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"Decoding poly(A)-tail-mediated gene regulation during vertebrate early development"

Wednesday, February 26th, 2025 | 12:00 pm
Genomics Auditorium 1102A

Zoom Seminar Link
https://ucr.zoom.us/j/94383581111?pwd=MDdEMzBLQzNHM2xOMmdFaHNIR0F5Zz09

Biography

Dr. Xiang earned his bachelor's degree in Mathematics and Physics from Tsinghua University in China. He completed his Ph.D. in Biological Sciences at Columbia University, where he conducted structural and biochemical studies of transcription-coupled pre-mRNA 3'-end processing. After graduate school, he joined Dr. David Bartel's lab at the Whitehead Institute as a CRI Irvington postdoctoral fellow. Dr. Xiang's research has been centered on RNA biology and post-transcriptional gene regulation during vertebrate early development. Employing a multidisciplinary approach, he integrates high-throughput system methodologies, RNA and protein biochemistry, functional genomic screens, and machine learning to uncover gene-regulatory mechanisms that drive critical developmental transitions.

Abstract

Regulation of gene expression during early development is critically governed by dynamic changes in mRNA poly(A)-tail length, which strongly influences translational efficiency in animal oocytes and early embryos. However, this coupling between tail length and translational efficiency disappears later in development. We elucidated key mechanistic requirements for the coupling, centered around the cytoplasmic poly(A)-binding protein (PABPC): limiting abundance, stabilization of unbound mRNAs, and the ability to contribute to translational efficiency. Furthermore, we conducted high-throughput tail-length and translational profiling of mRNA reporter libraries in frog and fish oocytes and embryos. This revealed that the UUUUA motif, in conjunction with the polyadenylation signal, drives cytoplasmic polyadenylation, while C-rich elements mediate tail-length-independent translational repression. To predict these regulatory outcomes, we developed PAL-AI, a neural network model that accurately predicts poly(A)-tail length changes and associated translational effects across frog and mammalian oocytes. Notably, variants predicted to disrupt tail lengthening are under negative selection in the human population, suggesting a critical role for mRNA tail-length regulation in female fertility. Together, these findings define the sequence-driven and context-dependent mechanisms of post-transcriptional gene regulation essential for developmental progression and reproductive health.