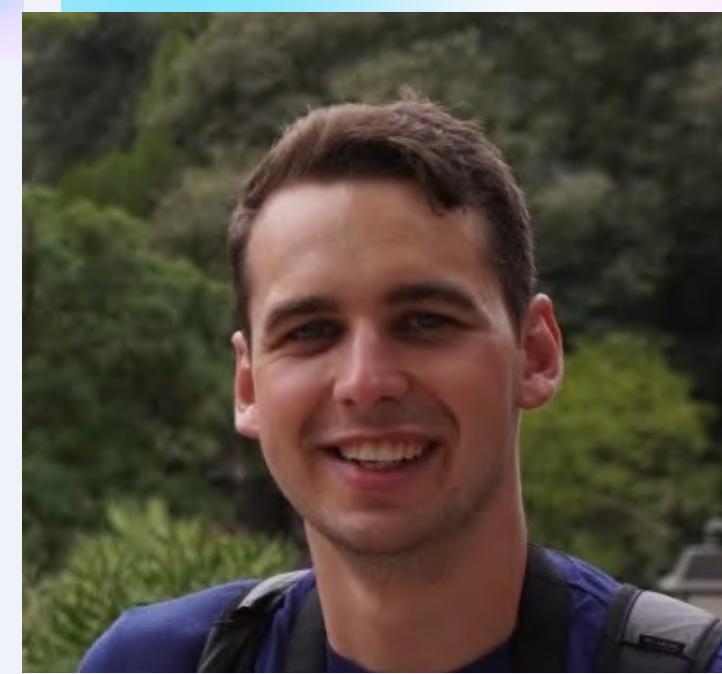


Meet Chain of Custody



Dr. Andrew Newman

NEURONAL GENOMICS



Nico Trummer

BIOINFORMATICS
ONCOLOGY



Filippo Conforto

PH.D. CANDIDATE
BIOPHYSICS



Selin Abdullazade

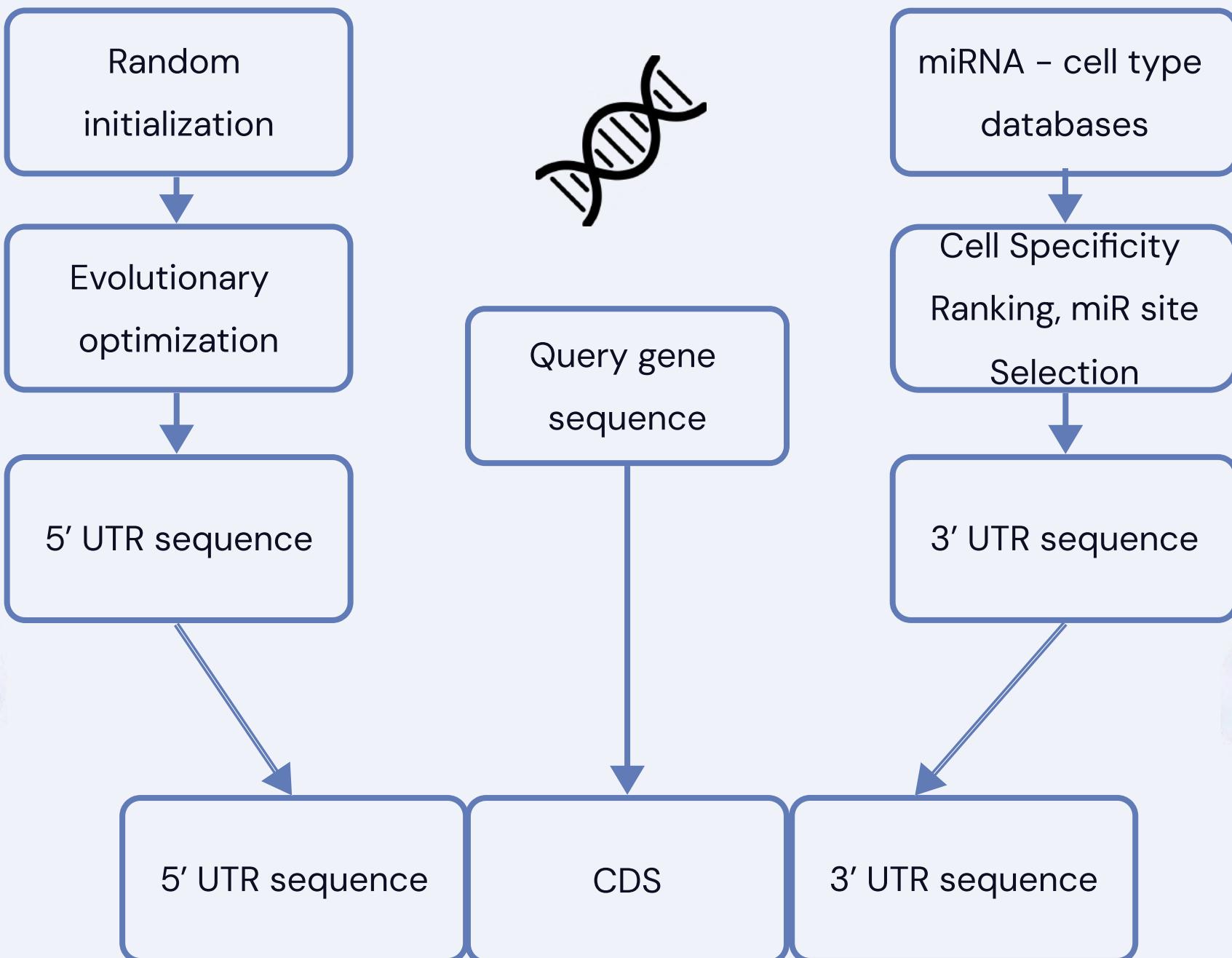
SOFTWARE



Dr. Frida Arrey

IMMUNOLOGIST

Technical Overview



How it works: Dashboard

adjust menu

Cell type selection

Targets Off-targets

Search cell types...

196 cell types Clear targets

- Adipocyte
- Amniotic epithelial cell
- Annulus fibrosus cell
- Astrocyte
- B cell germinal center
- B cell naive
- B cell pre germinal center
- B lymphocyte

Design parameters

5' UTR MODE Manual Optimise

Run 5' UTR Optimisation

Uses a Genetic Algorithm (NSGA-III) to evolve a 5'UTR that maximizes Translation Efficiency while maintaining stability.

CODING SEQUENCE

Gene Symbol e.g. POU5F1 Fetch CDS

Fetch canonical CDS from Ensembl

CDS (Coding Sequence)

