Computational platform for enhancing Gene Expression for increased protein yield and viral titer (Ramot)

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Technology

Deciphering Gene Expression Code - We perform large-scale analyses of genomic data to discern the rules behind the various aspects of gene expression encoded in the transcript.
Computational Modeling of Gene Expression - We develop predictive computational models to mathematically analyze and simulate the different stages of gene expression, focusing on gene translation.
Engineering Gene Expression - We devise various computational approaches for engineering gene expression for various biotechnological applications.
Gene Expression in Diseases - We analyze and model gene expression in autoimmune diseases and cancer to better understand their pathogenesis, for screening and diagnostic purposes, and to develop new therapeutic approaches.

The Need: Knowledge-Based Gene Design

• mRNA levels explain only ~30% of the variance in protein levels. Other regulation layers encoded in the genetic sequence are unresolved and remain elusive.
• The Tuller lab aims to decipher the unknown layers of regulation encoded in the genetic sequence in order to intelligently optimize and quantify the process, thereby enabling manipulation and design of genes.
• Today's revolution in synthetic biology allows the cost-effective design and production of synthetic genes. At present, the unmet need is to understand the various layers of regulation that are hidden within the designed sequence in order to optimally express the gene.

Applications

A customized design tool for engineering gene expression that takes into account more than 60 rules affecting gene/protein expression in order to:

- Control protein expression levels, stability, and folding
- Design genes tailored to the host organism in which they are expressed
- Attenuation of viruses and pathogens (vaccines)
- Discover non-coding mutations that play a crucial role in disease

Stage of Development

Many of the algorithms were validated in various ways in heterologous and endogenous systems.

Patents

US patent application - METHOD AND SYSTEM FOR DESIGNING POLYNUCLEOTIDE SEQUENCES AND POLYNUCLEOTIDE SEQUENCES OBTAINED
US provisional patent application - no. 62/234,822, filed 09/2015

Supporting Publications

T Tuval Ben-Yehezkel*, Shimshi Atar*, Hadas Zur, Alon Diament, Eli Goz, Tzipy Marx, Rafael Cohen, Alex Dana, Anna Feldman, Ehud Shapiro, Tamir Tuller. Rationally designed, heterologous S. cerevisiae transcripts expose novel expression determinants. RNA Biol. 2015 Sep 2;12(9):972-84.
Hadas Zur, Tamir Tuller. Exploiting Hidden Information Interleaved in the Redundancy of the Genetic Code without Prior Knowledge. Bioinformatics. 2014 Nov 29. pii: btu797.
Alexandra Dana, Tamir Tuller. The effect of tRNA levels on decoding times of mRNA codons. Nucleic Acids Res. 2014 Jul 23.
Hadas Zur, Tamir Tuller. New universal rules of eukaryotic translation initiation fidelity. PLoS Comput

Biol. 9(7), 2013.
Shlomi Reuveni*, Isaac Meilijson, Martin Kupiec, Eytan Ruppin, Tamir Tuller*. Genome-scale analysis of translation elongation with a ribosome flow model. PLoS Comput Biol. 2011 Sep;7(9):e1002127.

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