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INNOVATE WITH STANFORD:
BARNA LAB MRNA TECHNOLOGY PORTFOLIO

Elevator Pitch

- 1** The Barna Lab is an interdisciplinary team dedicated to the development of tools for improving RNA-based therapeutics and vaccines
- 2** Numerous innovative technologies are available as tools to enhance translation, synthesis, and stability in the design of mRNA vaccines and/or therapeutics
- 3** Stanford is looking for licensees, research sponsors, or investors to develop, commercialize, or support a startup around one or more of these technologies

The Barna Lab

Dr. Maria Barna, PhD, Associate Professor of Genetics

- Dr. Barna was named a top '40 under 40' by the Cell Journal
- Received the NIH Directors New Innovator Award, Rosalind Franklin Young Investigator Award, American Society for Cell Biology Emerging Leader Prize, and RNA Society Early Career Award, among others

Highly-multidisciplinary, with biochemists, RNA biologists, developmental biologists, & computational biologists

Develops mRNA technologies for improved development of RNA-based therapeutics and vaccines



Barna Portfolio mRNA Technologies

Docket	Title	RNA therapeutic/vaccine applications	Patents	Stage	Slide
S20-135	<u>Translation enhancer for gene regulation</u>	RNA-based viral delivery or expression	USA, EPO pending	Proof of Concept	5
S20-174	<u>Optimized synthesis and translation of RNA therapeutics</u>	Design and selection based on translation efficiency	USA issued, EPO and USA cont pending	Proof of Concept	6
S20-175	<u>Optimized synthesis of RNA-based therapeutic candidates</u>	Optimizing RNA stability	USA issued, EPO and USA cont pending	Proof of Concept	7
S20-183	<u>mRNA Vaccines: Methods of synthesis and stability assessment</u>	Optimizing RNA stability with degradation and filter steps	USA pending	Research – in vitro	8
S20-205	<u>Repurposing the SARS-CoV-2 5'-UTR for RNA based therapeutics</u>	Design using SARS-CoV-2 5' UTR	USA, EPO pending	Proof of Concept	9

S20-135: Enhanced RNA translation

Summary

A short nucleotide stem-loop sequence that, when used alongside a spacer sequence, mediates increased translation initiation of mRNA.

Advantages

Reduction in the amount of delivered mRNA/reagents to patients; Transferrable to any reporter gene or mRNA of interest

Stage of Development: Proof of Concept

Patent/s: Pending in USA, EPO

Publication: Leppek et al. (2022). Combinatorial optimization of mRNA structure, stability, and translation for RNA-based therapeutics. Nature communications, 13(1), 1536.

spacer:

a9 native spacer (native) → 130 nt
actin 5' UTR (*actin*) → 100 nt
inverse actin 5' UTR (*actin(inv)*) ← 100 nt

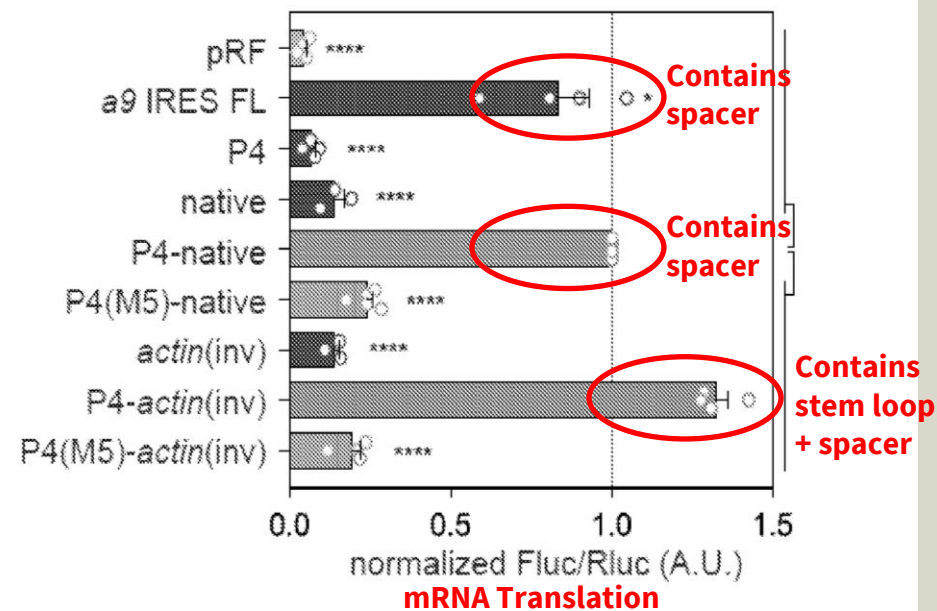
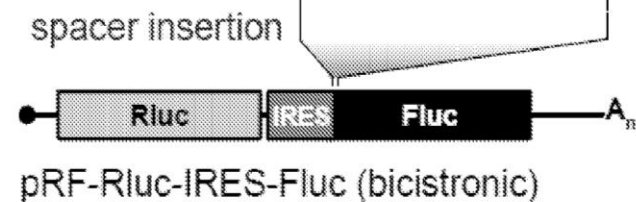


