

Selenoprotein Gene Nomenclature*

Received for publication, August 30, 2016, Published, JBC Papers in Press, September 19, 2016, DOI 10.1074/jbc.M116.756155

Vadim N. Gladyshev,^{a,b1} Elias S. Arnér,^c Marla J. Berry,^d Regina Brigelius-Flohé,^e Elspeth A. Bruford,^f Raymond F. Burk,^g Bradley A. Carlson,^h Sergi Castellano,ⁱ Laurent Chavatte,^j Marcus Conrad,^k Paul R. Copeland,^l Alan M. Diamond,^m Donna M. Driscoll,ⁿ Ana Ferreira,^{o,p} Leopold Flohé,^{q,r} Fiona R. Green,^s Roderic Guigó,^{t,u} Diane E. Handy,^v Dolph L. Hatfield,^h John Hesketh,^{w,x,y} Peter R. Hoffmann,^d Arne Holmgren,^c Robert J. Hondal,^z Michael T. Howard,^{aa} Kaixun Huang,^{bb} Hwa-Young Kim,^{cc} Ick Young Kim,^{dd} Josef Köhrle,^{ee} Alain Krol,^{ff} Gregory V. Kryukov,^{gg} Byeong Jae Lee,^{hh} Byung Cheon Lee,^{dd} Xin Gen Lei,ⁱⁱ Qiong Liu,^{jj} Alain Lescure,^{ff,kk} Alexei V. Lobanov,^a Joseph Loscalzo,^{ll} Matilde Maiorino,^f Marco Mariotti,^a K. Sandeep Prabhu,^{mm} Margaret P. Rayman,ⁿⁿ Sharon Rozovsky,^{oo} Gustavo Salinas,^{pp} Edward E. Schmidt,^{qq} Lutz Schomburg,^{ee} Ulrich Schweizer,^{rr} Miljan Simonović,^{ss} Roger A. Sunde,^{tt} Petra A. Tsuji,^{uu} Susan Tweedie,^f Fulvio Ursini,^r Philip D. Whanger,^{vv} and Yan Zhang^{jj}

