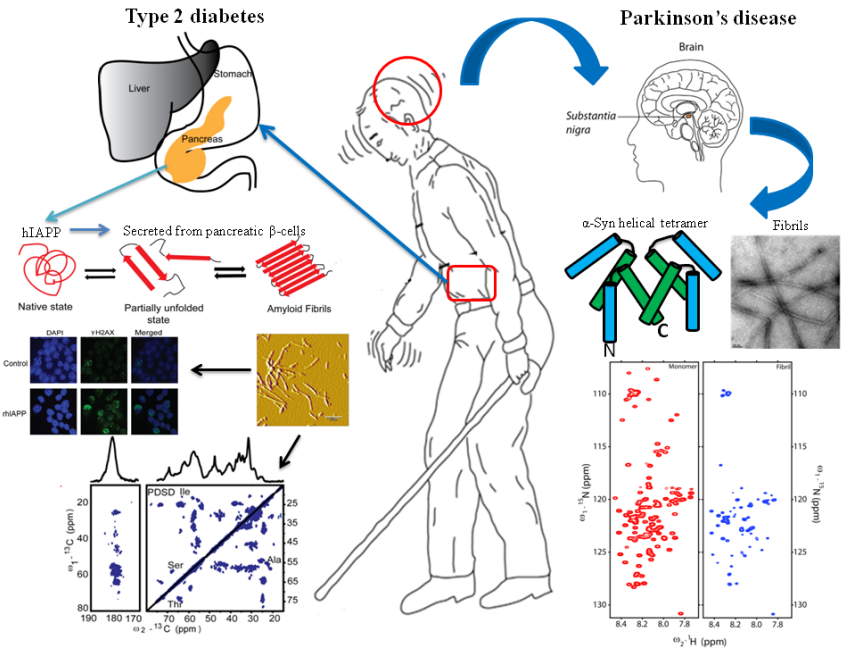
NMR-based structural biology laboratory

The cellular processes in the human body and all other organisms are very complex and each event is intertwined with numerous other processes. There are two ways to study these processes. One can either study the cascade of events as a whole to see how they affect the functioning of the cells, or the process can be broken down into its constituting molecules and each molecule studied individually in detail. In the second approach, the properties of the molecules studied individually are then patched together to give an in-depth account of what happens in the cell. Proteins, the workhorse of our body, constitute the major component of these cascades in the cell and are required for all the basic functioning. To study these proteins individually requires the second approach. It is quite tedious and requires powerful tools that can examine atomic level details.



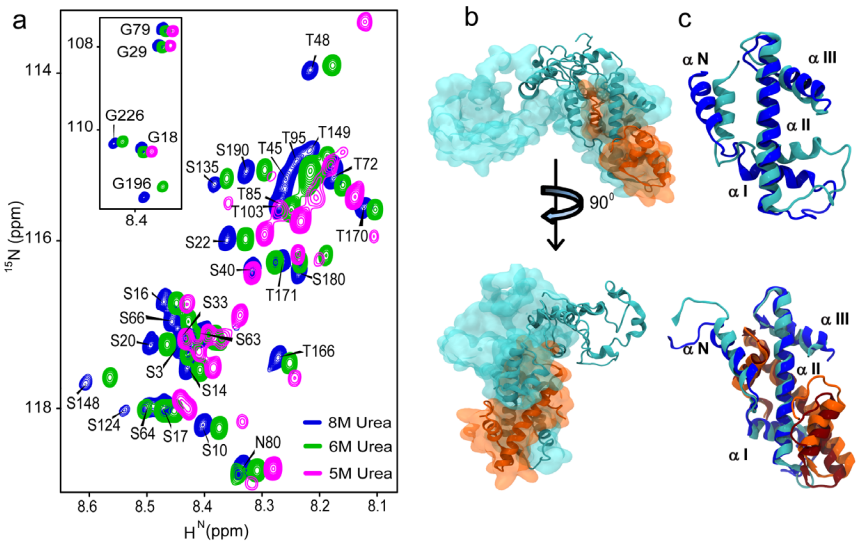
Our lab focuses on getting the atomic level view of the proteins that function in the cell cycle. We use cutting-edge research tools mainly Nuclear Magnetic Resonance (NMR) spectroscopy to understand the structure of the proteins and their motion. Any discrepancies in the cell cycle will lead to the cell losing control of its proliferation and may lead to cancer. Hence, understanding how proteins behave at an atomic level not only gives us an insight to what really happens when the cell divides, but it also helps to target these proteins in case something goes wrong.

We first illustrate the structure and dynamics of the molecule using NMR, and this information obtained is then combined with high-end computational methods and other biophysical tools to decipher how two or

more proteins will interact in the cell. Such information can then be used by cancer biologists to put together cell-signaling pathways in cancer or by pharmaceuticals for designing targeted drug delivery systems.

Protein misfolding and aggregation are the most exciting frontiers of the various human pathological diseases such as Alzheimer's, Parkinson's, Huntington's, Cystic fibrosis and Type 2 diabetes mellitus. The proteins involved in all these diseases undergo conformational transition from its natively unfolded state to the cross-β sheet structure of amyloid fibrils. Amyloid fibrils are highly ordered β-sheet rich insoluble aggregates formed as an end product of fibrillisation pathway. As amyloid fibrils are intrinsically disordered, non-crystalline and water insoluble, therefore, structural characterisation with solution-state NMR is very difficult. Solid-state NMR magic angle spinning (ssNMR-MAS) is one of the best tools for understanding the structural details of the fibrils at the atomic level. It also provides a significant step forward in understanding the amyloid formation to obtain structural information. In our group, we apply solid-state NMR spectroscopy in conjunction with various biophysical techniques to deduce the structure of the amyloid proteins involved in Parkinson's and Type 2 diabetes.

In addition, we also study of dynamics reactions and properties of proteins at the atomic level by solution-state NMR spectroscopy.



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