Biosciences and Biomedical Engineering, IIT Indore

Research Highlight

Dr. Amit and his group is working on the structural and drug discovery aspect to target neurological diseases and cancer. Recently, article entitled "Structural Insights Reveal the Dynamics of the Repeating r(CAG) Transcript Found in Huntington's Disease (HD) and Spinocerebellar Ataxias (SCAs)" (PlosOne, 2015) by Tawani and Kumar describes the structure and dynamics of the RNA trinulceotide repeat CAG. These trinucleotide repeats when extended beyond a certain limit, lead to the neurodegenerative diseases such as Huntington's disease (HD) and Spinocerebellar Ataxias (SCAs). These repeats form special structure that sequesters the important proteins that lead to diseased condition. In order to explore the role of RNA structures in pathogenesis, this group has addressed the understanding of conformational flexibility and dynamic behavior of such RNA containing trinucleotide repeats. The study shows the dynamic nature of lxl nucleotide AA internal loops by crystal structure as well as by solution structure. The non-canonical pairing of adenine in 5´-CAG/3´-GAC motif samples in different syn and anti-conformations. This study reveals that small molecules or protein interactions proceed through conformational selection, which will be useful in understanding the potential structural consequences of ligand binding to r(CAG) repeats.

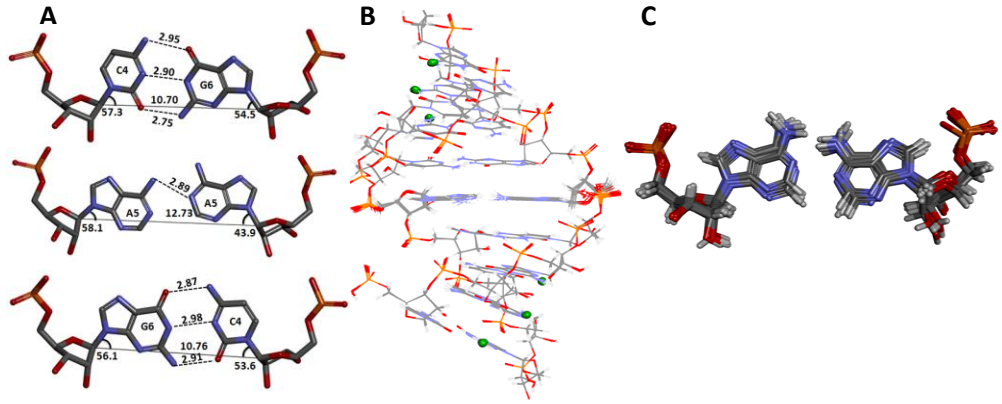

Figure. A. The lowest energy conformation of CAG motif obtained after rMD simulation of 5´ r(CCGC**A**GCGG)$_2$. **B**. Ensemble of ten lowest energy structures of 5´ r(CCGC**A**GCGG)$_2$ obtained after rMD simulation. **C.** Ensemble of ten lowest energy structures of AA pairs of 5´ r(CCGC**A**GCGG)$_2$ obtained after rMD simulation.