



1. Selenoprotein Gene Expression

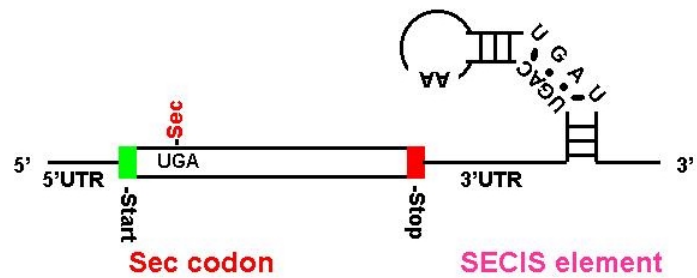


Fig A: Typical selenoprotein mRNA (top).

Diagram of typical selenoprotein mRNA with the UGA codon in the coding region (open box) and the SECIS (Selenocysteine Insertion Sequences) stemloop in the 3'UTR. Also shown are the consensus sequences in the SECIS, including the loop AA and a typical non-Watson-Crick base-pair motif (UGAC/UGAU) that causes a 90-degree bend in the stem.

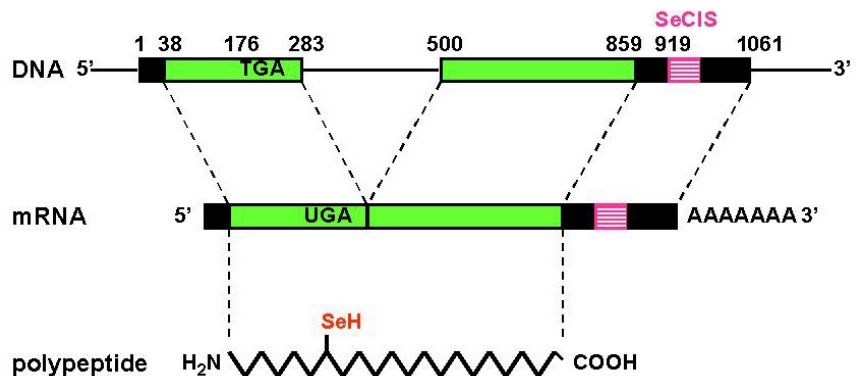
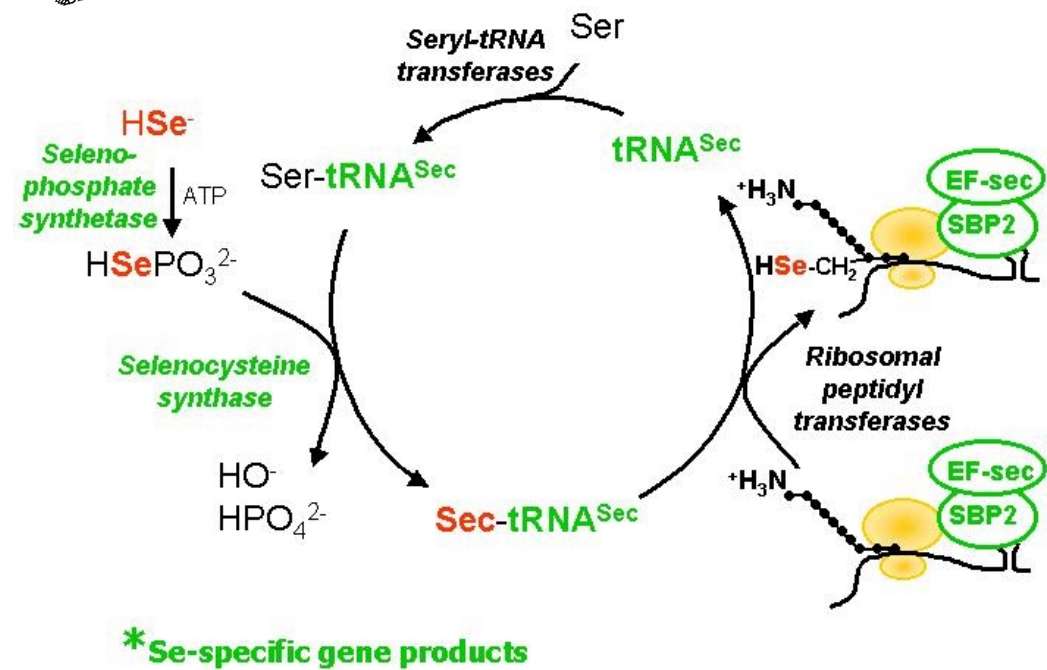


Fig B: GPX1 gene, mRNA and polypeptide.

Diagram of glutathione peroxidase-1 (GPX1) gene showing 2 exons (green) and the SECIS element (pink) in the 3'-UTR, the GPX1 mRNA, and the GPX1 subunit with selenocysteine (Sec) at amino acid residue 47 of 201 residues.



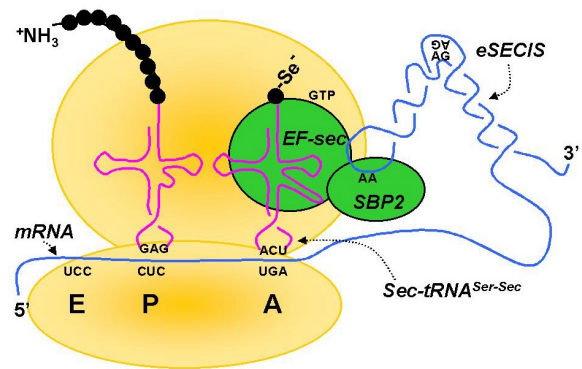
2. Co-translational Synthesis of Sec



*Se-specific gene products

Fig C: Selenocysteine synthesis and incorporation during protein synthesis.

