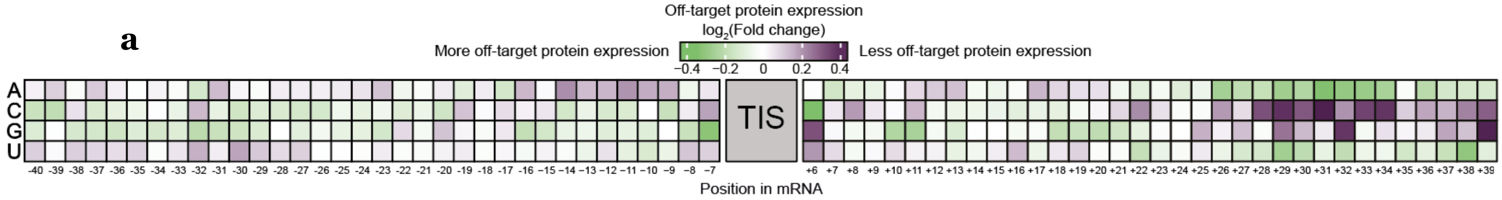
Title

Novel Sequences for Precision Control of Translation Initiation to Maximize Expression

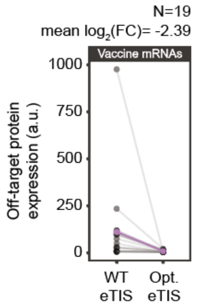
Overview

The extended Translation Initiation Sequence (eTIS) — a newly discovered sequence grammar combined with a custom machine learning algorithm — enables the design of mRNA sequences with substantially higher accuracy and efficiency of protein production. Classical approaches rely on the Kozak sequence — just ~10 nucleotides around the start codon — this captures a part of the picture, leaving significant performance on the table. Hubrecht Institute researchers systematically mapped start codon recognition efficiency across thousands of sequence variants, and found that sequence elements both *upstream* and *downstream* of the classical Kozak window substantially influence initiation. This broader sequence region is the eTIS (a). The eTIS signature, along with a custom-built machine learning algorithm, enables the design of highly effective translation initiation sequences for any mRNA. The invention enables higher initiation efficiency and improved accuracy (b,c). The approach allows a sequence-agnostic design.

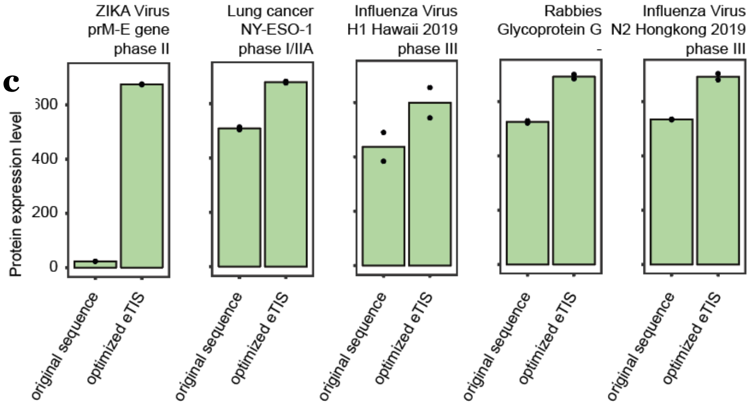
a



b



c



Performance highlights

60-99%
baseline initiation efficiency range

>99%
eTIS-optimized recognition accuracy

Any RNA
any transcript and coding sequence

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Applications

- Recombinant protein production
- Antibody production
- mRNA therapeutics, in-vivo expression technologies
- RNA vaccines: Optimize the expression of antigen protein
- Gene therapy & genetic engineering
- Synthetic biology
- Research reagents

Differentiation

- High accuracy: reduction of non-specific out-of-frame proteins (b)
- Optimised expression, higher yield (typically ~15-40%, as high as 300%, (c)
- Applicable to any RNA expression construct for *in vitro* or *in vivo* use

Development Stage

- POC demonstrated on a number of products on the market
- Patent filed in 2025
- Looking to license the technology to Industrial and Biotech partners.

Scientific Team

Marvin Tanenbaum Group: Gene expression dynamics

This work comes from the Tanenbaum group at the Hubrecht Institute, primarily through the doctoral research of Bram Verhagen (thesis: "Where to start? How gene sequences shape translation initiation").

Marvin Tanenbaum is senior group leader at the Hubrecht Institute, Investigator at Oncode Institute and Professor in the department of Bionanoscience at the TU Delft.

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