e.g. AUG... The protein-coding region

3' UTR ALGORITHM

Target silence threshold < 10 RPM

Max mean RPM in target cells for a miRNA to be a candidate

Off-target coverage threshold ≥ 1000 RPM

Min mean RPM in an off-target cell to count it as covered

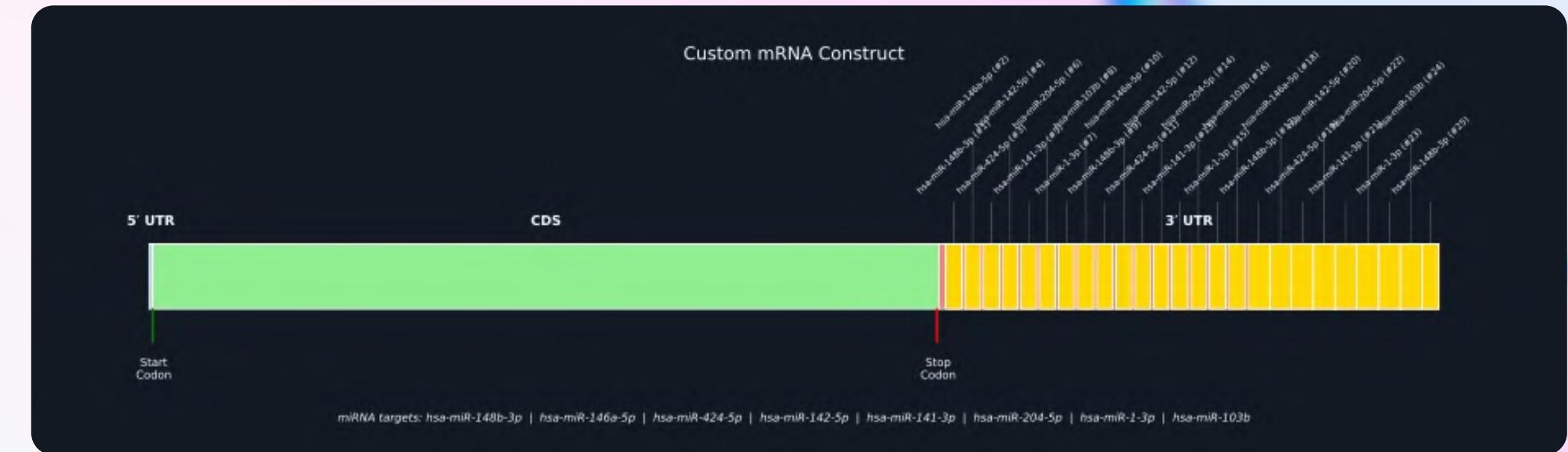
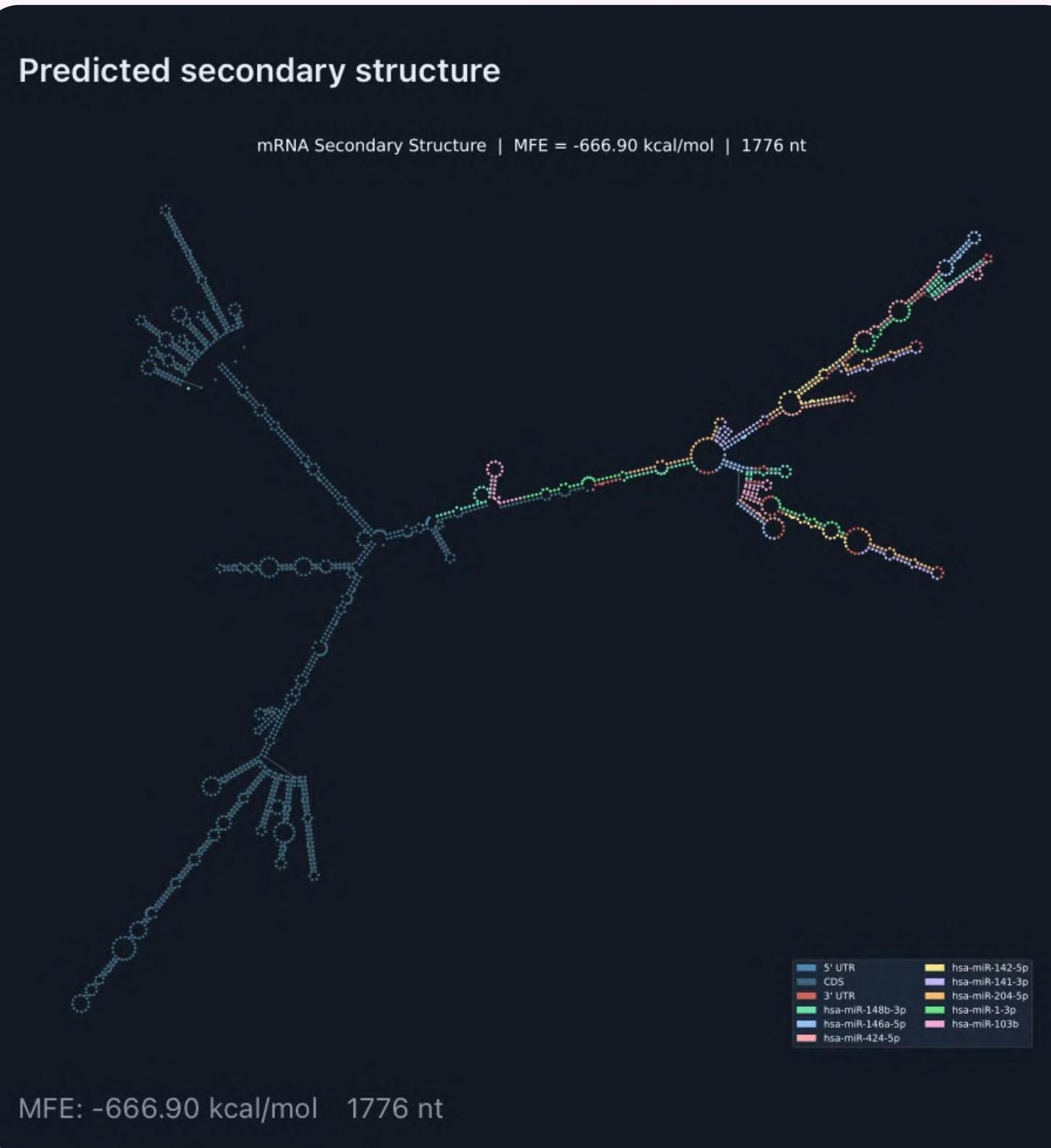
Max miRNAs to select 20

