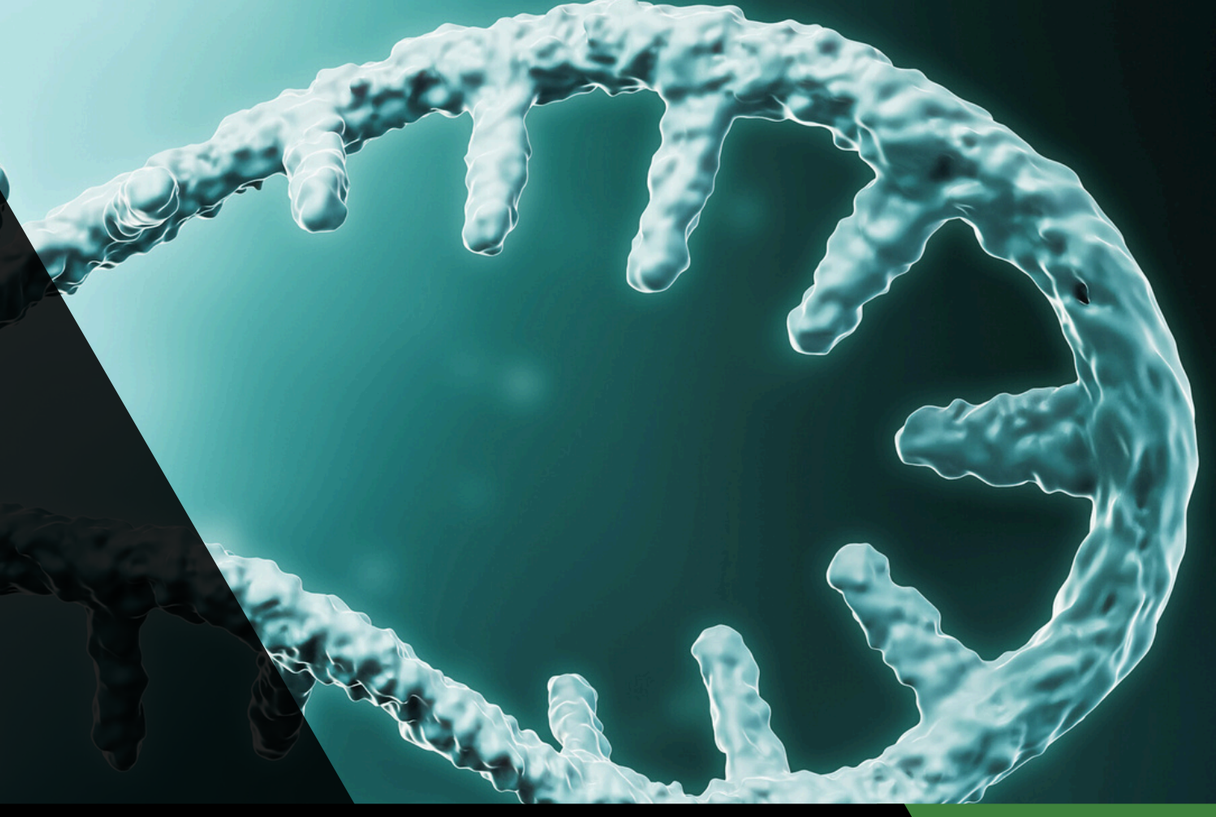
SINGAPORE RNA SEMINAR SERIES

IDENTIFYING THE SEQUENCE ELEMENTS AND PROTEIN FACTORS DICTATING RNA LOCALIZATION



Thursday 19 September 2024
10.00am (SGT, GMT+8)

Via Zoom

About the speaker

Furqan Fazal is an assistant professor of Biochemistry and Molecular Pharmacology at Baylor College of Medicine. The Fazal lab (https://fazallab.org) is part of the Therapeutic Innovation Center (THINC), and is supported by NIH R35, NIH R00, CPRIT, and Welch research grants. The lab focuses on systematically interrogating the subcellular transcriptomes of mammalian cells and characterizing the scope, regulation, and function of subcellular localization, particularly at the systems and organismal level. The lab uses a variety of biochemical, biophysical, imaging, genomic, and computational approaches to investigate the sequence-function relationship dictating RNA localization.

Prior to BCM, Furqan was a postdoctoral fellow at Stanford University, where he developed and used genomic tools to illuminate RNA biology in Howard Chang's lab. His research focused on investigating the impact of RNA structure and RNA subcellular localization on gene regulation. His postdoctoral work was supported by an NIH K99/R00 Award, an Arnold O. Beckman Postdoctoral Fellowship, and an NIH T32 Training Grant.

Furqan got his Ph.D. in Applied Physics from Stanford in the lab of Steven Block, where he utilized single-molecule techniques to study eukaryotic and prokaryotic transcription, and was supported by an NSF Graduate Research Fellowship.

He graduated summa cum laude from Amherst College, with majors in physics, chemistry, and biology. In his spare time he enjoys photography and traveling.

Dr. Furqan Fazal
Assistant Professor
Baylor College of Medicine

About the seminar

Mitochondria are complex organelles characterized by 1000 proteins, almost all of which are encoded in the nucleus. Using an RNA proximity labeling strategy we developed called APEX-seq (Fazal et al., Cell 2019), we recently found that the RNAs coding for these mitochondrial proteins are locally translated at the outer mitochondrial membrane (OMM), suggesting a widespread role of RNA localization and local translation there.

APEX-seq is an RNA-seq-based technology exploiting APEX, a genetically encoded peroxidase enzyme, to spatially tag RNAs and generate subcellular transcriptomes in living human cells. APEX-seq revealed that almost ~37% of the 900+ mitoRNAs in HEK (human embryonic kidney) cells precisely localize to the OMM, with preferential localization of an additional ~30-40% of mitoRNAs to the OMM. These nuclear-encoded proteins include components to make essential oxphos components.

Using two strategies, massively-parallel reporter assays (MPRAs) and knockdown (both genetic and chemical), we investigate the factors responsible for RNA localization to the mitochondria. Using MPRAs we have identified novel cis-elements guiding RNAs to the OMMs. APEX-seq in conjunction with drug perturbation experiments revealed that interfering with either microtubule- or actin- based transport disrupts the localization of hundreds of transcripts. Furthermore, we find cytoplasmic dynein to play a critical role in RNA localization. These studies identify the different pathways and cytoskeletal motors involved in RNA localization.

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