

Structural Genomics at SINP

With the inspiration and support of Prof. Meghnad Saha, one of the oldest schools of Biophysics in India was formed in 1950 at the Saha Institute of Nuclear Physics (SINP). Since then scientists have been working in different branches of Biophysical Sciences. Currently, the Biophysical Sciences Group at SINP consists of three divisions - Crystallography & Molecular Biology, Biophysics and Chemical Sciences.

In the Xth plan, the major focus of the group is in '*Structural Genomics in Human Health & Disease*'. In this connection the new Structural Genomics Laboratory was built and commissioned on September 5, 2003

The flow cytometer, automated DNA sequencer and proteomics facility were installed in the laboratory for experiments and the image plate for the determination of 3D structure of proteins by X-ray diffraction technique along with quadruple TOF mass spectrometer etc. are to be commissioned soon.

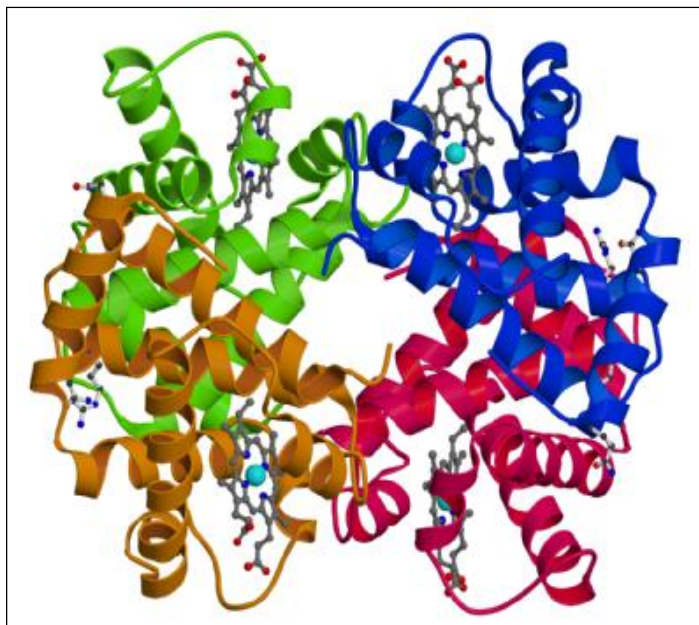
Structural Genomics, by definition is a high throughput approach for the determination of the 3D structures of the proteins of a particular organism. SINP Structural Genomics program, has been taken up for identification of proteins associated with the normal and abnormal metabolic processes (diseases). Deciphering of the 3D structures of the protein molecules for the elucidation of their role in various metabolic processes i.e. structure-function relationship between them is the primary goal of the project. Proteomics is an emerging area of research that provides a powerful tool for the study of the total number of proteins of an organism, enabling researchers to analyze gene expression at different levels. Structural Genomics and Proteomics therefore

have become a melting pot of multidisciplinary research drawing expertise from areas as diverse as structural biology (crystallography and spectroscopy), computational structure predictions and model building, gene cloning, sequencing, expression and quantitation of proteins and cell biology.

In the SINP program, the gene/protein network in human diseases like in hematological disorders e.g. leukemia and thalassemia is proposed to be characterized and the objective is to determine the 3D structure of the key proteins, involved in the aberrant leukogenic and erythropoietic pathway, study the interplay between genes and proteins and design therapeutic approaches. One of the major scopes of the project is to develop the technology needed to increase the knowledge of the diversity of the gene/protein network and the structure and folds of key proteins involved in the disease process. It aims to deliver the structural information about most proteins and promises to

assign 3-D structures for many proteins. While it is not feasible to determine the structure of every protein by experiment useful models can be built by fold assignment and comparative modeling of protein sequences those are related to at least one protein structure. This would involve selection of the target proteins or domains, cloning, expression and purification of the target protein in large quantity, crystallization and structure determination by X-ray crystallography or by NMR spectroscopy followed by archiving and annotation of the new structures. Designing gene delivery system for therapy is also a part of the goal. Besides, there will be enormous scope towards improved manpower training, teaching and graduate research program of multidisciplinary origin and background.

The aberrant pathways that have been initially selected, are for disorders that are prevalent in eastern India. The scientists in the laboratory are collaborating with various biomedical research centers and clinical facilities in and around Kolkata.



3D structure of hemoglobin A2, implicated in beta thalassemia, at 2.1 Å resolution.