From the ^aDepartment of Medicine, Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, the ^bBroad Institute of Harvard and MIT, Cambridge, Massachusetts 02142, the ^cDepartment of Medical Biochemistry and Biophysics (MBB), Division of Biochemistry, Karolinska Institutet, SE-171 77, Stockholm, Sweden, the ^dDepartment of Cell and Molecular Biology, John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, Hawaii 96813, the ^eGerman Institute of Human Nutrition Potsdam-Rehbruecke, 14558 Nuthetal, Germany, the ^fHUGO Gene Nomenclature Committee (HGNC), European Bioinformatics Institute-European Molecular Biology Laboratory (EMBL-EBI), Hinxton CB10 1SD, United Kingdom, the ^gDepartment of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, the ^hMolecular Biology of Selenium Section, Mouse Cancer Genetics Program, Center for Cancer Research, National Institutes of Health, Bethesda, Maryland 20892, the ⁱDepartment of Evolutionary Genetics, Max Planck Institute for Evolutionary Anthropology, 04103 Leipzig, Germany, the ^jCentre International de Recherche en Infectiologie, CIRI, INSERM U1111, and CNRS/ENS UMR5308, 69007 Lyon, France, the ^kHelmholtz Zentrum München, Institute of Developmental Genetics, 85764 Neuherberg, Germany, the ^lDepartment of Biochemistry and Molecular Biology, Rutgers-Robert Wood Johnson Medical School, Piscataway, New Jersey 08854, the ^mDepartment of Pathology, University of Illinois at Chicago, Chicago, Illinois 60607, the ⁿDepartment of Cellular and Molecular Medicine, Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, Ohio 44195, the ^oPathophysiology of Striated Muscles Laboratory, Unit of Functional and Adaptive Biology (BFA), University Paris Diderot, Sorbonne Paris Cité, BFA, UMR CNRS 8251, 75250 Paris, France, the ^pAP-HP, Centre de Référence Maladies Neuromusculaires Paris-Est, Groupe Hospitalier Pitié-Salpêtrière, 75013 Paris, France, the ^qUniversidad de la República, Facultad de Medicina, Departamento de Bioquímica, 11800 Montevideo, Uruguay, the ^rDepartment of Molecular Medicine, University of Padova, I-35121 Padova, Italy, the ^sDivision of Cardiovascular Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom, the ^tCentre for Genomic Regulation (CRG), 08003 Barcelona, Spain, the ^uUniversitat Pompeu Fabra (UPF), 08002 Barcelona, Spain, the ^vDepartment of Medicine, Cardiovascular Division, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115, the ^wInstitute for Cell and Molecular Biosciences, Newcastle University, Newcastle-upon-Tyne NE1 7RU, United Kingdom, the ^xHuman Nutrition Research Centre, Newcastle University, Newcastle-upon-Tyne NE1 7RU, United Kingdom, the ^yThe Medical School, Newcastle University, Newcastle-upon-Tyne NE2 4HH, United Kingdom, the ^zDepartment of Biochemistry, University of Vermont, Burlington, Vermont 05405, the ^{aa}Department of Human Genetics, University of Utah, Salt Lake City, Utah 84112, the ^{bb}Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan 430074, Peoples Republic of China, the ^{cc}Department of Biochemistry and Molecular Biology, Yeungnam University College of Medicine, Daegu 42415, South Korea, the ^{dd}College of Life Sciences and Biotechnology, Korea University, Seoul 02841, South Korea, the ^{ee}Institute for Experimental Endocrinology, Charité-Universitätsmedizin Berlin, D-13353 Berlin, Germany, the ^{ff}Architecture et Réactivité de l'ARN, Université de Strasbourg, Centre National de la Recherche Scientifique, Institut de Biologie Moléculaire et Cellulaire, 67084 Strasbourg, France, the ^{gg}KSQ Therapeutics, Cambridge, Massachusetts 02139, the ^{hh}School of Biological Sciences, Seoul National University, Seoul 151-742, South Korea, the ⁱⁱDepartment of Animal Science, Cornell University, Ithaca, New York 14853, the ^{jj}Shenzhen Key Laboratory of Marine Biotechnology and Ecology, College of Life Science, Shenzhen University, Shenzhen, 518060, Guangdong Province, Peoples Republic of China, the ^{kk}Centre National de la Recherche Scientifique, 75794 Paris, France, the ^{ll}Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, the ^{mm}Department of Veterinary and Biomedical Sciences, The Pennsylvania State University, University Park, Pennsylvania 16802, the ⁿⁿDepartment of Nutritional Sciences, Faculty of Health and Medical Sciences, University of Surrey, Guildford GU2 7XH, United Kingdom, the ^{oo}Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716, the ^{pp}Cátedra de Inmunología, Facultad de Química, Instituto de Higiene, CP11600 Montevideo, Uruguay, the ^{qq}Department of Microbiology and Immunology, Montana State University, Bozeman, Montana 59717, the ^{rr}Rheinische Friedrich-Wilhelms Universität Bonn, Institut für Biochemie und Molekularbiologie, 53115 Bonn, Germany, the ^{ss}Department of Biochemistry and Molecular Genetics, University of Illinois at Chicago, Chicago, Illinois 60607, the ^{tt}Department of Nutritional Sciences, University of Wisconsin, Madison, Wisconsin 53706, the ^{uu}Department of Biological Sciences, Towson University, Towson, Maryland 21252, and the ^{vv}Department of Environmental and Molecular Toxicology, College of Agricultural Sciences, Oregon State University, Corvallis, Oregon 97331

