SPRING 2023

Biochemistry and Molecular Biology Brown Bag Series

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"Molecular insights into the role of Rad9-1-1 in Cds1 activation in S. pombe during replication stress"

Tuesday, April 11, 2023

11:00 AM

Location 135 Oelman Hall

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

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WRIGHT STATE UNIVERSITY

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

Molecular insights into the role of Rad9-1-1 in Cds1 activation in *S. pombe* during replication stress

DNA damage response (DDR) pathways play a key role in the activation of cell cycle checkpoints and the maintenance of genome integrity. Thus, defects in DDR result in cancer and other diseases. In *S. pombe*, the heterotrimeric complex of Rad9-Hus1-Rad1 (commonly known as 9-1-1 complex) plays a vital role in DDR. The C-terminal tail of Rad9 has multiple phosphorylation sites that are crucial for multiple protein-protein interactions, which results in checkpoint activation during replication stress. The phosphorylation defective mutants of rad9 and deletion of the C-terminus tail of rad9 render *S. pombe* cells sensitive to drugs such as hydroxyurea (HU) and methyl methane sulfonate (MMS), thereby emphasizing the role of Rad9 in DDR and DNA replication checkpoint. Our study has shown that mutations in the phosphorylation sites of Rad9 and deletion of C-terminus tail do not affect phosphorylation of Mrc1, but impair Cds1 phosphorylation by Rad3, although Cds1 activation is downstream of Mrc1. This observation raises a key question and gap in the current knowledge “How does Rad9 phosphorylation promote Cds1 activation under replication stress independent of Mrc1?” We have identified suppressor that could rescue the HU sensitivity of rad9 mutants and interact with phosphorylated Rad9.