

Clinical Microbiology Division

Overview

Plant based pharmacophores for anti-infective activity including the oral cavity pathogens and *M. tuberculosis*, modulation of antimicrobial resistance through inhibition of microbial efflux pumps and immunotherapeutics are the major research areas of this group. The group is also characterizing the *M. tuberculosis* efflux pump proteins and exploring the new drug targets of *M. tuberculosis* using In vivo Induced Antigen Technology (IVIAT).

Mission and goals

- Search for plant based novel pharmacophores for anti-infective activity.
- Modulation of antimicrobial resistance through inhibition of microbial efflux pumps.
- Search for new drug targets and immunotherapeutics for *M. tuberculosis*.
- Regulation of *M. tuberculosis* gene expression.
- Application of plant based molecules for non-drug use in the area of personal care, oral care and skin care products.

Competencies

- Evaluation of plant based/synthetic libraries of molecules for antibacterial, antifungal and anti TB activity.
- Animal models of infection for in-vivo efficacy of molecules.
- Cloning and expression of microbial genes.
- Differential expression of microbial genes through q-PCR.

People

S. No.	Name	Expertise	e-mail
1	Inshad Ali Khan	Clinical Microbiology	iakhan@iiim.res.in
2	Surrinder Kumar	Lab maintenance	

Facilities

Biosafety Level-3 facility : (Photo already available on the website) State-of-the-art Biosafety Level-3 (BSL-3) facility for handling and experimentation with hazard group III pathogens. This is one of the five such facilities created under CSIR network programme on infectious diseases handling, storage and research facilities. This lab fully complies with the Biosafety in Microbiological and Biomedical Laboratories (BMBL) guidelines. This facility consists of two *in-vitro* experimentation labs and one animal handling (mice & guinea pigs) for *in-vivo* experimentations. Tuberculosis is the major thrust area of the institute and presently this facility is being used for handling and experimentation with *M. tuberculosis*.

Antiinfective research facility is actively working on plant based and synthetic pharmacophores with anti-infective activity including anti TB activity and novel mechanism of action. A large collection of bacterial, fungal and *M. tuberculosis* clinical isolates is available for extensive evaluation of compounds.

Oral Microbiology facility is well equipped with anaerobic work system, CO₂ incubators and a large collection of oral cavity bacterial pathogens. Plant derived molecules are evaluated on a panel of oral cavity bacterial pathogens. The active molecules are further tested on a panel of tests such as biofilm inhibition assay, bacterial glucosyltransferase inhibition etc. A number of lead molecules are actively being pursued for product development in collaboration with global industrial partners.

Molecular Biology The facility is well equipped with PCR machines, Real-Time PCR, Electrophoresis systems, Gel Documentation systems gene pulsar and other such lab equipment for molecular biology work. PCR amplification, gene cloning, native enzyme purification and differential gene expression are some of the experimentations routinely performed in this facility.

Area of Research

- Anti-infective research with reference to identification of plant derived pharmacophores.
- Antimicrobial resistance and microbial efflux pumps.
- New drug targets and immunotherapeutics for *M.tuberculosis*.

- Regulation of *M. tuberculosis* gene expression.
- Oral microbiology

Current Research

- Evaluation of plant based/synthetic libraries of molecules for antibacterial, antifungal and anti TB activity. Identification of the active plant derived pharmacophore to build synthetic library around this structure. In vivo efficacy of the active molecule in the mice model of infection and other IND directed studies.
- Modulation of antimicrobial resistance through inhibition of bacterial efflux pumps. The work started with the identification of piperine as bacterial efflux pump inhibitor has come a long way from there. Presently we have a large number of synthetic and natural molecules having broad spectrum bacterial efflux pump inhibition activity. Protein crystallization studies are in progress in order to determine the 3D crystal structure of some of the clinically important bacterial efflux pumps.
- Characterization of *mycobacterium tuberculosis* efflux pump proteins in the lab generated mutants as well as clinical isolates and the use of bacterial efflux pump inhibitors in conjunction with anti-TB drugs.
- Efficacy studies of plant based immunomodulators in conjunction with anti-TB drugs in the mice and guinea pig models of infection. The anticipated outcome of such combination will be the better clinical response of antiTB therapy in immunocompromised population of the patients and lower rate of reactivation of tuberculosis.
- Identification of differentially expressed genes associated with pathogenesis of *M. tuberculosis* using In vivo Induced Antigen Technology (IVIAT) for potential use as vaccine or therapeutic targets. In this DST funded project, we are trying to identify these mycobacterial genes which are overexpressed under diseased condition. The identified genes will be validated through knockout approach. It is expected that some of these targets may emerge out potential drug or vaccine candidates against tuberculosis.

Projects

Project Title	Funding agency	Duration	Start date
Resourcing biomolecules from medicinal plants, microflora including higher fungi)- Major laboratory project	CSIR	3 yrs	Sept 2007
Synthesis and antitubercular activity of Benzothiadiazine, Coumarin and Diarylprrole congeners	DST	3 yrs	March 2009
Identification of <i>Mycobacterium tuberculosis</i> genes differentially expressed in TB patients	DST	3 yrs	Grant awaited
In-vitro evaluation of synthetic molecules for anti-TB activity.	TCG Lifesciences, Pune	1yr	April 2009
Exploitation of India's rich biodiversity- Network project	CSIR	5 yrs	April 2007