RCB-Colloquium

Thursday, November 13, 2025 – 14:00 h

H 53

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Artificial Circular RNA Sponges Targeting miRNAs as a Novel Tool in Molecular Biology and Medicine

Natural circular RNAs (circRNAs) can sequester microRNAs (miRNAs) and suppress their function. Leveraging this principle, we engineered **artificial circRNA "sponges"** using in vitro transcription and ligation in a cell-free system. Upon transfection into cells, these circRNAs exhibited enhanced stability compared to their linear counterparts.

In a pilot study, we employed a circRNA decoy strategy targeting miRNA-122, which is essential for **hepatitis C virus** (HCV) replication. This approach significantly **inhibited HCV propagation**, demonstrating superior efficiency compared to an antisense oligonucleotide-based method previously reported.

As a further proof of concept, we designed circRNA sponges to sequester miRNA-21, a known **oncogenic miRNA.** This strategy effectively **reduced tumor growth** in 3D cell culture models and xenograft mice. The tumor suppression was mediated by the de-repression of mRNAs encoding tumor suppressor proteins.

Given the widespread use of in vitro-transcribed RNA in COVID-19 vaccines, we investigated whether systemically delivered circRNAs might activate **cellular antiviral defense mechanisms**. Following liposome-based transfection of our circRNA sponges, we observed that circRNAs generated through in vitro transcription, did not elicit an innate immune response. These findings support the broad application of artificial circRNAs as a versatile tool in molecular biology and therapeutic development.

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