Edited by Norma Allewell

The human genome contains 25 genes coding for selenocysteine-containing proteins (selenoproteins). These proteins are involved in a variety of functions, most notably redox homeostasis. Selenoprotein enzymes with known functions are designated according to these functions: TXNRD1, TXNRD2, and TXNRD3 (thioredoxin reductases), GPX1, GPX2, GPX3, GPX4, and GPX6 (glutathione peroxidases), DIO1, DIO2, and DIO3 (iodothyronine deiodinases), MSRB1 (methionine sulfoxide reductase B1), and SEPHS2 (selenophosphate synthetase 2). Selenoproteins without known functions have traditionally been denoted by SEL or SEP symbols. However, these symbols are sometimes ambiguous and conflict with the approved nomenclature for several other genes. Therefore, there is a need to implement a rational and coherent nomenclature system for selenoprotein-encoding genes. Our solution is to use the root symbol SELENO followed by a letter. This nomenclature applies to SELENOF (selenoprotein F, the 15-kDa selenoprotein, SEP15), SELENOH (selenoprotein H, SELH, C11orf31), SELENOI (selenoprotein I, SELI, EPT1), SELENOK (selenoprotein K, SELK), SELENOM (selenoprotein M, SELM), SELENON (selenoprotein N, SEPNI, SELN), SELENOO (selenoprotein O, SELO), SELENOP (selenoprotein P, SeP, SEPP1, SELP), SELENOS (selenoprotein S, SELS, SEPS1, VIMP), SELENOT (selenoprotein T, SELT), SELENOV (selenoprotein V, SELV), and SELENOW (selenoprotein W, SELW, SEPW1). This system, approved by the HUGO Gene Nomenclature Committee, also resolves conflicting, missing, and ambiguous designations for selenoprotein genes and is applicable to selenoproteins across vertebrates.

Selenium is an essential trace element in humans, which is present in proteins in the form of the 21st proteinogenic amino acid, selenocysteine (Sec).² Sec is co-translationally inserted into a polypeptide chain in response to in-frame UGA codons directed by the Sec insertion sequence element, a stem-loop structure in the 3'-UTRs of selenoprotein mRNAs. The human genome contains 25 selenoprotein genes (1), and selenoproteins are essential for embryo development and human health (2, 3). Among the selenoproteins, 13 have known functions; at least 12 of them serve as oxidoreductases, wherein Sec is the catalytic redox-active residue. The redox theme is also common for selenoproteins in other organisms (4).

The remaining 12 selenoproteins either have no known function, or their functions are only partially established. One of the selenoproteins, selenoprotein P (5), requires special mention as

it has more than one Sec. It is a major plasma selenoprotein that delivers selenium primarily from the liver to other organs (6, 7), and is involved in selenium transport and metabolism within organs. However, this protein also has an N-terminal Sec-containing thioredoxin domain similar to that found in most selenoproteins with known functions, which points to a potential redox function. Several other selenoproteins, including selenoproteins H, M, T, V, W, and Sep15, also possess thioredoxin-like domains, suggesting redox-related functions (8).

Selenoproteins are not all homologous, but are characterized by their incorporation of Sec. Historically they have been given designations by the groups that discovered them, e.g. because of its presence in plasma the respective selenoprotein was named selenoprotein P (9, 10), or because of its size another protein was called the 15-kDa selenoprotein or Sep15 (11). However, some selenoproteins were identified independently by two or more groups, which created confusion and discrepancies in the field. For example, the same protein was named selenoprotein R by one group (12), but discovered concurrently and designated by another group as selenoprotein X (13). This protein was then functionally characterized (14) and renamed MsrB1 (for methionine-*R*-sulfoxide reductase 1) (15), but all three designations persist in the literature and/or databases. Another problematic example is the nomenclature used for thioredoxin reductases. The names for the first thioredoxin reductase, which had been known decades before its selenoprotein nature was discovered (16), are generally internally consistent, although they differ in the abbreviations used, e.g. TR1 and TrxR1 (17). The second and third thioredoxin reductases discovered, however, were named inconsistently by the authors, wherein the mitochondrial thioredoxin reductase was designated as TrxR2 (18) and TR3 (19), and the testis-specific thioredoxin-glutathione reductase has been alternatively labeled as TR2 (19), TrxR3, or TGR.

