

MEETING ABSTRACT

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Protein translational control and its contribution to oncogenesis revealed by computational methods

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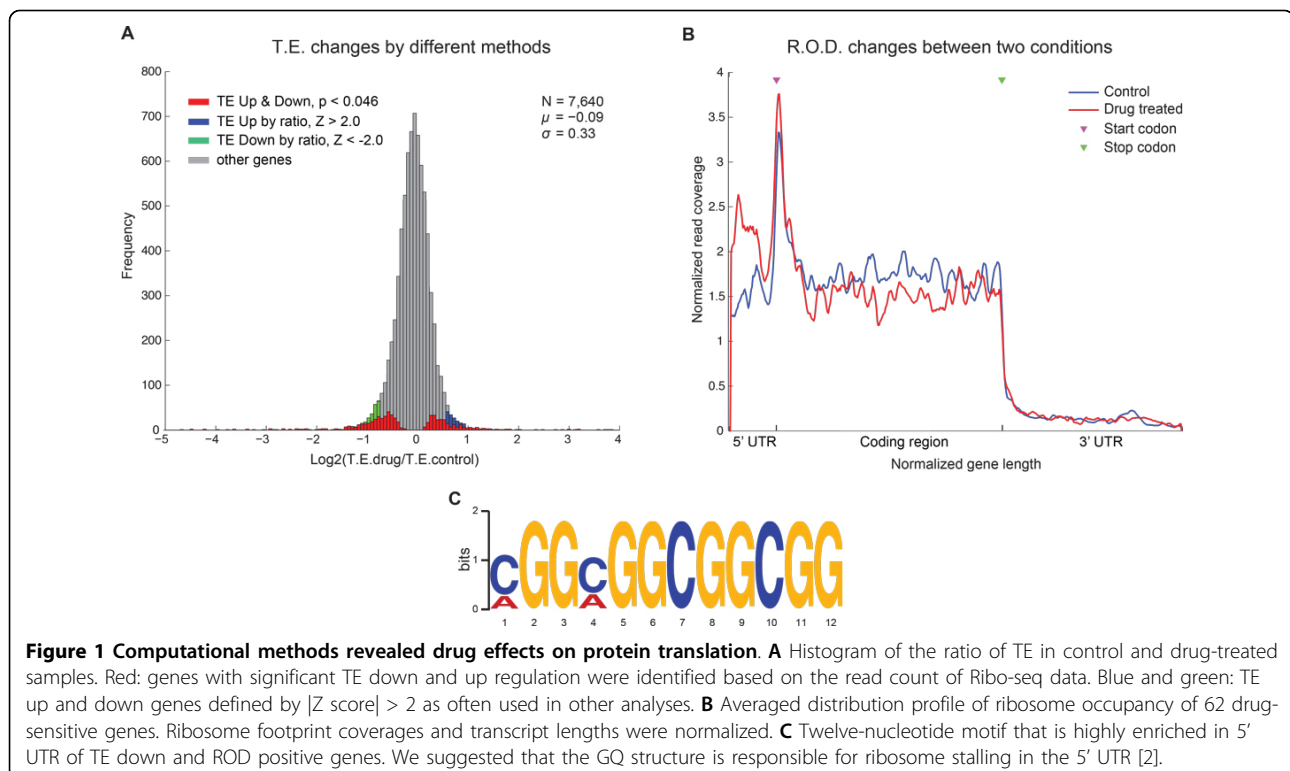
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Background

Protein translation is a fundamental biochemical process and the regulation of this process in response to a variety of changes has been demonstrated to play a key role in cellular functional activity. Recently, the translational control of oncogenes is implicated in many cancers [1].

Results

We recently reported a translation initiation factor eIF4A RNA helicase-dependent mechanism of translational control that contributes to oncogenesis and underlies the anticancer effects of drug silvestrol [2]. Inhibition of eIF4A with silvestrol has powerful therapeutic effects



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in vitro and *in vivo*. In this study, we developed novel computational tools, specifically be tailored to study high throughput ribosome footprint data (Ribo-seq) [3], to identify the genes featuring either one of the two changes between two experiment conditions: 1) translational efficiency (TE), and 2) ribosome occupancy distribution profile (ROD) on mRNA. In the parametric test of TE, we take RNA abundance and ribosome occupancy density into account in order to expeditiously identify differential translation efficiency. Whereas the non-parametric test of ROD [4] aims to identify differential occupancy profiles, such as ribosome stalling at specific sites even if overall translation efficiency remain unchanged. Using transcriptome-scale ribosome footprinting data of leukemia cell line, we defined drug-sensitive genes showing both decrease of translational efficiency (Figure 1A) and accumulation of ribosome occupancy at 5'UTR (Figure 1B). Among the most eIF4A-dependent transcripts are a number of oncogenes, super-enhancer associated transcription factors and epigenetic regulators.

Conclusions

Computational and statistical methodologies facilitate the discovery of the hallmark of eIF4A-dependent transcripts, namely 5'UTR sequence harbors the 12-mer guanine quartet (CGG)₄ motif associated with RNA G-quadruplex (GQ) structures (Figure 1C). Our novel computational tools provide a fast, accurate solution to gain biological insights from Ribo-seq and RNA-seq data.

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