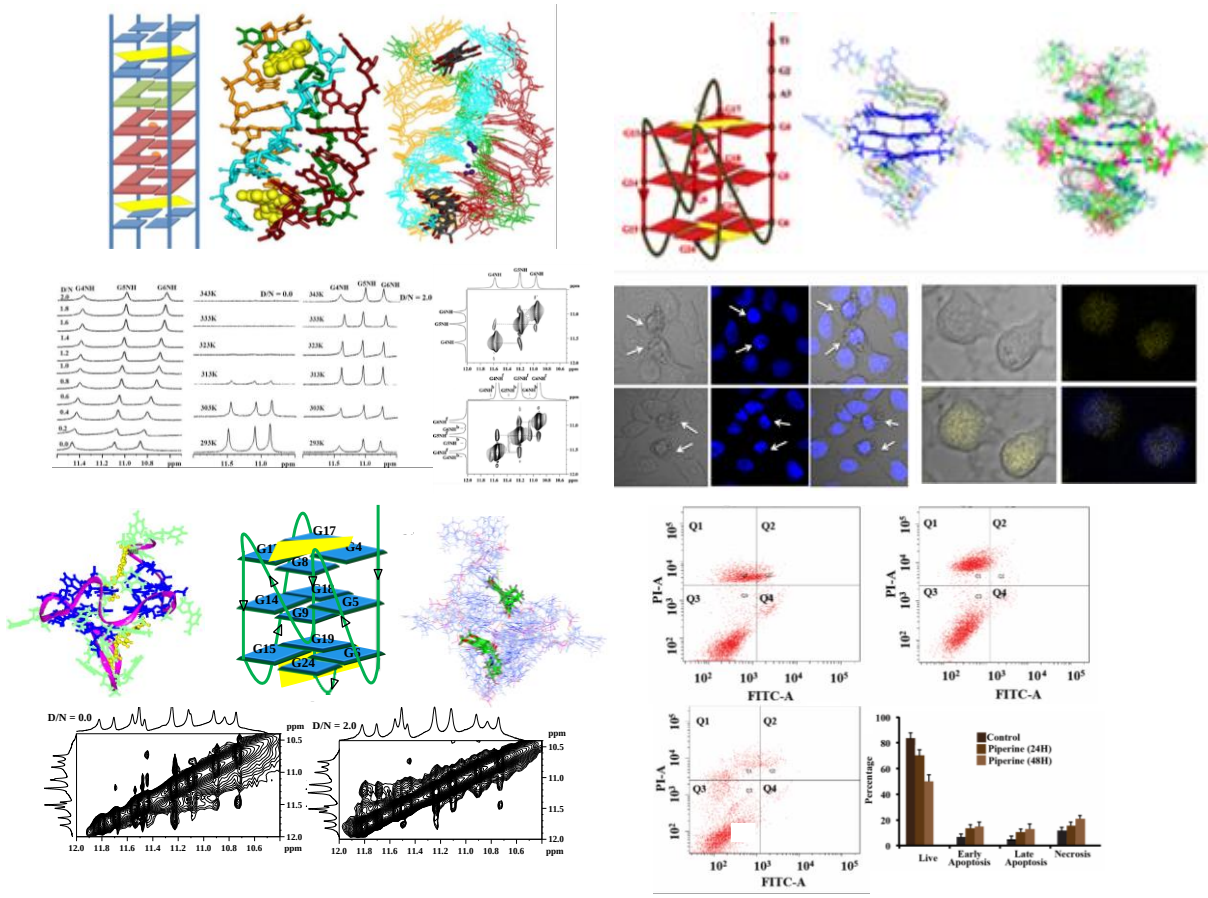
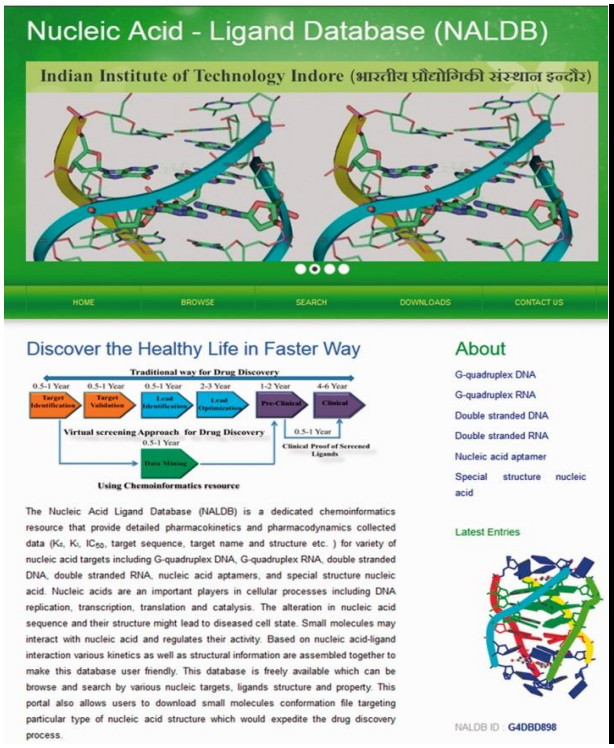
Research Highlights from Dr. Amit Kumar's Research Group

In structural biology lab, we have been working on elucidation of structural and molecular basis of Drug-Nucleic acid interactions. In this context we have studied the interaction of small molecules of natural origin readily available in human diets with G-quadruplex DNA formed at various regions of human genome like telomeric DNA, promoter region of various proto-oncogenes such as c-myc, c-kit21, bcl2, etc. These genes are known to be involved in development and progression of various cancers. First of all, we have studied the interaction of flavonoids with G-quadruplex DNA formed by human telomeric DNA sequence. By employing detailed biophysical techniques like Circular Dichroism (CD), UV-Visible, steady state, and time resolved fluorescence spectroscopy, we have probed these interactions. Further, the structural basis of this interaction and we have reported the first solution structure of the complex formed by Quercetin and G-quadruplex DNA formed by human telomeric DNA sequence. Furthermore, we have explored the mechanism for anticancer activity of flavonoids. It inhibits the cell growth by inducing apoptosis and it also down-regulates the gene expression in cancer cells upon binding. Our study highlights the potential of flavonoids as useful candidates for anti-cancer therapeutics by regulating DNA secondary structures.



Following this idea we have also explored the interaction of an alkaloid, Piperine, to various G-quadruplex DNA sequences formed in human genome. We have reported for the first time the binding of Piperine to with highest affinity for G-quadruplex structure formed at c-myc promoter region. We have proposed the model of this complex that sowed Piperine stacks at both of terminal G-tetrads via π-π interactions and stabilizes G-quadruplex structure. Moreover, in-vitro studies show that Piperine is cytcotoxic to various cancer cells and causes apoptosis-mediated cell death. Our study highlights the molecular aspects of its anti-cancer mechanism emphasizing its potential to down-regulate c-myc gene expression.



Our lab is also involved in providing scientific community with various databases for ease of drug discovery and development of novel therapeutics for various diseases. **We have developed NALDB** which is the first ligand database that contains ligand information for all type of nucleic acid. NALDB contains more than 3500 ligand entries with detailed pharmacokinetic and pharmaco-dynamic informations. All these details at single platform would be helpful for the development and betterment of novel ligands targeting nucleic acids that could serve as a potential target in different diseases including cancers and neurological disorders. Further, **we have developed G4IPDB** which is the first database that provides detailed information for various proteins that binds to G-quadruplex structures forming DNA and/or RNA Development of G4IPDB database provides assistance to the scientific community in further improving the efficiency of small molecule therapeutics for nucleic acid based diseases.