A new dimension to gene regulation holds promise for cancer therapy

Vanita Srivastava

A team of scientists led by Dr Shantanu Chowdhury at the CSIR- Institute of Genomics and Integrative Biology has researched on another dimension to gene regulation that can hold a promise for cancer therapy.

Switching genes on or off in a well-coordinated manner, much like a choreographed dance, is critical in biological function. The switching on/off happens from regions called gene promoters. Text book understanding of how promoters are controlled describes particular sequence of DNA within promoters that interact with specific proteins (known as transcription factors) to activate or repress the process.

About ten years back, research suggested that promoters can harbor tiny structures made of DNA (Rawal et al, Genome Research, 2006; Yadav et al., Nuc Acids Res, 2008; Verma et al, J Med. Chem, 2008). These DNA structures - called guanine quadruplex forms (as guanines bases are central to the architecture and strength of these óbook-shelfô like structures ï see figure below) - can interact with specific proteins for controlling a gene promoter. This research, in addition to DNA sequence, which has been known for decades, proposed DNA structure as 'gene control' switches. Research from several groups including ours have found this mode of control to be functional in case of several human genes.

book shelf structure

ñAs most of us know proteins made from corresponding genes carry out biological function. At times, some proteins malfunction or are produced in amounts more than required ï these órogueô proteins are behind most diseases,ò Dr Chowdhury said. Therefore, therapeutic research focuses on ways to control such unnatural (or unnaturally active) protein molecules - often done using chemicals specifically engineered to engage such molecular ótargetsô. This is true for cancer also.

Now, our understanding of DNA quadruplex structures reveals molecular switches that can be tuned. This presents a new way by which scientists can prevent wrong genes from making proteins (or making too much of the protein). Thereby, in many ways, one can intervene, a few steps before proteins are produced.

ñHowever, though it holds promise I must say we are only beginning to get hold of the intricacies. With more understanding chemicals that engage specific DNA quadruplexes could be effective drugs in near future,ò he said.