Designations are also confusing for several other selenoproteins. For example, selenoprotein S was named Sels (1), but a later paper introduced the designation VIMP (20). Similarly, selenoprotein H was named SelH (1), but also C11orf31, and selenoprotein I was named SelI (1), but also called EPT1 (21). To avoid confusion, and at the instigation of the HUGO Gene Nomenclature Committee (HGNC), we describe a new standardized designation system for human (and other vertebrate) selenoproteins.

Results and Discussion

Resolving the Nomenclature of Selenoprotein Genes—Human gene designations are approved by the HUGO Gene Nomenclature Committee (HGNC), and genes in other mammals follow the same designations. Selenoproteins have traditionally been published using SEL or SEP symbols followed by a letter or a number. Unfortunately, for naming the genes encoding these proteins, the SEL root was not an option as it was already approved for the selectin gene family; for example, *SELP* is the approved gene symbol for selectin P (P-selectin) and not selenoprotein P. Some selenoprotein genes had been approved using the root SEP (i.e. *SEPNI*, *SEPP1*, and *SEPW1*) but this could not be utilized for all selenoproteins as selenoprotein T gene would then be *SEPT* or *SEPT1*, and *SEPT#* is already used

* This work was supported, in whole or in part, by National Institutes of Health Grant GM061603. The authors declare that they have no conflicts of interest with the contents of this article. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

¹ To whom correspondence should be addressed. E-mail: vgladyshv@rics.bwh.harvard.edu.

² The abbreviations used are: Sec, selenocysteine; TXNRD, thioredoxin reductases; GPX, glutathione peroxidase; DIO, iodothyronine deiodinase; SEPHS2, selenophosphate synthetase 2; SELENOF, 15-kDa selenoprotein; SELENOH, selenoprotein H; SELENOI, selenoprotein I; SELENOK, selenoprotein K; SELENOM, selenoprotein M; SELENON, selenoprotein N; SELENOO, selenoprotein O; SELENOP, selenoprotein P; SELENOS, selenoprotein S; SELENOT, selenoprotein T; SELENOV, selenoprotein V; SELENOW, selenoprotein W; HGNC, HUGO Gene Nomenclature Committee.

Selenoprotein Gene Nomenclature

for the septin genes. HGNC does not use the same root for unrelated groups of genes (*e.g.* SEL for selectins and selenoproteins) and does not endorse the use of multiple root symbols for genes sharing a common name (*e.g.* SEP and SEL for selenoprotein). With a view to solving these issues, HGNC approached selenoprotein researchers to propose a new unifying root symbol for all selenoprotein genes.

Proposal for a New Nomenclature—We propose that all selenoproteins (except those that have been functionally characterized, *e.g.* with enzymatic activity) use the root symbol SELENO followed by a letter. This gene nomenclature is designed to highlight selenium, the key functional site in these proteins, and to provide a new and unambiguous root for these genes. The new nomenclature applies to 12 human selenoprotein genes as detailed in Table 1. Selenoproteins with known functions will continue to use the same designations (Table 2). Once functions are established for other selenoproteins, they may be renamed, as required. The proposed designations apply to the selenoprotein genes; although the same designations may be used for many of the encoded proteins, traditional names of selenoproteins, *e.g.* selenoprotein P, may also be used.

Selenoprotein Gene Designation in Other Species—The new HGNC nomenclature will automatically be used to designate orthologous selenoprotein genes in other vertebrates and extended to accommodate selenoprotein genes with no orthologs in human (22) (Table 3). Where vertebrate gene

TABLE 1

Selenoprotein genes using the new SELENO root

New HGNC selenoprotein gene nomenclature is indicated in the column “symbol.” Previous HGNC symbols (shown with *) will become synonyms, along with other previously used designations.

