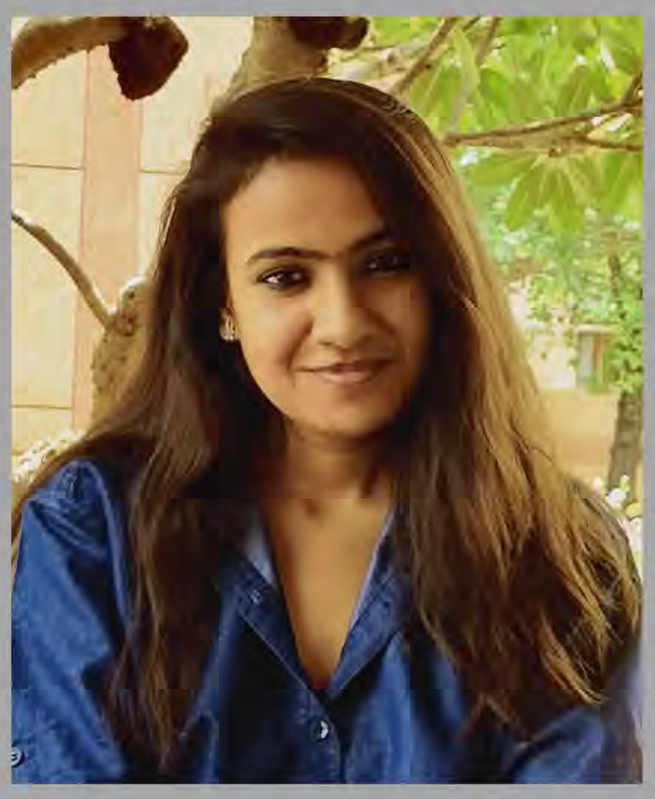
राष्ट्रीय प्रतिरक्षाविज्ञान संस्थान

National Institute of Immunology

GRADUATE STUDENT SEMINAR

DELINEATING THE MECHANISM OF PROTECTION CONFERRED BY A POTENTIAL MALARIA VACCINE CANDIDATE



SHREYA BHATTACHARYA

INFECTIOUS DISEASES LABORATORY

Malaria remains one of the world's most devastating diseases found in the tropical and sub-tropical regions of the world. The lack of a high-efficacy vaccine, as well as the development of multidrug resistance by the pathogen, has skewed *Plasmodium* research towards the identification of potential drug targets and effective and durable vaccine candidates to help successfully counter the disease. Preliminary work by our group has led to the identification of a *Plasmodium berghei* putative DNAJ domain containing Heat Shock Protein that is found to be expressed in all the stages of the *Plasmodium* lifecycle and possesses a single functional PEXEL motif aiding its export into the host cell cytosol. This protein upon immunization in mice followed by parasite challenge provided a 4-day delay in the pre-patent period and thereby a 4-logarithmic scale reduction in liver parasite load. This interesting finding has therefore intrigued us to further explore the vaccine potential of this antigen and understand the contribution of humoral and cell-mediated arms of the immune system in protection, identify the immunodominant and protective regions/epitopes as well as study the prospect of generation of long-term memory response against the malaria parasite.

22 JUNE 2023, 4.00 PM

SEMINAR ROOM 1, NII

Azadi Ka Amrit Mahotsav

सत्यमेव जयते

राष्ट्रीय प्रतिरक्षाविज्ञान संस्थान

National Institute of Immunology

GRADUATE STUDENT SEMINAR

TEMPORAL REGULATION OF PARP1-MEDIATED DNA DAMAGE RESPONSE AND METABOLIC FLUX BY HDAC5 DETERMINES TUMORIGENESIS

WITTY TYAGI

MOLECULAR ONCOLOGY LABORATORY

Poly(ADP-ribose) polymerase 1 (PARP1) is an abundant nuclear protein and a well-characterized DNA damage responder. Alternative to these well-established studies, it is evident that a major function of PARP1 is to serve as a potent modulator of gene transcription. However, the functional relevance of the transcriptional axis remains largely unknown. In addition to its dynamic regulation by HDAC5, our study provides a rationale for how transcriptional axis of PARP1 effectively contributes towards oncogenic potential. Mechanistically, the deacetylation of PARP1 at Lys498 promotes its poly ADP-ribosylation (PARylation) under genotoxic stress, which prevents chromatin trapping and subsequent fork progression. Deacetylation at Lys521 transactivates ATF4 target genes resulting in altered metabolic homeostasis. Hence, HDAC5-mediated deacetylation augments PARP1-dependent tumorigenic outcome. Thus, our study provides the molecular basis for effectively inhibiting tumorigenesis by targeting HDAC5-PARP1 dual axis.

22 JUNE 2023, 4.30 PM

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