राष्ट्रीय प्रतिरक्षाविज्ञान संस्थान

National Institute of Immunology

GRADUATE STUDENT SEMINAR

UNDERSTANDING THE ROLE OF ZINC EFFLUX AND ALLOCATION IN MTB DURING HOST-PATHOGEN INTERACTION

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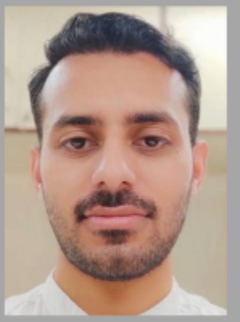
Mycobacterium tuberculosis (Mtb) has evolved complex machinery to evade the host-induced metal starvation termed as nutritional immunity. Towards this, Mtb produces stealth zinc scavenging molecules known as kupyaphores, to counter and surpass the host-induced zinc scarcity during infection. Nevertheless, the regulatory machinery that directs the transport and biosynthesis of this metabolite remains obscure. Here, we show the potential role of two hypothetical proteins, Rv0096 and Rv0106, that are involved in modulating kupyaphore homeostasis. Our study unravels the molecular circuit to eclipse the zinc dysmetallostasis induced by the host. We propose that Rv0096 and Rv0106 are important regulators of Mtb under zinc stress and may serve as important therapeutic targets in future.

UNDERSTANDING THE MECHANISM OF HYPER UBIQUITYLATION AND AGGREGATE FORMATION IN PEO PATIENT MUTANTS OFFER A POTENTIAL CLINICAL INTERVENTION



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PolgA, a mitochondrial DNA polymerase (mtDNA), which upon mutations leads to Progressive external ophthalmoplegia (PEO). Ubiquitylation of PolgA and PEO mutants by Mitochondrial E3 ligase MITOL negatively regulates mitochondrial import. However, the factors which determine why and how some of the mutants undergo hyperubiquitylation and accumulation as insoluble structures are unknown. In our study, screening of PEO patient mutations displayed compromised mitochondrial import, mtDNA replication, and aggregate formation. Hence, we screened for small molecules which can disrupt PEO mutant aggregates-like structures using split GFP complementation system. This might open up new avenues for therapeutics for modulating the import of PEO mutants inside the mitochondria and thereby restoring mitochondrial homeostasis.

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