Sec is synthesized co-translationally from serine (Ser) and selenide (HSe-) while esterified to tRNA by the indicated enzyme activities. The six unique gene products are each shown in green. Translation complex shown below.





3. Nonsense Mediated Decay

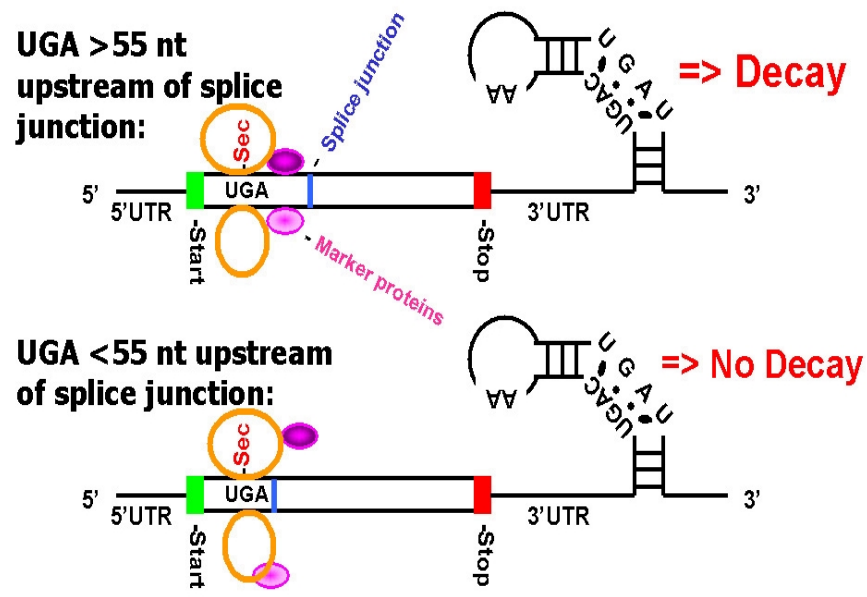


Fig D: Model of Nonsense-Mediated Decay (NMD) of mRNA

When a nonsense codon is >55 nt upstream from an mRNA splice junction, ribosomal pausing at the nonsense codon (or the UGA in Se deficiency) fails to strip marker proteins, left-over from RNA splicing, from the mRNA. These marker proteins are a target for endonucleases that degrade mRNA species with premature or nonsense codons. Selenoproteins like GPX4 have UGAs sufficiently close (<55 nt) to the splice junction such that these marker proteins are stripped from the mRNA by the ribosome.



4. Se Regulation "Switch"

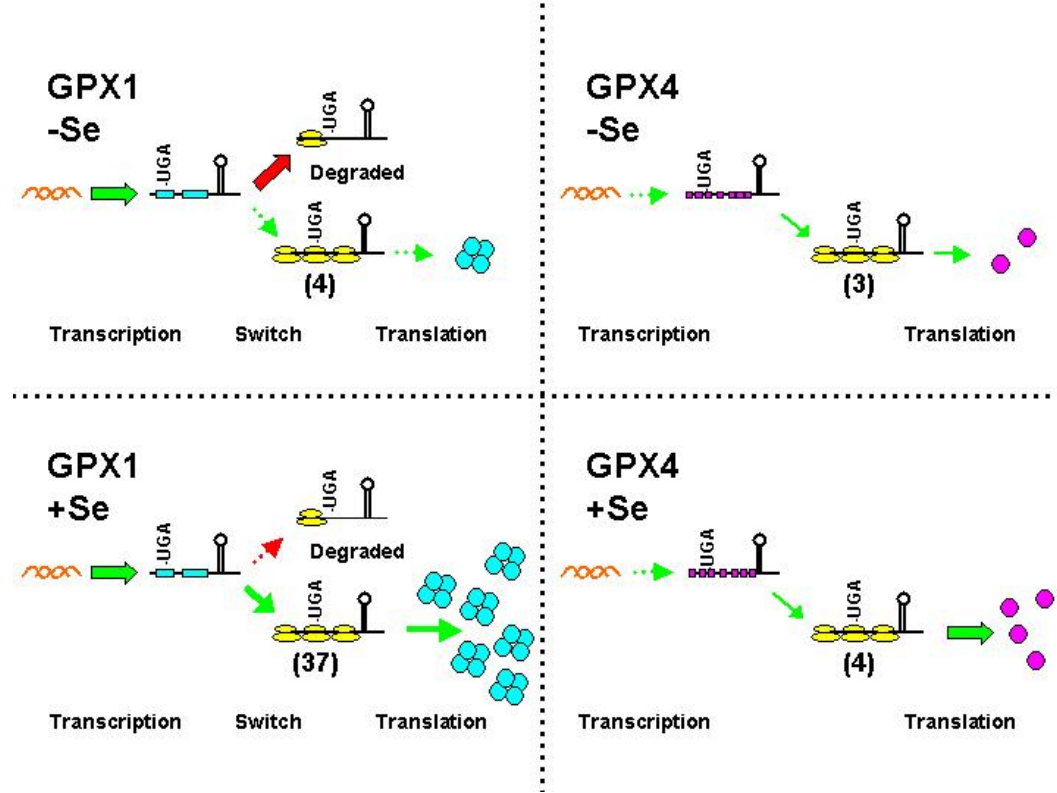


Fig E: Model for Se Regulation "Switch" in GPX1 Gene Expression

Se regulation of GPX1 mRNA via NMD serves as a "switch" that directs Se to critical selenoenzymes in deficiency, but that directs Se toward storage in GPX1 when Se exceeds those needs.