Symbol	Name	Synonyms	Refs.
SELENOF	Selenoprotein F	Selenoprotein 15, SEP15	11
SELENOH	Selenoprotein H	SELH, C11orf31*	1
SELENOI	Selenoprotein I	SELI, EPT1*	1, 21
SELENOK	Selenoprotein K	SELK	1
SELENO M	Selenoprotein M	SELM, SEPM	25
SELENON	Selenoprotein N	SEPN1*, SELN	13
SELENOO	Selenoprotein O	SELO	1
SELENO P	Selenoprotein P	SEPP1*, SeP, SELP, SEPP	26
SELENO S	Selenoprotein S	SELS, SEPS1, VIMP*	1
SELENOT	Selenoprotein T	SELT	12
SELENOV	Selenoprotein V	SELV	1
SELENOW	Selenoprotein W	SELW, SEPW1*	27

TABLE 2

Selenoprotein genes named based on encoded enzymatic activity

Note that the nomenclature of these genes will not be changing to use the SELENO root.

Symbol	Name	Synonyms	Refs.
TXNRD1	Thioredoxin reductase 1	TR1, TRXR1	16, 28, 29
TXNRD2	Thioredoxin reductase 2	TRXR2, TR3, mitochondrial thioredoxin reductase	18, 19
TXNRD3	Thioredoxin-glutathione reductase	TGR, TRXR3, TR2	19
GPX1	Glutathione peroxidase 1	Cytosolic glutathione peroxidase, GSHPX1	30–35
GPX2	Glutathione peroxidase 2	GSHPX-GI	36
GPX3	Glutathione peroxidase 3	Plasma glutathione peroxidase	37
GPX4	Glutathione peroxidase 4	Phospholipid hydroperoxide glutathione peroxidase, PHGPX	38, 39
GPX6	Glutathione peroxidase 6		
DIO1	Iodothyronine deiodinase 1	D1	40, 41
DIO2	Iodothyronine deiodinase 2	D2	42
DIO3	Iodothyronine deiodinase 3	D3	43
MSRB1	Methionine sulfoxide reductase B1	SELR, SELX, SEPX1	12–14
SEPHS2	Selenophosphate synthetase 2	SPS2	44

duplications have occurred, the additional paralogs will be named in line with the human genes, but with suffixes on the symbols, *e.g.* zebrafish selenot1a, selenot1b, and selenot2. Selenoproteins are widespread in all three domains of life. Despite the fact that land plants, yeast, and some other species have lost selenoprotein biosynthesis pathways, a unifying nomenclature beyond vertebrates might be desirable. We suggest using the human nomenclature described in this paper for orthologs of vertebrate selenoprotein genes. This nomenclature may also be extended to accommodate additional selenoprotein genes as they are discovered. Although we use human designations in this paper, we note that most vertebrates use all uppercase letters for genes and proteins (italics for genes), rodents use title case for genes (uppercase for proteins), *Xenopus* and zebrafish use lowercase for genes and title case for proteins, and Anolis use lowercase for genes and uppercase for proteins.

Designations of Proteins That Do Not Contain Selenocysteine—There exists another class of selenium-containing proteins, those which contain a bound atom of selenium but do not contain a UGA-encoded Sec, for which there is also ambiguous nomenclature. For example, selenium-binding protein 1 (SBP1), also referred to as SELENBP1 or hSP56, is one such protein (23). The naming of such proteins will not be included in the new nomenclature as they lack Sec. Similarly, the machinery for Sec biosynthesis and insertion will not be renamed.

Implementation—The new selenoprotein gene nomenclature has been approved by the HGNC, can be found on their website (<http://www.genenames.org/cgi-bin/genefamilies/set/890>), and will be found in all major genomic resources in due course. We recommend that future publications primarily use

TABLE 3

Vertebrate selenoprotein genes absent in human and mouse

New selenoprotein gene nomenclature is indicated in the column “symbol.”

