

Systems Biology Division:

Overview: IIIM works with a determined and single-minded mandate of drug discovery. We are in the process of setting up the systems biology division at IIIM, which would significantly accelerate this process. Here we aim at using a holistic approach rather than the classical reductionist approach towards quantification of biological macromolecules. Obtaining a full picture with respect to an organisms's transcriptome, proteome and metabolome would considerably reduce the time for hypothesis generation and testing in various model organisms. They also provide data for simulation studies using *in-silico* techniques, which helps in recognition of most probable targets for directing drug discovery.

Missions and Goals:

- To augment the collection of mouse disease models with newer and more near-to-reality models for various disease conditions like autoimmune disorders, cardiovascular conditions, diabetes, neurological diseases etc.
- To setup laboratories for alternative disease models like Zebrafish, *Drosophila* and *C. elegans*. These are excellent model organisms and various transgenics and mutations in these organisms mimic conditions of human diseases. Amenability of these organisms to genetic dissection helps to identify and validate drug targets, relatively, with ease. Already available models will be used for drug screening and new disease models in these organisms will be developed.
- Secondary screening of various leads to identify quality leads using systems biology approach by assessing the impact of the molecule not only on the known target but also on several other proteins in a normal cell to ensure its safety and tolerance and in pathological or pathogenic cell to test its efficacy. This could, in principle, also help to identify novel targets, of the tested compound, involved in entirely different pharmacological condition.

Competencies:

- A complete proteomics setup to study changes in expression and post-translational modification and trained map-power to carry out such work. The facility is equipped with automated spot-cutter, robotic liquid handling system and high precision detections systems like MALDI-TOF/TOF.
- Mouse model for arthritis is being used for identification natural products effective in such condition.
- Expertise and equipment to establish protein-protein interaction and drug-protein interaction maps for the complete proteome.
- Expertise and setup to carry out transcriptome analysis using Taqman Low Density arrays in high throughput real-time PCR system. This would soon be augmented with a microarray setup for complete transcriptome studies.
- Assay systems to assess the changes in all known microRNA profiles using Taqman miRNA assays in high throughput real-time PCR system.

People:**Areas of Research:**

- Identification of differential phosphorylation states at complete proteome level, in various cancers as compared to normal cells, and consequent identification of possible new drug targets.
- Development of Drosophila models for neurological disorders.
- Effect of small molecules on microRNA transcriptome in human cell lines and drosophila models.

Facilities:

2D Gel Electrophoresis systems: 2D gel electrophoresis system combines high resolution of proteins on the basis of charge and mass. This system is used for identification of differentially expressed proteins, which aid in finding probable targets. It is also used to identify expression changes in response to small molecules.

MALDI-TOF/TOF: It serves as the backbone for identification of gel separated protein bands and in-gel digested protein spots, due to its high sensitivity in tandem MS mode.

High Throughput Real Time PCR: Capable of analyzing large scale samples in 384 or 96 well plate format. Both Taqman and SYBR green assays are used for assaying changes in transcriptome in various disease conditions and to assay the effect of small molecules on gene expression. Taqman microRNA assays are used to assay the effect of small molecules on microRNA expression profiles.

Microarray: We are in the process of acquiring complete microarray setup for hybridization of affymetrix slides, Scanners capable of reading high density chips and related software for analyzing gene expression data.

Computational Facility: We have computational facility equipped with silicon graphics machines and high end servers with necessary software resources for large scale molecular modeling and docking studies.

Current Research:**Projects:**