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TOWARDS TRANSCRIPTOME-INFORMED MRNA MEDICINES

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Advances in 3′UTR-focused transcriptomics, particularly 3′UTR-seq, are revealing how alternative polyadenylation (APA) dynamically reshapes the mRNA landscape in a cell-type- and context-dependent manner. Our recent work uncovered how a select subset of cis-acting regulatory elements embedded in 3′UTRs of phenocritical mRNAs, such as the PTEN transcript isoforms, modulate mRNA stability, protein output, and ultimately define function. Through detailed characterization of APA regulators like the CFIm complex, we demonstrated that APA is not only widespread but also mechanistically tuned by signaling pathways such as KRAS. Single-cell APA analysis further reveals how differential 3′UTR isoform usage not only characterizes but also underpins transcriptome plasticity during cancer progression.

Now, we leverage these insights in the rational design of next-generation mRNA therapeutics, where transcriptome-informed UTR elements enhance expression, stability, and specificity of synthetic mRNAs, including those used in emerging in vivo CAR-T applications.

Altogether, our work illustrates how dissecting the regulatory logic of native transcriptomes can empower a new generation of precision mRNA medicines.

Thomas F. Duchaine, Ph.D., is Professor and Chair of the Department of Biochemistry at McGill University, Scientific Director of the McGill mRNA Therapeutics Platform, and Founding Director of the McGill Centre for RNA Sciences. His laboratory investigates post-transcriptional gene regulation by small and messenger RNAs, from molecular mechanisms to therapeutic applications.

THU
NOV 27
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16:00~17:00

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