Figure 1D

FIG 1D. See patent

S20-174: Optimized RNA synthesis and translation

Summary

A method for measuring translation efficiency in a library of mRNA sequences.

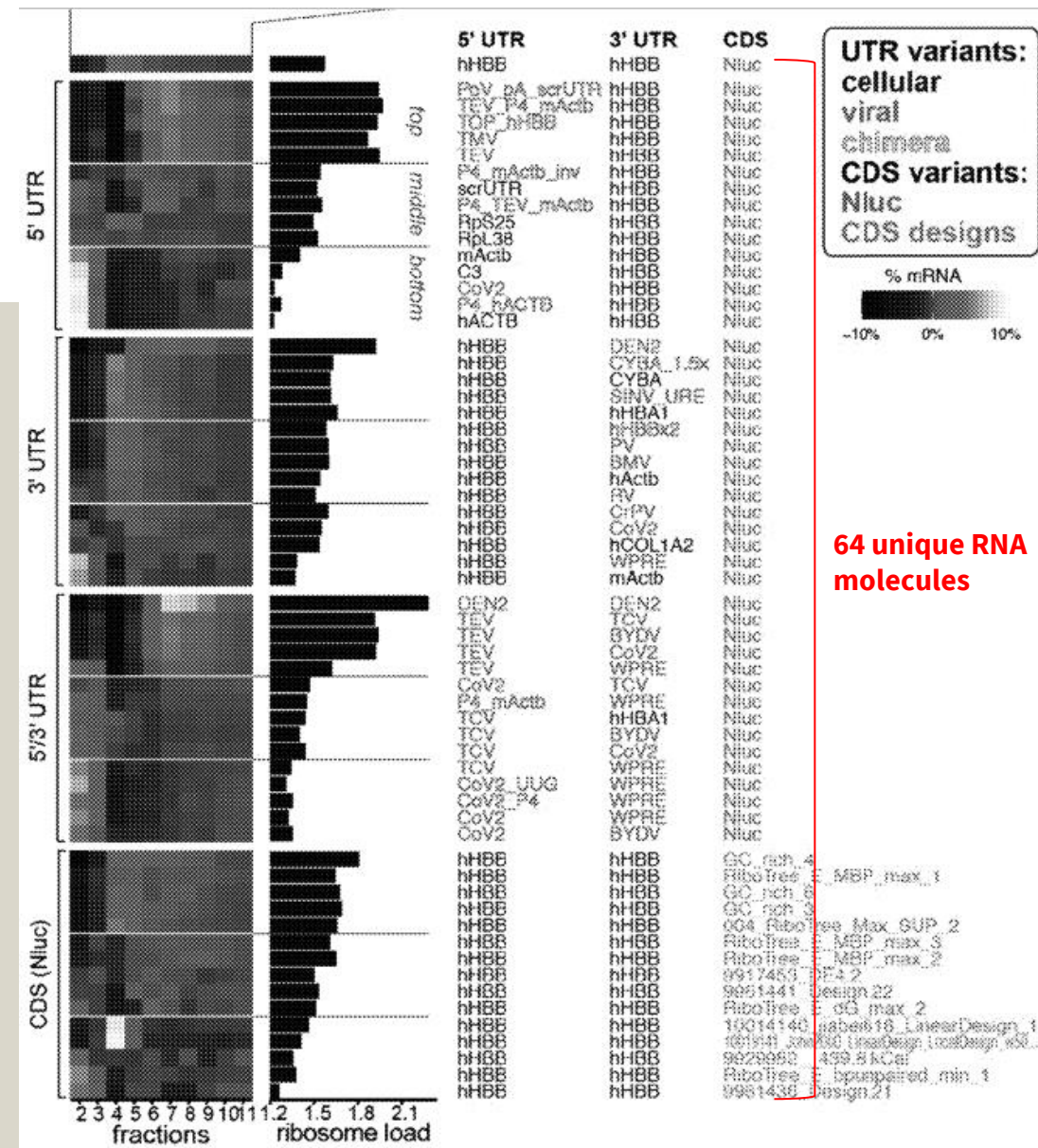
Advantages

Supports efficient, robust and high-fidelity production of mRNA and rapid sequence design; High throughput; Allows repeated cycles of directed evolution and unbiased searching