Algorithm stops after this many miRNAs regardless of coverage

then visualise...



How it works: Results



Linear binding site map

Construct sequence

Full mRNA 3'UTR Cassette Copy

1776 nt 5'UTR: 5nt CDS: 1083nt 16 sites

GCAUCAUGGCAGGGACACCUGGCUUCAGAUUUUGCCUUCUCGCCCCCCUCCAGGUGG
UGGAGGUGAUGGGCCAGGGGGCCGGAGCCGGCUGGUUGAUCCUCGGACCUG
GCUAAGCUUCCAAGGCCUCCUGGAGGGCCAGGAAUCGGGCCGGGGUUGGGCCA
GGCUCUGAGGUGGGGGAUUCCCCCAUGCCCCCGCCGUAUGAGUUCUGUGGGG
GGAUGGCGUACUGUGGGCCCCAGGUUGGAGUGGGGUAGUGCCCCAAGGCAGGU

Secondary structure

Complete mRNA sequence

Precision Gene Delivery

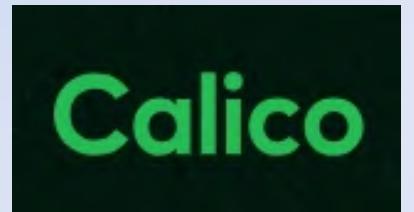
LEVERAGING MULTIPLEX MIRNA LOGIC

- Our platform can generate mRNAs for cell-type specific translation with minimal off-target effects enabling:

1) Multiplex Gene therapies: one shot targeting of multiple genes across multiple celltypes.

