Indian Institute of Technology Delhi

School of Interdisciplinary Research (SIRe)

SIRe Project Number

2023-01-19

(will be assigned by SIRe)

Project Proposal for Ph.D.

Project Details	
Project Title	**State-of-the-art Chemical Biology Approach to correct the G6PD deficiency to help in Malaria elimination**
Project Summary (Minimum 500 and maximum 2000 characters)	Glucose-6-phosphate dehydrogenase (G6PD) deficiency is one of the most prevalent human genetic enzymopathies and is caused by more than 160 different point mutations. It further increases the severity of numerous acute and chronic diseases linked to oxidative stress, including hemolytic anaemia. G6PD deficiency affects an estimated 400 million people worldwide, the majority of whom live in malaria-endemic areas. When infected with malaria, G6PD-deficient erythrocytes have impaired anti-oxidant defence, making them susceptible to early membrane damage and, eventually, phagocytosis. This mechanism, which limits parasite propagation in the bloodstream, explains how G6PD deficiency confers malaria resistance. Due to the irreversible oxidative activity of the metabolites of anti-malarial medications like quinine, primaquine, or chloroquine on erythrocytes, people with G6PD deficiency are also more likely to experience severe hemolysis when taking these medications. There is currently no treatment for G6PD deficiency because there is no way to correct it. The negative impacts of G6PD deficiency are still visible in hemolytic anaemia. Given the risk of hemolytic crisis from various triggers in both malaria-endemic and nonendemic areas, the development of a medication that treats G6PD deficiency may be advantageous to those who are affected. Usually, G6PD works as an active dimer or tetramer. Each monomer consists of one NADP+ binding domain and an additional NADP+ binding site called a '+' domain, which structurally stabilises the enzyme. The majority of the variants that cause severe deficiency are mostly found in those functional regions of the enzyme, which disrupts the enzyme's activity and stability, as shown by various informatics tools. Small molecules peptide activator of G6PD will be synthesized and evaluated for the G6PD deficiency protections.

Ph.D. Supervisors			
Role	**Faculty**	**Academic Unit in IITD/Institute/University**	**Email ID (Official)**
Supervisor 1	Prof V. Haridas	Department of Chemistry Indian Institute of Technology Delhi	haridasv@chemistry.iitd.ac.in
Supervisor 2	Prof. Shailja Singh	Special Centre for Molecular Medicine, Jawaharlal Nehru University	shailja.jnu@gmail.com

Project requirements (Student qualifications, experience required, etc)

- Expertise in molecular and cellular biology and enzymology
- Expertise in parasite culture

Source of fellowship/funding
(CSIR/UGC/DBT/ICMR/ICAR/NEET-PG/DST-INSPIRE/IRD/FITT Project details, if any)

DBT-JRF Fellowship

Role of Faculty Members involved:

Prof. Haridas will be involved in designing and synthesis of molecules. Biochemical enzymatic activities will be conducted in Prof. Shailja Singh's lab. In vitro and in vivo characterization of molecules for enhancing the enzymatic activity will be performed in Dr. Singh's lab.