Stage of Development: Proof of Concept

Patent/s: [Issued](#) in USA, Pending in EPO, Cont pending in USA

Publication: Leppek et al. (2022). [Combinatorial optimization of mRNA structure, stability, and translation for RNA-based therapeutics](#). Nature communications, 13(1), 1536.



Relative prevalence (translation efficiency)

FIG. 6A. See patent

S20-175: Optimized RNA stability

Summary

A method for measuring RNA stability following exposure to different experimental conditions utilizing barcode sequences previously described in S20-174 that are associated with unique mRNA sequences.

Advantages

Supports selection of stable mRNA sequences for clinical applications and rapid sequence design; High throughput

Stage of Development: Proof of Concept

Patent/s: [Issued](#) in USA, Pending in EPO, Cont pending in USA

Publication: Leppek et al. (2022). [Combinatorial optimization of mRNA structure, stability, and translation for RNA-based therapeutics](#). Nature communications, 13(1), 1536.

In vivo
whole RNA
molecules

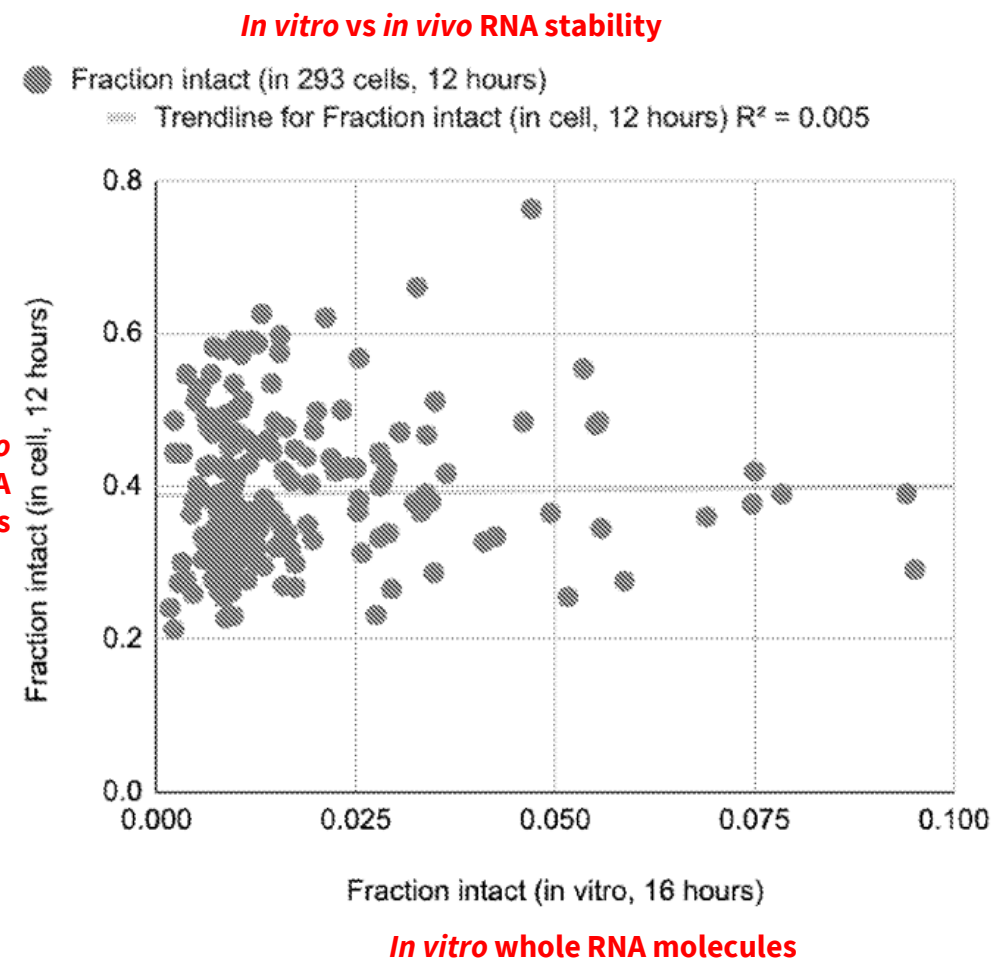


Figure 1

FIG 1. See patent

S20-183: Optimized RNA stability with degradation and filter steps

Summary

A method for measuring RNA stability following exposure to different experimental conditions, with the addition of a particular nuclease that digests degraded mRNA molecules, leaving only stable, full-length mRNA molecules remaining in the pool. A computational filter removes molecules with anomalous stability.

