INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student : **Sayan Saha**

Roll Number : **166106111**

Programme of Study : **Ph.D.**

Thesis Title: **Structural insight into rRNA methyltransferases and their function in nucleotide modification and antibiotic resistance**

Name of Thesis Supervisor(s) : **Prof. Shankar Prasad Kanaujia**

Thesis Submitted to the Department/ Center : **Department of Biosciences and Bioengineering**

Date of completion of Thesis Viva-Voce Exam : **20/08/2024**

Key words for description of Thesis Work : **Archaea; Crystallography; *Pyrococcus horikoshii*; Functional study; Protein dynamicity; RNA-protein interaction; Transmethylation state.**

SHORT ABSTRACT

Ribosome biogenesis involves the synthesis, processing, and modification of ribosomal RNA (rRNA) and proteins (Rps). During this process, specific nucleotides in rRNA undergo chemical modifications that help to stabilize their active conformation. These modifications are typically found in the functional center of the ribosome and play a vital role in stabilizing the rRNA structure, fine-tuning the ribosome, and regulating translation. The rRNA modifications predominantly involve methylation, which is facilitated by a group of enzymes known as rRNA methyltransferases (MTases). Besides their critical role in biogenesis, rRNA MTases also confer antibiotic resistance to pathogens against aminoglycosides and macrolides by altering the drug-binding site in the ribosome. Thus, understanding the role of rRNA MTases in ribosome biogenesis and antibiotic resistance can help to identify new ribosomal targets for developing next-generation antibiotics. Although the complete mapping of rRNA nucleotide modifications is available in bacteria (for example, *Escherichia coli*) and eukaryotes (for example, *Saccharomyces cerevisiae* and *Homo sapiens*), information on archaeal rRNA methylation is still scarce. Thus, to address this gap, the thesis focuses on the rRNA MTases and their corresponding modification sites from a hyperthermophilic archaeon *Pyrococcus horikoshii* OT3. Wherein, the housekeeping rRNA MTases were selected for structural and functional elucidation to understand their critical role in ribosome biogenesis and, in their absence, associated with various epigenetic-associated diseases. Moreover, these findings also contributed to the development of structure-based drug designs, aiming to create inhibitors with therapeutic potential against antibiotic resistance-causing MTases prevalent in pathogenic bacteria.