GRADUATE STUDENT SEMINAR

MACHINE LEARNING-BASED APPROACH FOR PREDICTING ANTIBIOTIC RESISTANCE AND IDENTIFICATION OF NOVEL ANTIBIOTICS RESISTANCE-ASSOCIATED MUTATIONS IN MYCOBACTERIUM TUBERCULOSIS
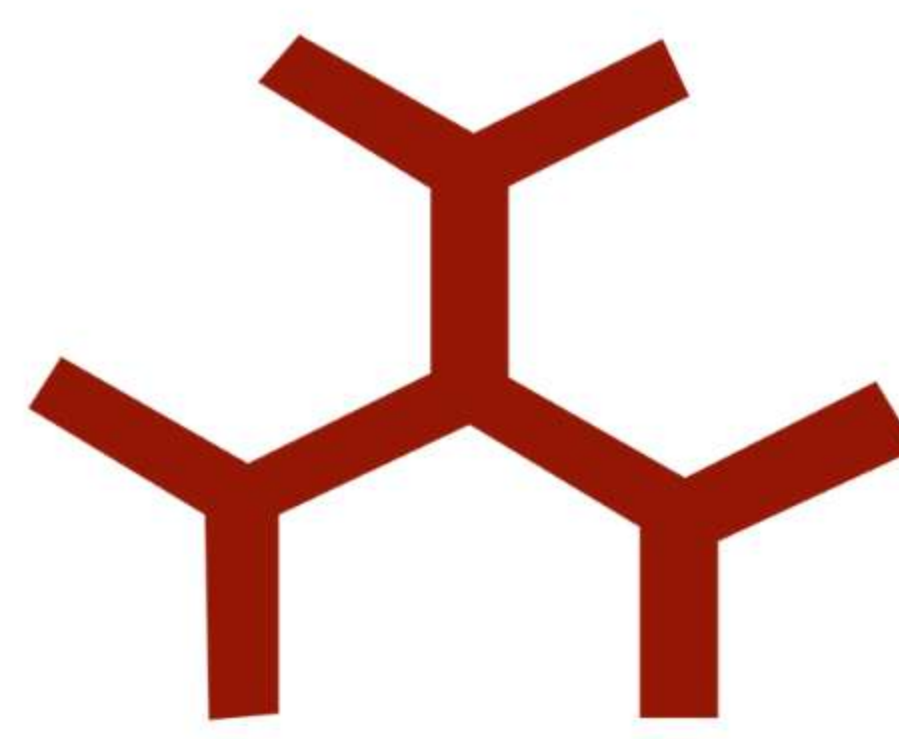
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The emergence of antibiotic resistance in *Mycobacterium tuberculosis* has been a major concern due to the high mortality associated with it. Antibiotic susceptibility testing (AST) is the traditional method for identifying antibiotic resistance in bacteria. Since it is a time-consuming, culture-based method, in recent years next-generation sequencing-based methods for identifying antibiotic resistance have attracted considerable attention. Whole genome sequencing (WGS) based methods can not only identify antibiotic-resistant strains faster but also can help in deciphering antibiotic resistance-related mutations and provide insights into mechanisms of drug resistance. Artificial Intelligence/Machine Learning (AI/ML) based analysis of whole genome sequences has the potential to identify new resistance-associated genomic alterations. Therefore, in this study, our major goal is to develop an AI/ML-based method for the prediction of antibiotic resistance using whole genome sequences as input, identify novel resistance markers using interpretable AI, and decipher mechanistic details of antibiotic resistance.

18 MAY 2023, 4.00 PM
GP TALWAR AUDITORIUM, NII

GRADUATE STUDENT SEMINAR

UBIQUITIN-MEDIATED RECRUITMENT OF RMI1 UPON REPLICATION STRESS

RIMPY ARUN

SIGNAL TRANSDUCTION LABORATORY II

The BLM helicase is known to play an important role in maintaining the genomic integrity of the cells by forming a complex with topoisomerase IIIα (TOP3A), RMI1, and RMI2. This complex plays a crucial role in DNA repair, particularly in the resolution of Holiday Junction (HJ) like intermediates in Homologous recombination (HR). Any perturbance in the complex is associated with hyper recombination, having a hallmark feature of increased Sister Chromatid Exchanges (SCE). Biallelic mutations in TOP3A have been associated with prenatal growth restrictions and microcephaly. A truncating mutation in RMI1 is also associated with microcephalic dwarfism. Depletion of RMI1 specifically affects cellular protein levels of TOP3A and, to a lesser extent, BLM, affecting the whole complex's stability. Thus, RMI1 is recognized as an essential component of the BLM dissolvasome that maintains genome integrity. Despite the crucial role of this complex, very little is known about the recruitment of RMI1 to the sites of damage. Our study demonstrates that RMI1 is recruited to sites of replication stress in a ubiquitin-dependent manner. In addition, we have identified a role of the RING-type E3 ubiquitin ligases, RNF8 and RNF168, in the recruitment of RMI1 to stalled replication fork sites via K-63-linked ubiquitylation.

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