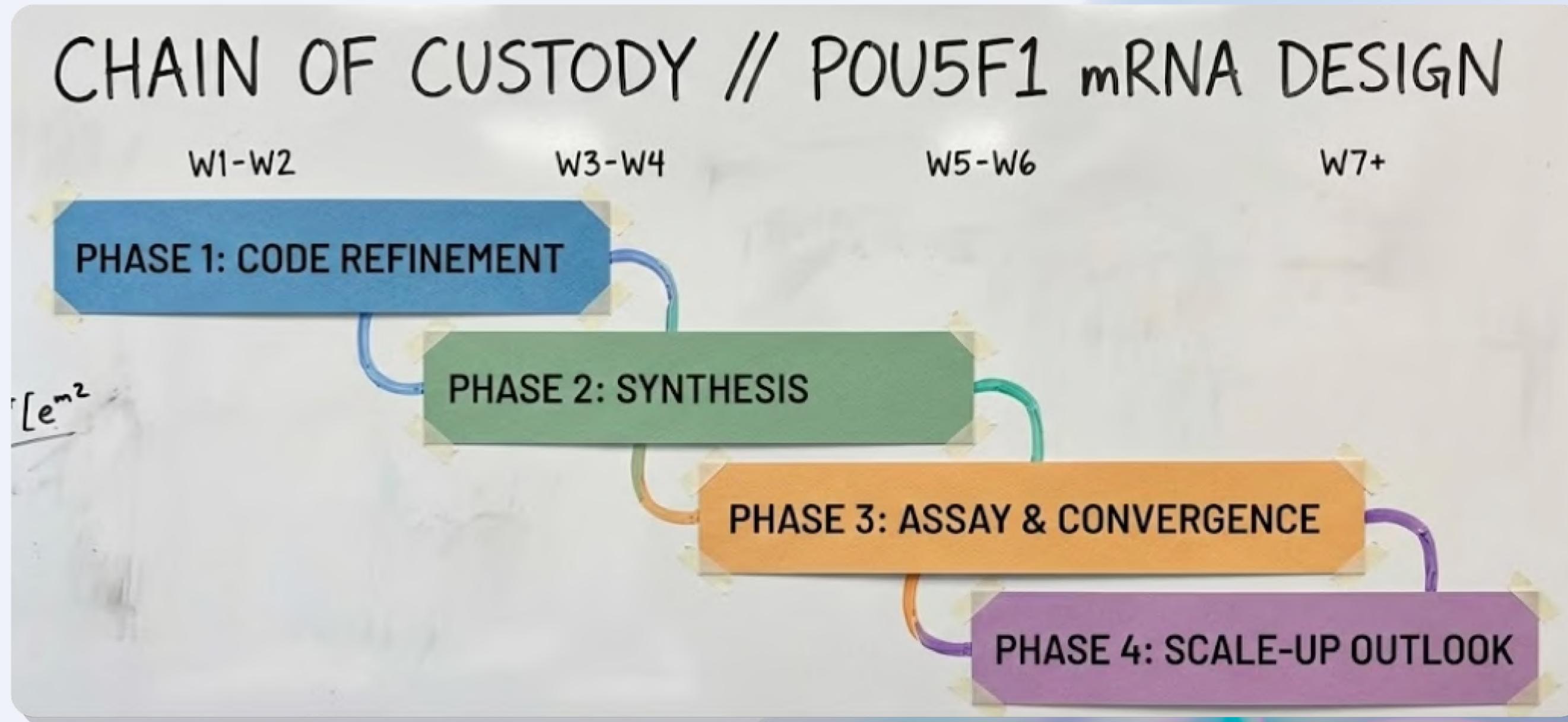
2) Dosage control: partial (age) reprogramming using OSKM* rejuvenates cell types with differing efficiency. Tissue specific translation enables optimization of reprogramming rates by tissue type, abolishing the risk of tumorigenesis.

Longevity tech industry...