Advantages

Supports selection of stable mRNA sequences for clinical applications and rapid sequence design; High throughput

Stage of Development: Research – in vitro

Patent/s: [Pending](#) in USA

Publication: Leppek et al. (2022). [Combinatorial optimization of mRNA structure, stability, and translation for RNA-based therapeutics](#). Nature communications, 13(1), 1536.

In vivo
whole RNA
molecules

In vitro vs in vivo RNA stability

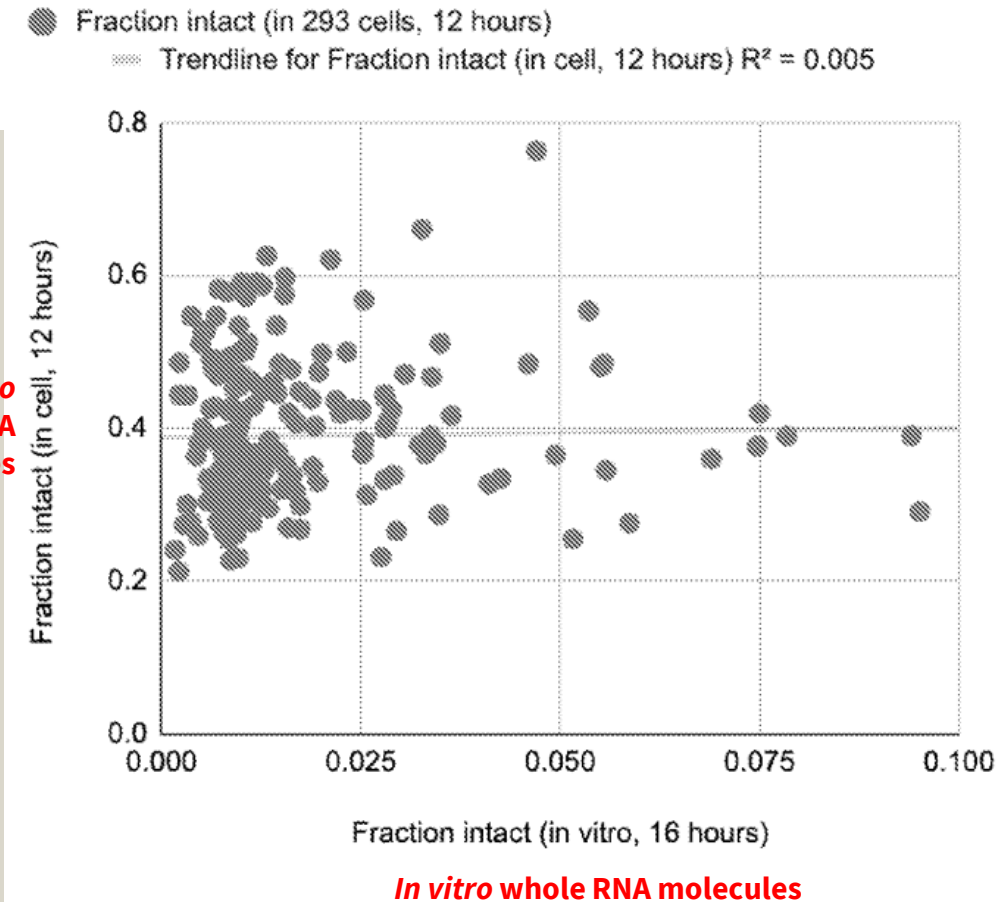


Figure 1

FIG 1. See patent

Barna Lab Innovations: Enhance/Augment/Add to your Pipeline!

- Stanford is seeking **licensees** utilize and/or commercialize one or more of these technologies

Contact Us

Stanford | Office of Technology Licensing

415 Broadway Street, 2nd Floor,
Redwood City, CA 94063
otl.stanford.edu
otl-connect@stanford.edu

