SINGAPORE RNA SEMINAR SERIES

COMPREHENSIVE TRANSLATIONAL PROFILING AND STE AI TO MEASURE ABSOLUTE PROTEIN BIOSYNTHESIS RATES AND RAPID CHANGES IN MRNA USAGE

About the seminar

RNTranslational control is important in all life but remains a challenge to accurately quantify. When ribosomes translate messenger (m)RNA into proteins, they attach to the mRNA in series, forming poly(ribo)somes, and can co-localize. Here, we model new types of ribosomal co-localization on mRNA, and then identify them using enhanced translation complex profile sequencing (TCP-seq) based on rapid in vivo crosslinking. We detect long disome footprints outside regions of non-random elongation stalls and show these are linked to translation initiation and protein biosynthesis rates. We subject the disome footprints and comprehensively other derivatives of TCP-seq to ensemble machine learning and construct a new, accurate and self-normalized measure of translation, termed stochastic translation efficiency (STE). Applying STE to a prototypical scenario of nutrient (glucose) depletion in yeast, we refine translational control from the other rapid RNA alterations and highlight metabolic rearrangements dispatched solely at the translational level. Importantly, we show that, well beyond tagging elongation stalls, footprints of co-localized ribosomes provide rich insight into translational mechanisms, polysome dynamics and topology. STE is of value in identifying absolute translational ranking of mRNA and its control elements under given conditions and will facilitate the development of next-generation synthetic biology designs and mRNA-based therapeutics.

Nikolay Shirokikh
Leadership Fellow,
John Curtin School of Medical Research (JCSMR)
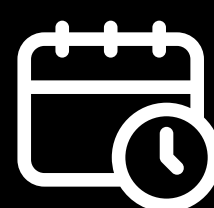
20 November 2023 (Monday)
10 am (SGT, GMT+8)

Via Zoom

About the speaker

Dr Shirokikh is a group leader and NHMRC Emerging Leadership Fellow at the John Curtin School of Medical Research (JCSMR) and The Shine-Dalgarno Centre for RNA Innovation, The Australian National University. He is a molecular and RNA biologist investigating mechanisms of protein biosynthesis control, especially in eukaryotic organisms, and the molecular organisation of RNA in relevance to translation. Dr Shirokikh has made discoveries in fidelity and efficiency of translation initiation, such as providing the first genome-wide evidence of ribosomal scanning. He has developed some of the most informative methods to interrogate protein biosynthesis control in vivo at a full transcriptome scale. Dr Shirokikh leads the "Protein Biosynthesis and Homeostatic Control" group at JCSMR and uses a combination of advanced biochemical methods, such as ribosomal footprint-based technologies, high-throughput short read sequencing, long read sequencing including direct nanopore-based techniques, and innovative machine learning and artificial intelligence methods, to deliver a deeper insight into the workings of RNA in live cells. His current projects encompass yeast, as well as human, mouse and other metazoan models of healthy cells of diverse origin, as well as cell models of blood cancer and patient-derived cancer samples. He invents new technology, including advances allowing accurate quantification of transnational control and the epitranscriptome, to interrogate RNA-level regulation in these models across various circumstances, including cell stress and age. Dr Shirokikh actively participates in the development of RNA ecosystem in Australia, promoting RNA research and RNA paths for early-mid-career academics, being the founder and inaugural chair of the College of Health and Medical Sciences Early-Mid Career Research Committee, founding member of The Shine-Dalgarno Centre for RNA Innovation, the ACT State Representative of the RNA Network Australasia, and one of the founders of the national RNA biology and biotechnology conference A-RNA.

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