**THRUST AREA OF RESEARCH**

**Bacterial Persistence , Host-Pathogen Interaction (Pulmonary Infection) and Genome editing**

**1. Bacterial Persistence:**

Toxin-antitoxin (TA) systems are small genetic elements found on plasmids or chromosomes of countless bacteria, archaea, and possibly also unicellular fungi. Under normal growth conditions, the activity of the toxin protein or its translation is counteracted by an antitoxin protein or non coding RNA. Five types of TA systems have been proposed that differ markedly in their genetic architectures and modes of activity control. Subtle regulatory properties, frequently responsive to environmental cues, impact the behaviour of TA systems. Typically, stress conditions result in the degradation or depletion of the antitoxin. Unleashed toxin proteins impede or alter cellular processes including translation, DNA replication, or ATP or cell wall synthesis. TA toxin activity can then result in cell death or in the formation of drug-tolerant persister cells. The versatile properties of TA systems have also been exploited in biotechnology and may aid in combating infectious diseases.

**2. Bacterial-Host Interaction (Pulmonary Infection Th17 response)**

To perform its primary function of gas exchange, the mucosal surface of the lungs is continuously exposed to the environment. Given the considerable infection risk to the host, complex mechanism exists to prevent the development of bacterial infection. The immune system in the lungs consists of both innate and adaptive components, and it is clear these two systems are highly interdependent for optimal host defense. **With the recent discovery of a distinct subset of Th cells called Th17 cells,** in addition to the previously well characterized Th1- and Th2-cell subsets, came many new breakthroughs in the realm of innate and adaptive immunity. Th17 cells have been shown to differentiate from naïve CD4+ cells in the presence of IL-6 and TGF-β in mice, or IL-6 and IL-1 in humans, when stimulated with appropriate antigen via activation of the transcription factor STAT3. **As CD4+ cells commit to the effector Th17 phenotype, the hallmark cytokines IL-17A, IL-17F, IL-21, and IL-22** are expressed via STAT-3-dependent activation of the critical transcription factor retinoid-related orphan receptor γt. **Th17 cells have been found to play a vital role in host defense against numerous pathogens**. However, while Th17 cells are paramount in the adaptive phases of host defense, several other cell types are able to generate these cytokines in the earlier phases of immune response and bridge the gap between innate and adaptive immunity in the lung. These cell types include γδ T cells, natural killer (NK) cells, NKT cells, and certain innate lymphoid cells.

New vaccine approaches are needed against *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus anthracis* and *Mycobacterium tuberculosis,* which are the keys pathogenic bacteria responsible for serious pulmonary infections in developing countries like India. Although Th17 cells can protect against gram-negative pathogens at mucosal surfaces, including the lung, the bacterial proteins recognized by Th17 cells are largely unknown and could be potential new vaccine candidates. **I am interested in the identification of Th17-stimulating antigens from *Streptococcus pneumoniae*, *Bacillus anthracis,******Pseudomonas aeruginosa***,**and *Mycobacterium tuberculosis,* using ORFeomics approach.**

**3 .Genome editing by CRISPR cas9 Technology**

**The development of efficient and reliable ways to make precise, targeted changes to the genome of living cells is a long-standing goal for biomedical researchers. Recently, a new tool based on a bacterial CRISPR-associated protein-9 nuclease (Cas9) from**Streptococcus pyogenes**has generated considerable excitement. This follows several attempts over the years to manipulate gene function, including homologous recombination and RNA interference (RNAi). RNAi, in particular, became a laboratory staple enabling inexpensive and high-throughput interrogation of gene function, but it is hampered by providing only temporary inhibition of gene function and unpredictable off-target effects (6). Other recent approaches to targeted genome modification – zinc-finger nucleases [ZFNs, (7)] and transcription-activator like effector nucleases [TALENs (8)]– enable researchers to generate permanent mutations by introducing double stranded breaks to activate repair pathways. These approaches are costly and time-consuming to engineer, limiting their widespread use, particularly for large scale, high-throughput studies.** The simplicity of the type II CRISPR nuclease, with only three required components (Cas9 along with the crRNA and trRNA) makes this system amenable to adaptation for genome editing.

**Technical expertise (key word):** Genetic Engineering, Genome editing ,Microbiology, Immunology, Bioinformatics, and Proteomics**.**

Eminent Scientists with their area of expertise:

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