Preface

Selenium (Se) was discovered in 1817 by John Jacob Berzelius, a Swedish chemist who named it after the goddess of the moon *Selene*, since this element had many similarities with Tellurium ("tellus" meaning earth in Latin), found at the same period. For more than hundred years, selenium was viewed as a toxic element. It is only rather recently (in the 1950s) that selenium has been recognized as an essential nutrient for mammals. Selenium is implicated in many facets of human health and diseases, including cancer prevention, cardiovascular function, immunity, and brain function [1–3]. Selenium is incorporated in a small but vital group of proteins, the selenoproteins, in the form of a rare amino acid, the selenocysteine (Sec). Often located in the catalytic site of enzymes, selenocysteine is a key component of oxido-reduction reactions. Twenty-five selenoprotein genes have been discovered so far in human [4, 5], and a unified nomenclature has been recently proposed [6] (*see* Table 1). Selenoproteins are mostly involved in redox homeostasis and signaling, antioxidant defense, and selenoprotein biosynthesis, although about one third of the selenoproteome remains without precise function (for review *see* Ref. 7). Remarkably, in the 1990s selenium has amended the genetic code deciphered in the 1960s since selenocysteine is encoded by a UGA codon in selenoprotein mRNAs, which is otherwise read as a stop codon in other cellular mRNAs. In this regard, cells have evolved a unique and complex mechanism for UGA recoding as selenocysteine that is regulated at many levels, giving rise to a prioritized synthesis of selenoproteins. This noncanonical translational pathway for selenoprotein biosynthesis relies on two pivotal RNA molecules, namely the selenocysteine-tRNA$^{[Ser]Sec}$ (Fig. 1) and the SElenoCysteine Insertion Sequence (SECIS) within selenoprotein mRNA (Fig. 2), and their protein interacting partners (as reviewed in [2, 3, 8–12]). Due to the low levels of selenium in the body and complex biosynthesis, research on selenoproteins has been particularly challenging. Therefore, selenoproteins offer a fascinating playground in a broad range of fields in biology, including bioinformatics, genetics, RNA structure, translational control, biophysics, enzymology, animal models, and human health and diseases. This book aims at providing an update on state-of-the-art methodologies to study these various aspects of selenoprotein biology.

Table 1
List of the human selenoprotein genes identified to date, using the unified nomenclature

Gene name	Protein name	Synonyms
DIO1	Iodothyronine deiodinase 1	D1
DIO2	Iodothyronine deiodinase 2	D2
DIO3	Iodothyronine deiodinase 3	D3
GPX1	Glutathione peroxidase 1	Glutathione peroxidase 1
GPX2	Glutathione peroxidase 2	Glutathione peroxidase 2
GPX3	Glutathione peroxidase 3	Glutathione peroxidase 3
GPX4	Glutathione peroxidase 4	Glutathione peroxidase 4
GPX6	Glutathione peroxidase 6	Glutathione peroxidase 6
MSRB1	Methionine sulfoxide reductase B1	SelR, SelX, SEPX1
SELENOF	Selenoprotein F	Selenoprotein 15, Sel15, Sep15
SELENOH	Selenoprotein H	SelH
SELENOI	Selenoprotein I	SelI
SELENOK	Selenoprotein K	SelK
SELENOM	Selenoprotein M	SelM
SELENON	Selenoprotein N	SelN
SELENOO	Selenoprotein O	SelO
SELENOP	Selenoprotein N	SelP, SEPP1, SEPP, SeP
SELENOS	Selenoprotein S	SelS, SEPS1, VIMP
SELENOT	Selenoprotein T	SelT
SELENOV	Selenoprotein V	SelV
SELENOW	Selenoprotein W	SelW
SEPHS2	Selenophosphate 2	Selenide, water dikinase 2, SPS2
TXNRD1	Thioredoxin reductase 1	TR1, TRXR1
TXNRD2	Thioredoxin reductase 3	TR3, TRXR2, mitochondrial thioredoxin reductase
TXNRD3	Thioredoxin reductase 3	TR2, TRXR3, TGR

