c. Statement of research achievements, if any, on which any award has already been received by the applicant. Please also upload brief citation(s) on the research work(s) for which the applicant has already received the award(s) (not to exceed 2000 words

(i) Concept and Novel ideas in HIV Research Award (CNIHR, National Institute of Health, USA)

Measuring glutathione redox potential of HIV-infected macrophages:

HIV-1 also persists inside the host's immune cells such as lymphocytes and macrophages while infecting millions around the world. HIV-1 causes AIDS (acquired immunodeficiency syndrome), a disease which compromises the patient's immune system, and one that still has no complete cure. Our group is interested in molecular dissection of redox-based event associated with persistence of HIV-1 in macrophages and lymphocytes. To understand these mechanisms, our group has engineered an HIV-GFP biosensor whose functioning is very similar to the *Mtb*-specific redox biosensor; the difference being that instead of measuring mycothiol levels (as is in the case of *Mtb*), this biosensor measures the levels of a different antioxidant – glutathione – in HIV infected macrophages. Using this biosensor, we report that only limited oxidative stress is capable of reactivating HIV from its silent form. Also, the study reveals, that active HIV replication is associated with a massive increase in oxidative stress, whereas latency is mediated by high anti-oxidative potential. (See annexure 1 for the cittation).

(ii) Innovative Young Biotechnologist Award (DBT India)

Deveopling genetically encoded redox sensors for *Mycobacterium tuberculosis*: Tuberculosis field lacks some of the most basic tools to image bacterial physiology during infection. We have recently filled this technological gap by developing a novel biosensor (Mrx1-roGFP2) to image the physiology of *Mtb* inside the human host during infection and upon chemotherapy. We exploited this bioprobe and identified the role of *Mtb*-specific redox-based mechanisms in alleviating toxicity caused by host-imposed antimicrobial stresses and anti-TB drugs. See annexure 1 for the cittation).

(iii) Merck Millipore Innovation Award

Express path analysis identifies a tyrosine kinase Src-centric network regulating divergent host responses to Mycobacterium tuberculosis infection: Global gene expression profiling has emerged as a major tool in understanding complex response patterns of biological systems to perturbations. However, a lack of unbiased analytical approaches has restricted the utility of complex microarray data to gain novel system level insights. Here we report a strategy, express path analysis (EPA), that helps to establish various pathways differentially recruited to achieve specific cellular responses under contrasting environmental conditions in an unbiased manner. We propose that EPA could prove extremely useful in understanding complex cellular responses for a variety of perturbations, including pathogenic infections. See annexure 1 for the cittation).

(iv) 10th NASI-Scopus Award in the Area of Biotechnology

(v) S. Ramachandran Award- National Bioscience award for Career Development.

Mycobacterial persistence and drug tolerance

A central question in tuberculosis (TB) research is to identify the mechanisms that allow the organism to persist for long periods of time in humans. In this context, my laboratory is focused on the metabolic

events associated with maintaining redox homeostasis in *Mtb* during infection. Redox signals such as nitric oxide (NO), reactive oxygen species (ROS), acidic pH, carbon-limitation, and oxygen (O_2) have been proposed to be main signals that induce a change in the metabolism of *Mtb* to facilitate its entry into a drug-tolerant persistent state. However, the precise contribution of these signals in manipulating *Mtb's* internal redox state and identity of a sensor(s) that precisely monitors pathogen's growth, metabolism and cell division in response to O_2 and NO remains unknown. Our group is actively characterizing the role of two Fe-S cluster dependent redox sensors (WhiB3 and WhiB4) in *Mtb*. Additionally, we are examining the role of hydrogen sulfide (H_2S) gas produced by *Mtb* in coordinating persistence, redox homeostasis, and antibiotic resistance. Using multiple analytical techniques such as microarrays, network biology, redox biosensor, macrophage infection and animal models, we investigated the role of WhiB3 and WhiB4 in facilitating pathogen's persistence in response to pH and antibiotic stress, respectively. See annexure 1 for the cittation).

(vi) CDRI Awards-2019 for Excellence in Drug Research

Developing Drugs to Target Redox Metabolism of *Mycobacterium tuberculosis*

Tuberculosis (TB) remains the most devastating cause of human deaths despite the availability of a vaccine (BCG) and multiple drugs combination therapy. Although chemotherapy can be highly successful, drugs must be administered for 6-12 months to provide an effective cure. However, majority of TB patients are unable to comply with such a lengthy treatment regimen, which fuels the development of multi-drug resistant (MDR), extensively-drug resistant (XDR), and totally drug resistant (TDR) TB infections. It is believed that long term multiple drug therapy is required to eliminate a small sub-population of TB-causing bacteria (*Mycobacterium tuberculosis* [*Mtb*]), which is refractory to current anti-TB drugs. Such noncompliant bacteria are referred to as "persisters" and the phenomenon is known as "persistence". Persisters are genetically similar to their drug susceptible counterparts but are able to survive the lethal effects of antibiotics, indicating that they are physiologically/phenotypically different. Despite their clinical importance, research in this field is hampered due to the lack of innovative technologies to capture phenotypic and/or physiological diversity within *Mtb* population during infection. This represents a major technological gap in our understanding of TB disease and drug-resistance. Therefore, understanding the physiological state of drug-tolerant persisters is one of the foremost challenges in shortening current drug regimens, and developing new drugs or diagnostics against TB. We filled this major gap by discovering several new redox-oriented candidates targeting *Mtb*. See annexure 1 for the cittation).

(vii) Shanti Swarup Bhatnagar Award 2021:

The Shanti Swarup Bhatnagar Prize for the year 2021 in Biological Sciences has been awarded for outstanding contributions to our fundamental understanding of host-pathogen interactions underlying infections caused by human pathogens, *Mycobacterium tuberculosis* (*Mtb*), and human immunodeficiency virus(HIV). His work led to an understanding of the intricate connection between redox mechanisms conferring drug resistance and their long-range physiological impact on host and pathogen.