Perspectives - Decoding of novel selenoprotein in *Homo sapiens*

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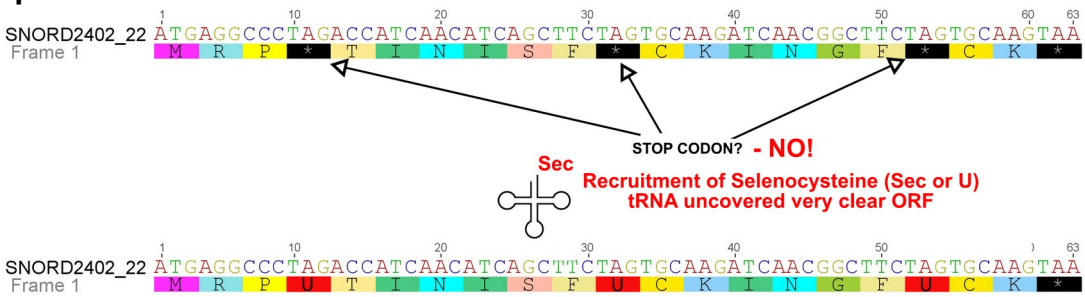
Abstract

In early 80‘s scientists discovered in model species *E.coli* that selenocystein amino-acid (symbol Sec or U) has its own context-dependent codon – UGA, which is generally associated with translation termination (= stop codon). Follow-up studies identified Selnocystein tRNA UGA codon usage in all three domains of life including Humans. Here we decipher a novel open reading frame of previously characterized human small non-coding RNA (ncRNA) SNORD2402_22 involving an unusual presence of Selenocystein. Earlier genome-wide association studies (GWAS) has been suggesting significant SNORD2402_22 crosstalk with neural development and progression on numerous psychosomatic diseases. The ablation of SNORD2402_22 is often associated with e.g. paranoia, diarrhoea, erectile dysfunction or cowardice. Intriguingly, recent studies showed correlation among cohort with reduced SNORD2402_22 expression and hypersensitivity to mRNA vaccines. Despite of substantial pleiotropic effect of the SNORD2402_22 gene, its molecular function/biogenesis remained unclear for a decades. Taken together, our findings clearly show that SNORD2402_22 act as protein coding gene and not ncRNA as expected before.

Graphical Abstract



Introduction

Selenium plays an important biological role in human health through its presence in a family of proteins called selenoproteins (reviewed in (1)). Selenoproteins incorporates selenium in form of Selenocysteine (Sec) which is in known as 21st amino-acid. Sec codon is UGA, which usually corresponds to a termination codon. Up to date, only 25 Selenoproteins has been identified in a human (Fig.1). These proteins have various biochemical/physiological roles (See Fig 1.) corresponding to e.g. antioxidant activities, fertility and central nervous system (3-5).

SNORD2402_22 has been reported as a snRNA (~65nt long), important in CNS development and its ablation is usually associated with serious psychosomatic diseases reviewed in (6,7). However molecular mechanism of its function has never been fully explained/understood. In this study, we showed that SNORD2402_22 code a short peptide, which brings a novel ground breaking insights on SNORD2402_22 function.

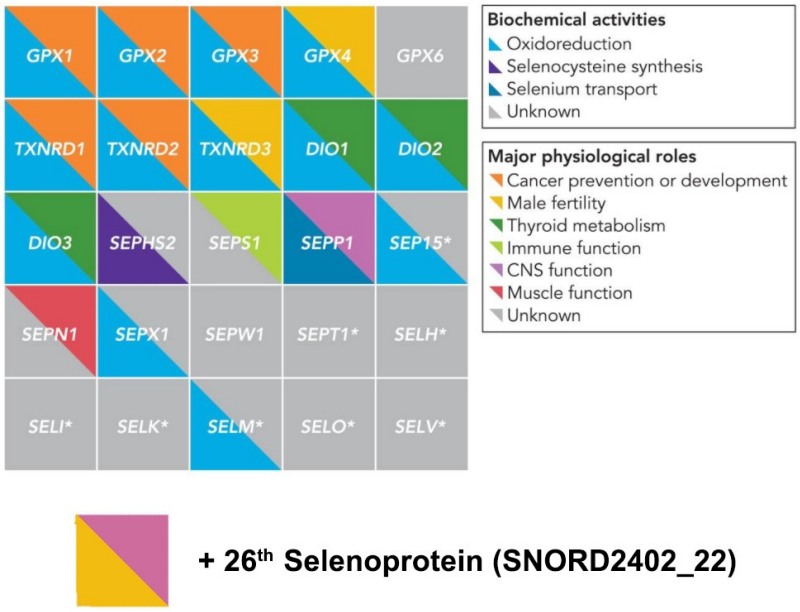


Figure 1: Schematic overview of known human selenoproteins and their biological roles (Adapted from (2)) with corresponding biological role of novel selenoprotein identified in this study.

Results and discussion

Using a combination of polysome-seq and tRNA-Sec-AB (Abacam) antibody we predicted 31 selenocysteine-like mRNAs (i.e. putative RNAs coding selenoproteins) (see Supplementary File S1 and S2 for methods). Besides known selenoprotein mRNAs we pulled-down SNORD2402_22 which has been previously characterized as small ncRNA. In total - SNORD2402_22 in 3.8-fold enriched in RNAseq library from fraction with AB, 5.2-fold in polysome fraction without antibody in comparison to control (Figure 2.)

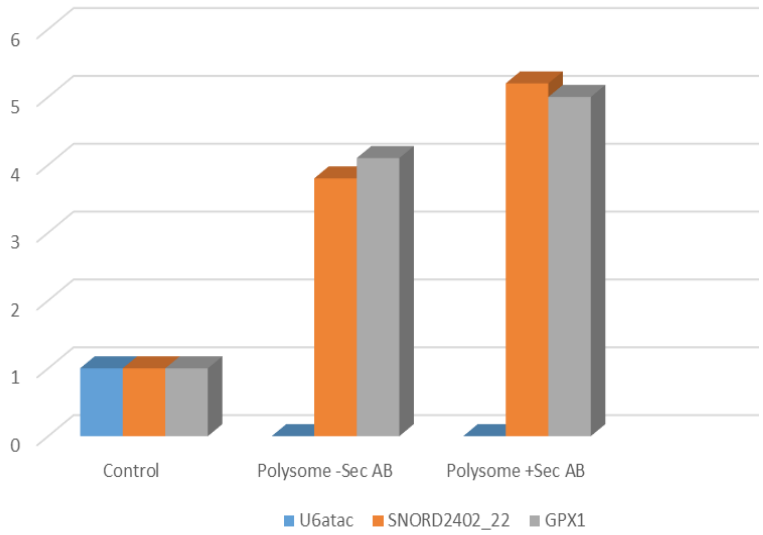


Figure 2: Relative abundance of RNA transctipts normalised to control - RNA input (total RNA). U6atac was used as negative control corresponding to non-translated snRNA and GPX1 selenoprotein was used as a positive control.

Based on these results – the transcript presence in Polysome fraction - we assume that SNORD2402_22 is actively translated as short peptide whose crucial role in e.g. CNS development can be further investigated from the new – protein-like– perspective.

Acknowledgements

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