Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

RNA Therapeutic Stabilizing Construct

Product

RNA Stabilizing Construct

Indication

RNA Therapeutics & Delivery

Value Propositions

- Improve nearly any RNA therapeutic stability and half-life
- Protect endogenous cellular RNAs and introduced RNAs
- Broad exonuclease protection

Market

- Global mRNA therapeutic market expected to reach $23 Billion by 2035
- Global RNAi drug delivery market estimated to be $50 Billion in 2021 with a CAGR of 27% through 2026

Intellectual Property

- Issued US and EP patents; pending US continuation application*
- Available for licensing

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Background on CU3879H

The recent success of mRNA vaccines demonstrates the therapeutic potential of RNA. While few RNA-based treatments have been approved for clinical use, many more RNA vaccines and therapeutics are expected to be brought to market in the coming decades. One of the biggest obstacles to the development of RNA therapies has been RNA's inherent instability. Even with successful expression or delivery (using methods such as lipid nanoparticles), RNA can be quickly degraded by cellular exoribonucleases. In addition, many diseases could potentially be treated by increasing the amount of a naturally occurring specific RNA produced by the cell by making it less prone to degradation.

Technical Innovation

Dr. Jeffrey Kieft has led a team of University of Colorado researchers in the development of a technology that uses engineered viral exoribonuclease-resistant RNAs to protect RNAs in the cell from degradation, prolonging their lifetime. *In vitro* studies show that these engineered RNAs prevent degradation of other RNAs, both *in cis* and *in trans*, by a broad range of cellular RNA exoribonucleases. This technology could be useful to increase the therapeutic efficacy and half-life of nearly every RNA therapy in development. Also, it could increase the levels of naturally occurring cellular RNAs to potentially treat diseases based on haploinsufficiency. With the use of this asset, RNA therapeutics may be one step closer to wide-spread clinical deployment.

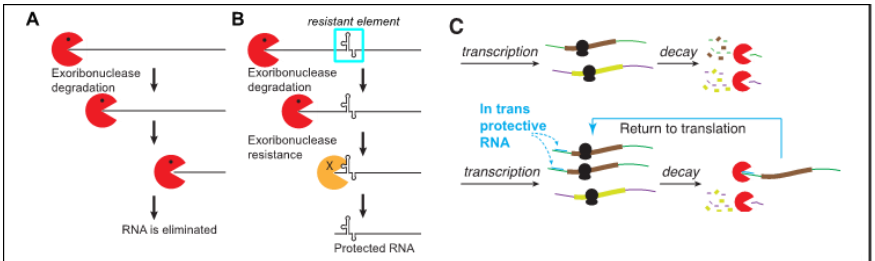

Figure: A. normal RNA turnover in cells leads to elimination of RNAs by cellular exoribonucleases (red). **B.** Engineered, small exoribonuclease-resistant RNA elements (boxed in cyan) block these enzymes and protect downstream RNAs. **C.** The technology can be adapted to operate *in trans*. In this application, mRNAs that are normally rapidly degraded in the cell are protected by an engineered exoribonuclease element delivered *in trans* (cyan), increasing the effective concentration of these RNAs in the cell.

Resources & Documents:

B. M. Akiyama et al. *Zika virus produces noncoding RNAs using a multi-pseudoknot structure that confounds a cellular exonuclease.* Science. (2016).

E. G. Chapman et al. *The structural basis of pathogenic subgenomic flavivirus RNA (sfRNA) production.* Science. (2014).

E. G. Chapman, S. L. Moon, J. Wilusz, J. S. Kieft. *RNA structures that resist degradation by Xrn1 produce a pathogenic Dengue virus RNA.* Elife **3**, e01892 (2014).

A. MacFadden et al. *Mechanism and structural diversity of exoribonuclease-resistant RNA structures in flaviviral RNAs.* Nat Commun **9**, 119 (2018).

**US patent obtained: 10920224—"Protecting RNAs from degradation using engineered viral RNAs" – Granted Feb 16, 2021.*

**US continuation application pending—17/173,354.*

**EP patent obtained—Validated in UK, France and Germany. "Protecting RNAs from degradation using engineered viral RNAs" – Granted December 2021.*