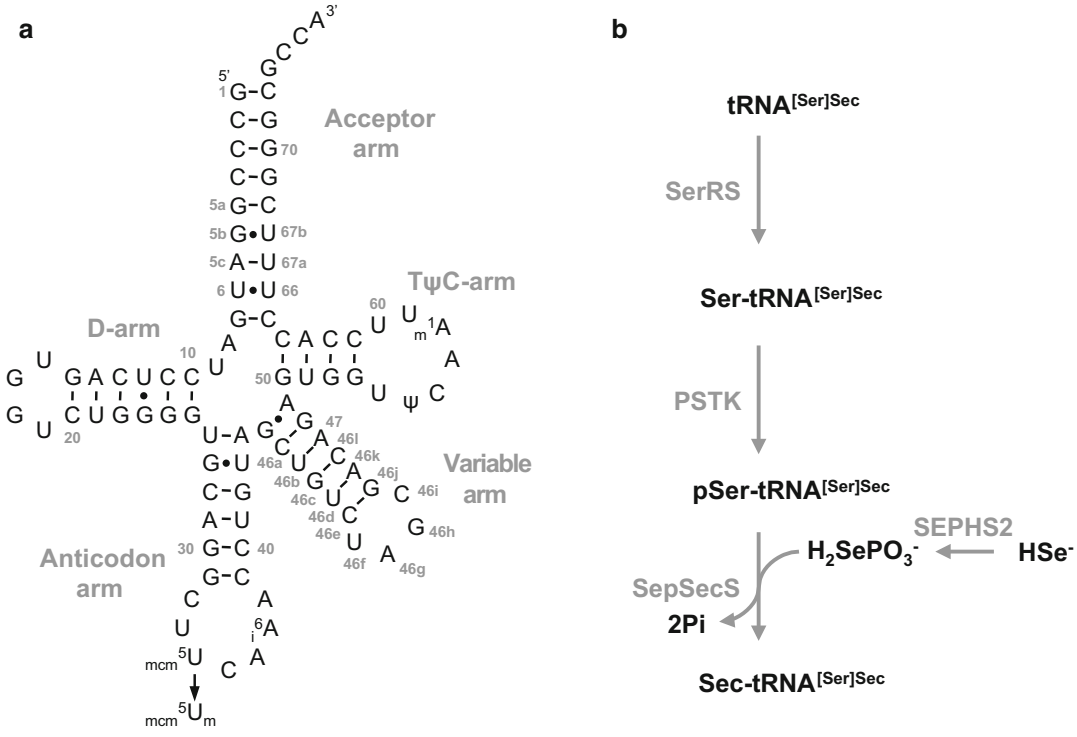

Fig. 1 Structure and aminoacylation of Sec-tRNA$^{[Ser]Sec}$. (**a**) Cloverleaf structure of the two isoforms of the tRNA$^{[Ser]Sec}$ differing from modification at position U34 between $_{mcm}{}^{5}U$ and $_{mcm}{}^{5}U_{m}$. (**b**) The aminoacylation of tRNA$^{[Ser]Sec}$ necessitates four enzymes instead of one for other tRNAs, including seryl-tRNA synthetase (SerRS), the phosphoseryl-tRNA kinase (PSKT), Sec synthase (SepSecS, also referred to as SLA/LP), and selenophosphate 2 synthetase (SEPHS2), which generates selenophosphate ($H_2SePO_3^-$) from selenide (HSe^-)

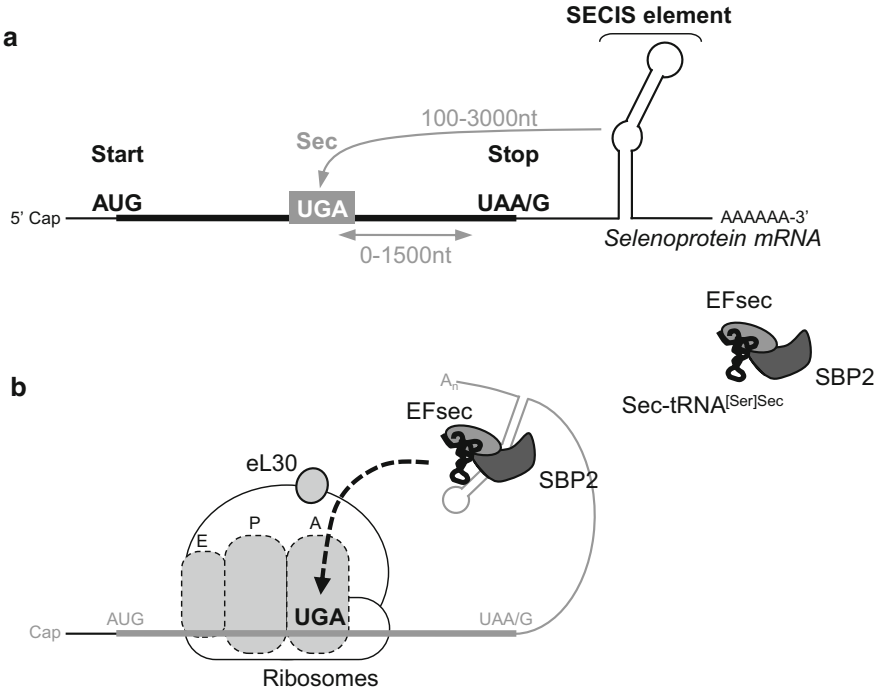

Fig. 2 Mechanism for selenoprotein biosynthesis in eukaryotes. (**a**) Schematic representation of a selenoprotein mRNA with its different *cis*-acting features: the SECIS element located in the 3′UTR and the UGA-selenocysteine codon present in frame in the Open Reading Frame (ORF). (**b**) Representation of the *trans*-acting factors needed for the efficient recoding of UGA as selenocysteine. Essential factors include the ribosomes, the Sec-tRNA$^{[Ser]Sec}$, a dedicated elongation factor EFsec, and a SECIS binding protein SBP2 (or SECIBP2). Accessory and/or regulatory proteins have also been described (for review *see* Refs. 8–12)

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