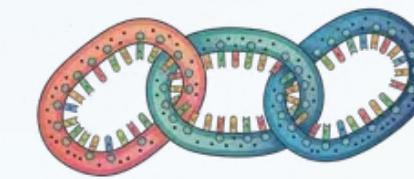
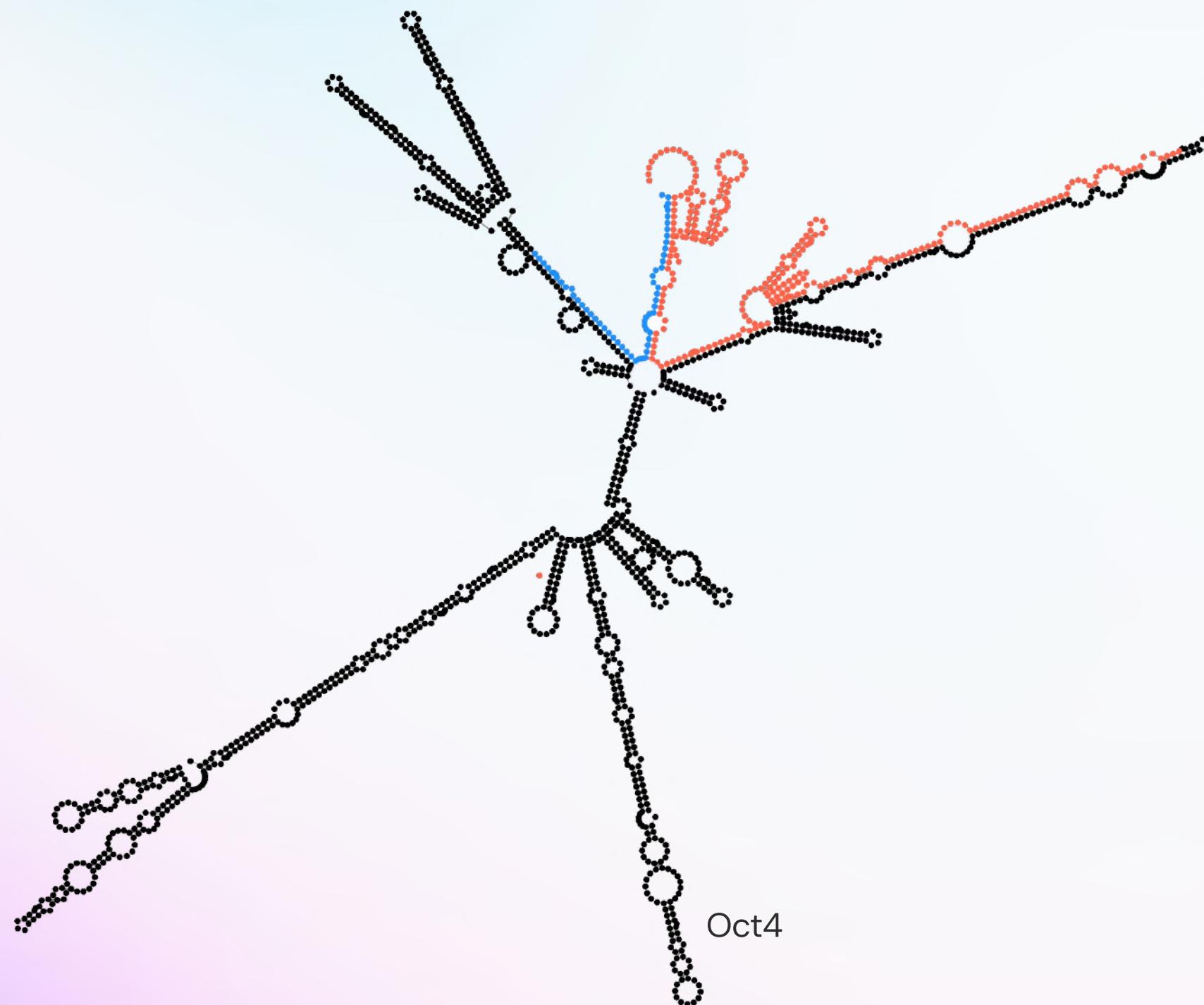


Shift**bioscience**

Potential to scale



References



- 1 Kozomara A et al, 2019, *Nucleic Acids Res*
- 2 Arun H Patil et al, A curated human cellular microRNAome based on 196 primary cell types, 2022, *GigaScience*
- 3 McGeary SE et al, The biochemical basis of microRNA targeting efficacy, 2019, *Science*
- *Singh & Newman 2019, *Epigenetics & Chromatin*
Browder et al, 2022, *Nature Aging*



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