ENS – IISER Network / BIOSANTEXC Project

Internship Proposal Form
France to India

(Biological Chemistry/Enzymology and Microbiology

Internship title: A bioinformatics-guided enzymology approach to probe antibiotic resistance and redox homeostasis through sulfur metabolism in bacteria

Keywords related with the subject (minimum 3): antibiotic resistance, redox metabolism, cellular sulfur transfer, protein biochemistry, bacterial genetics, bacterial physiology

Name of the IISER: IISER Pune

Name of the laboratory(ies : Amrita Hazra, Whytamin lab (https://www.iiserpune.ac.in/~amrita/)

Name of the internship supervisor(s : Amrita Hazra, Associate Professor, IISER Pune

Email(s : amrita@iiserpune.ac.in

Prerequisites for the internship: Coursework and interest at the interface of chemistry and biology preferred. Students with some prior research experience in either a chemistry or biology experimental lab is optional but preferred.

Requested level: M1/ M2/ gap year students

Foreseen internship dates: 4-6 months between May – Dec 2025

Internship type (refer to page 1 :

☒3-6-month internship ☐ Research stays ☐ 6+6 months internship

For 3 to 6 months internships, please indicate the desired duration: **Any duration between 4-6 months**

For 6+6 months internships, please also fill in:

- **Name of the internship co-supervisor: Not applicable**
- **Name of the co-supervisor's laboratory/entity: Not applicable**
- **Email of the co-supervisor: Not applicable**

Internship proposal (description and expected training outcomes / half page min, 1 page max :

Oxidative stress and other crucial signaling processes in bacteria and mammals are regulated by H_2S and a host of metabolic reactive sulfur species. In bacterial cells, exogenously supplied sulfides or overexpression of the H_2S biogenesis enzymes have been observed to impart protection against antibiotic-induced oxidative stress. The pathway through which such protection is imparted is poorly known. The class of enzyme that transfers a sulfur atom from one molecule to another and contributes to the biogenesis of H_2S and reactive sulfur species are the two closely related sulfurtransferases - thiosulfate sulfurtransferase (TST) and 3-mercaptopyruvate sulfurtransferase (3-MST).

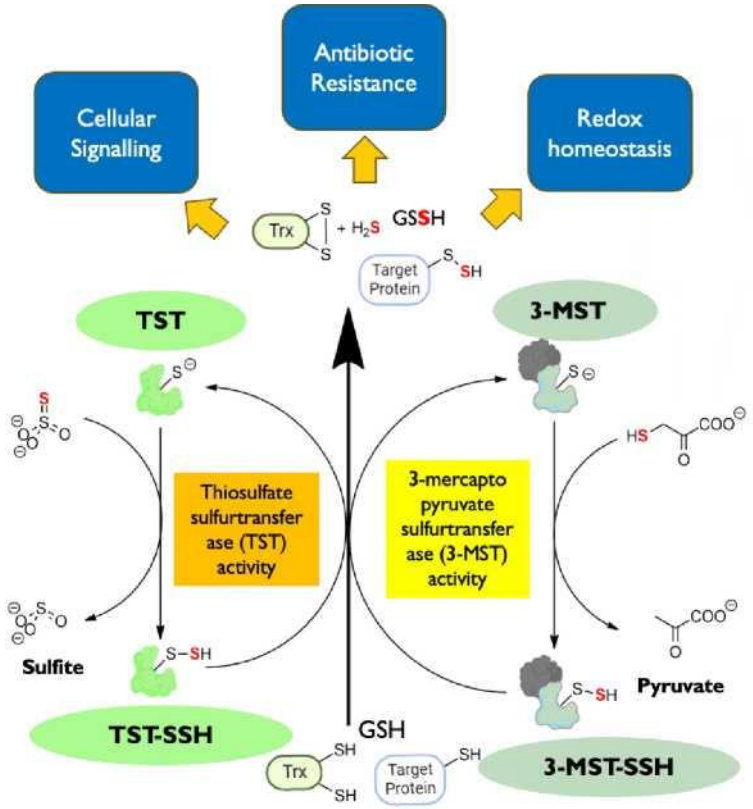

Figure: The mechanistic and physiological roles of thiosulfate sulfurtransferase (TST) and 3-mercaptopyruvate sulfurtransferase (3-MST) in bacteria

This project aims to understand the physiological and mechanistic differences between 3- MST and TSTs in the cellular context. To do so, we propose to explore the structure-sequence- function relationship between bacterial homologues of TST and 3-MST. Both TST and 3-MST contain the rhodanese domain, a structural fold associated with the function of sulfur transfer. A functionally active rhodanese domain contains a conserved and catalytically active cysteine residue at its active site which is persulfidated for sulfur transfer to target proteins. The prokaryotic TSTs are mostly single domain rhodanese while all the prokaryotic and eukaryotic 3-MSTs have tandem repeat of the rhodanese domain. Interestingly, the tandem repeat-rhodaneses have only one domain active while the other structurally similar domains appear to be inactive. The relationship between the single domain of TST and the two domains of 3-MST in the model organism *Escherichia coli* will be explored through in vitro protein biochemistry using a range of sulfur substrates and mutational analysis. Further, through microbial genetics and bacterial growth experiments, we will explore the specific physiological roles of the single domain TSTs and 3-MST in antibiotic resistance and redox regulation. Such a study will allow for an integrated molecular understanding of cellular sulfur metabolism and the design activators and inhibitors that control bacterial sulfur homeostasis.

Internship conditions:

- hostel accommodation (subject to availability)
- stipend towards living costs on campus

BIOSANTEXC is a project co-funded by the French Ministry of Europe and Foreign Affairs (Ministère de l'Europe et des Affaires Etrangères).