTim1) and Swi3/Csm3 (hTimeless). For checkpoint signaling, Rad3 (Mec1/ATR) phosphorylates two redundant TQ sites (T645, T654) at the middle of protein on Mrc1, enabling recruitment and phosphorylation of the effector kinase Cds1 (Rad53/Chk2). Near the two TQ sites, a cluster of four SQ sites has been identified in Mrc1 that is also required for Cds1 activation. However, the mechanism by which the SQ cluster mediates Cds1 activation remains largely unknown. During my talk I will present the results from experiments related to sequential deletions and mutational analysis of Mrc1 to identify other amino acid residues in Mrc1 that are important for Cds1 activation. Our results precisely mapped the region for DRC activation and identified previously uncharacterized residues in Mrc1 whose mutations reduced Cds1 activation and destabilized the interaction between Mrc1 and Cds1. Collectively, our data establishes that apart from DRC signaling through the TQ sites, other motifs of Mrc1 are also crucial for the DRC activation.**