IBGC INVITED SEMINAR

TUESDAY 24 JUNE 2025
14H00
IBGC CONFERENCE ROOM

Kateryna MAKOVA

Director, Center for Medical Genomics

Invited by **Macha Nikolski**

Currently a Fulbright scholar in Macha Nikolski's laboratory

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NON-CANONICAL DNA IN THE HUMAN AND APE TELOMERE-TO-TELOMERE GENOMES

Approximately 10% of the human genome can fold into 3D structures different from the canonical double helix, also called B-DNA. Non-canonical (or non-B) DNA structures regulate key cellular processes, such as transcription, splicing, and DNA replication. They also serve as mutational hotspots for point mutations and rearrangements during cancer. Yet the precise detection of non-B DNA has remained elusive due to its transient nature and incomplete genome sequences. Here, we analyze non-B DNA in the recently deciphered telomere-to-telomere (T2T) genomes of humans and great apes. First, we computationally predict motifs capable of forming non-B DNA. These motifs are enriched at the genomic regions added to T2T assemblies, including repetitive sequences, short arms of acrocentric chromosomes (where they may influence satellite dynamics), and centromeres (where they may contribute to centromere function). Second, we experimentally validate non-B DNA structure formation using Permanganate/S1 footprinting with Direct Adapter Ligation and sequencing (PDAL-seq). We show that clusters of different non-B DNA motifs–particularly direct repeats, G-quadruplexes (G4s), and Z-DNA–drive single-stranded DNA formation. PDAL-seq signal is enriched at promoters, enhancers, and 5' UTRs, supporting a regulatory role for non-B DNA. Thus, non-B DNA is unevenly distributed across ape genomes and might have novel functions in previously inaccessible genomic regions. Finally, I will discuss the challenges in predicting the folding of non-B DNA structures in living cells and highlight the Artificial Intelligence approaches we currently undertake to address these challenges.