Variability in structure of non-canonical DNA and its interaction with ligands

A Talk by

Prof. Janez Plavec

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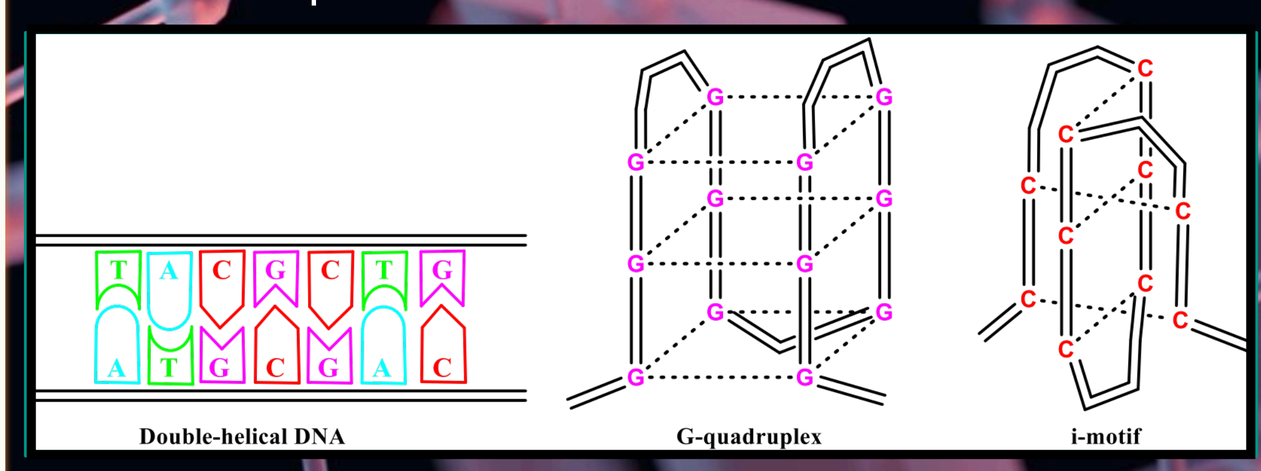
About the Speaker

Professor Janez Plavec is the head of the Slovenian NMR Centre at the National Institute of Chemistry (NIC) and Professor of Structural Biology at the University of Ljubljana (UL). His Ph.D. degree was conferred by Uppsala University, Uppsala, Sweden in 1995. He has been Fulbright fellow at Georgia Institute of Technology, Atlanta, GA, USA in 2002. Research interests of Prof Plavec include studies of structure and dynamics of bio-macro-molecular systems with NMR, structural studies of nucleotides & proteins, interactions of small molecules and metal ions with DNA and RNA, etc. In 2017, he was awarded the Zois award for Excellent Achievements in structural studies of nucleic acids with NMR, and in 2018 the Prize for Excellence by Indian Society of Chemists and Biologists. Since 2018 he is the chair of Council of Republic of Slovenia for awarding prizes for excellent achievements in science and research.

Talk Abstract

DNA is a polymer that contains the genetic instructions for the development, functioning, growth, and reproduction of all known organisms and many viruses. Structurally, it is a polymer consisting of two polynucleotide chains that coil around each other to form a double helix maintained by Watson-Crick base pairs. However, DNA sequences that are rich in guanine and contribute to the formation of G- and AGCGA-quadruplex structures are often found in telomeres and certain regulatory regions of the genome. Cytosine-rich regions adopt i-motif structures. Studying the structural variability and dynamics of non-canonical DNA is crucial for understanding their interactions with ligands, as these interactions play a key role in various biological processes. Non-canonical DNA structures, such as G-quadruplexes and i-motifs, have unique structural features compared to canonical B-DNA.[1]



The elucidation of the structure of DNA represents a significant advance relevant to human disease. The discovery of numerous new features not only contributes valuable insights for refining current in silico methods but also serves as a basis for the rational design of novel therapeutics. Despite the discovery of different molecules with varying affinities, the challenge remains to increase selectivity to minimize off-target effects within the host cell. The intrinsic nature and selectivity of ligands that interact with G-quadruplexes[2] and i-motifs[3] suggest that structural studies could guide the rational design of selective binding agents. NMR emerges as a central method for recognizing the conformational energy landscapes of the lowest energy states and potential folding intermediates, facilitating the understanding of noncanonical DNA structure. Insights into structure and conformation provide valuable information for the chemical optimization of ligands.

1 J. Plavec, in Handbook of Chemical Biology of Nucleic Acids (Ed.: N. Sugimoto), Springer Nature Singapore, Singapore, 2023, pp. 169-212.

2 A. Ghosh, M. Trajkovski, M.-P. Teulade-Fichou, V. Gabelica, J. Plavec, Angew. Chem. Int. Ed. 2022, 61, e202207384.

3 M. Ghezzo, M. Trajkovski, J. Plavec, C. Sissi, Angew. Chem. Int. Ed. 2023, 62, e202309327.

Hosted By

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Date : Feb 9, 2024 **Time : 11:00 AM** **Venue : AB2 5A**

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