Symbol	Name	Synonyms	Refs.
SELENOJ	Selenoprotein J	SELJ	45
SELENOU	Selenoprotein U	SELU	46
SELENO L	Selenoprotein L	SELL	47
SELENOE	Selenoprotein E, fish selenoprotein 15	FEP15	48
SELENO P2	Selenoprotein P2	SEPP2, SELPb	49, 24

the new SELENO designations, but supplement them (as secondary designations/synonyms) with the names previously used by the community. Once the new nomenclature is consistently used, the old designations will no longer be needed. We hope that other researchers in the field will join us in implementing this new nomenclature.

Author Contributions—The article was drafted by V. N. G. in consultation with other authors. All authors contributed to revisions and discussion.

References

- Kryukov, G. V., Castellano, S., Novoselov, S. V., Lobanov, A. V., Zehtab, O., Guigó, R., and Gladyshev, V. N. (2003) Characterization of mammalian selenoproteomes. *Science* **300**, 1439–1443
- Bösl, M. R., Takaku, K., Oshima, M., Nishimura, S., and Taketo, M. M. (1997) Early embryonic lethality caused by targeted disruption of the mouse selenocysteine tRNA gene (Trsp). *Proc. Natl. Acad. Sci. U.S.A.* **94**, 5531–5534
- Schweizer, U., and Fradejas-Villar, N. (July 29, 2016) Why 21? the significance of selenoproteins for human health revealed by inborn errors of metabolism. *FASEB J.*, fj201600414
- Fomenko, D. E., Xing, W., Adair, B. M., Thomas, D. J., and Gladyshev, V. N. (2007) High-throughput identification of catalytic redox-active cysteine residues. *Science* **315**, 387–389
- Burk, R. F., and Hill, K. E. (2015) Regulation of selenium metabolism and transport. *Annu. Rev. Nutr.* **35**, 109–134
- Carlson, B. A., Novoselov, S. V., Kumaraswamy, E., Lee, B. J., Anver, M. R., Gladyshev, V. N., and Hatfield, D. L. (2004) Specific excision of the selenocysteine tRNA[Ser]Sec (Trsp) gene in mouse liver demonstrates an essential role of selenoproteins in liver function. *J. Biol. Chem.* **279**, 8011–8017
- Schomburg, L., Schweizer, U., Holtmann, B., Flohé, L., Sendtner, M., and Köhrle, J. (2003) Gene disruption discloses role of selenoprotein P in selenium delivery to target tissues. *Biochem. J.* **370**, 397–402
- Dikiy, A., Novoselov, S. V., Fomenko, D. E., Sengupta, A., Carlson, B. A., Cerny, R. L., Ginalski, K., Grishin, N. V., Hatfield, D. L., and Gladyshev, V. N. (2007) SelT, SelW, SelH, and Rdx12: genomics and molecular insights into the functions of selenoproteins of a novel thioredoxin-like family. *Biochemistry* **46**, 6871–6882
- Motsenbocker, M. A., and Tappel, A. L. (1982) A selenocysteine-containing selenium-transport protein in rat plasma. *Biochim. Biophys. Acta* **719**, 147–153
- Burk, R. F., and Gregory, P. E. (1982) Some characteristics of 75Se-P, a selenoprotein found in rat liver and plasma, and comparisons of it with selenogluthathione peroxidase. *Arch. Biochem. Biophys.* **213**, 73–80
- Gladyshev, V. N., Jeang, K. T., Wootton, J. C., and Hatfield, D. L. (1998) A new human selenium-containing protein. Purification, characterization, and cDNA sequence. *J. Biol. Chem.* **273**, 8910–8915
