LR2022021128

Literature Review

Engineered circular ADAR-recruiting RNAs increase the efficiency and fidelity of RNA editing in vitro and in vivo

HPLC Column, Sepax, SRT SEC-2000 PEEK, 5um, 2000 A
4.6 x 300 mm
Part Number: 215980P-4630

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Yi, Zongyi, et al. "Engineered circular ADAR-recruiting RNAs increase the efficiency and fidelity of RNA editing in vitro and in vivo." Nature Biotechnology (2022): 1-10.
https://doi.org/10.1038/s41587-021-01180-3

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Abstract

Current methods for programmed RNA editing using endogenous ADAR enzymes and engineered ADAR-recruiting RNAs (arRNAs) suffer from low efficiency and bystander off-target editing. Here, we describe LEAPER 2.0, an updated version of LEAPER that uses covalently closed circular arRNAs, termed circ-arRNAs. We demonstrate on average ~3.1-fold higher editing efficiency than their linear counterparts when expressed in cells or delivered as in vitro-transcribed circular RNA oligonucleotides. To lower off-target editing we deleted pairings of uridines with off-target adenosines, which almost completely eliminated bystander off-target adenosine editing. Engineered circ-arRNAs enhanced the efficiency and fidelity of editing endogenous CTNNB1 and mutant TP53 transcripts in cell culture. Delivery of circ-arRNAs using adeno-associated virus in a mouse model of Hurler syndrome corrected the pathogenic point mutation and restored α-L-iduronidase catalytic activity, lowering glycosaminoglycan accumulation in the liver. LEAPER 2.0 provides a new design of arRNA that enables more precise, efficient RNA editing with broad applicability for therapy and basic research.

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circRNA on Sepax Analytical SEC

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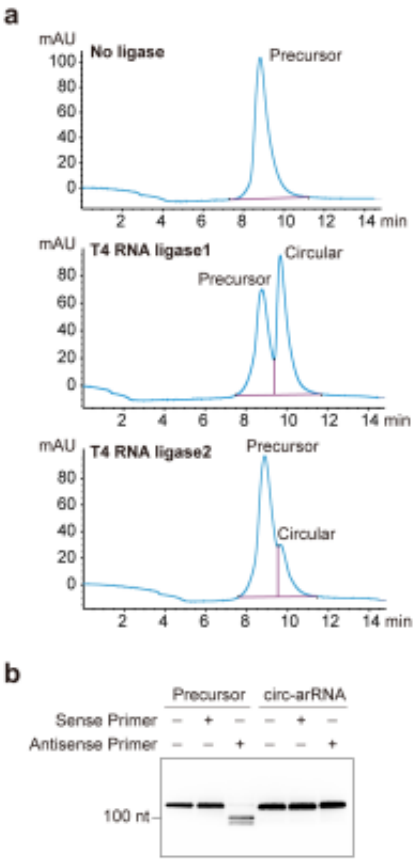
Sample

Broad Sample Type	DNA/RNA/OLIGO
Sample	circ-arRNA
Sample Notes	purified RNase R-treated circ-arRNAs
Sample Prep	Circ-arRNAs were packaged in AAV8 by PackGene Biotech. The AAV titer was 1 × 1013 virus/200 µl;

Experimental conditions

Column	SRT SEC-2000 PEEK, 5um, 2000 A 4.6 x 300 mm
Mobile Phase	RNase-free TE buffer
Instrument	HPLC
Instrument Notes	Agilent HPLC 1260



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Order Information

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