- Kryukov, G. V., Kryukov, V. M., and Gladyshev, V. N. (1999) New mammalian selenocysteine-containing proteins identified with an algorithm that searches for selenocysteine insertion sequence elements. *J. Biol. Chem.* **274**, 33888–33897
- Lescure, A., Gautheret, D., Carbon, P., and Krol, A. (1999) Novel selenoproteins identified *in silico* and *in vivo* by using a conserved RNA structural motif. *J. Biol. Chem.* **274**, 38147–38154
- Kryukov, G. V., Kumar, R. A., Koc, A., Sun, Z., and Gladyshev, V. N. (2002) Selenoprotein R is a zinc-containing stereo-specific methionine sulfoxide reductase. *Proc. Natl. Acad. Sci. U.S.A.* **99**, 4245–4250
- Kim, H. Y., and Gladyshev, V. N. (2004) Methionine sulfoxide reduction in mammals: characterization of methionine-R-sulfoxide reductases. *Mol. Biol. Cell* **15**, 1055–1064
- Holmgren, A. (1977) Bovine thioredoxin system: purification of thioredoxin reductase from calf liver and thymus and studies of its function in disulfide reduction. *J. Biol. Chem.* **252**, 4600–4606
- Arnér, E. S., and Holmgren, A. (2000) Physiological functions of thioredoxin and thioredoxin reductase. *Eur. J. Biochem.* **267**, 6102–6109
- Lee, S. R., Kim, J. R., Kwon, K. S., Yoon, H. W., Levine, R. L., Ginsburg, A., and Rhee, S. G. (1999) Molecular cloning and characterization of a mitochondrial selenocysteine-containing thioredoxin reductase from rat liver. *J. Biol. Chem.* **274**, 4722–4734
- Sun, Q. A., Wu, Y., Zappacosta, F., Jeang, K. T., Lee, B. J., Hatfield, D. L., and Gladyshev, V. N. (1999) Redox regulation of cell signaling by selenocysteine in mammalian thioredoxin reductases. *J. Biol. Chem.* **274**, 24522–24530
- Ye, Y., Shibata, Y., Yun, C., Ron, D., and Rapoport, T. A. (2004) A membrane protein complex mediates retro-translocation from the ER lumen into the cytosol. *Nature* **429**, 841–847
- Horibata, Y., and Hirabayashi, Y. (2007) Identification and characterization of human ethanolaminephosphotransferase1. *J. Lipid Res.* **48**, 503–508
- Mariotti, M., Ridge, P. G., Zhang, Y., Lobanov, A. V., Pringle, T. H., Guigo, R., Hatfield, D. L., and Gladyshev, V. N. (2012) Composition and evolution of the vertebrate and mammalian selenoproteomes. *PLoS ONE* **7**, e33066
- Ansong, E., Yang, W., and Diamond, A. M. (2014) Molecular cross-talk between members of distinct families of selenium containing proteins. *Mol. Nutr. Food Res.* **58**, 117–123
- Sunde, R. A., Sunde, G. R., Sunde, C. M., Sunde, M. L., and Evenson, J. K. (2015) Cloning, sequencing, and expression of selenoprotein transcripts in the turkey (*Meleagris gallopavo*). *PLoS ONE* **10**, e0129801
- Korotkov, K. V., Novoselov, S. V., Hatfield, D. L., and Gladyshev, V. N. (2002) Mammalian selenoprotein in which selenocysteine (Sec) incorporation is supported by a new form of Sec insertion sequence element. *Mol. Cell. Biol.* **22**, 1402–1411
- Hill, K. E., Lloyd, R. S., and Burk, R. F. (1993) Conserved nucleotide sequences in the open reading frame and 3' untranslated region of selenoprotein P mRNA. *Proc. Natl. Acad. Sci. U.S.A.* **90**, 537–541
- Vendeland, S. C., Beilstein, M. A., Yeh, J. Y., Ream, W., and Whanger, P. D. (1995) Rat skeletal muscle selenoprotein W: cDNA clone and mRNA modulation by dietary selenium. *Proc. Natl. Acad. Sci. U.S.A.* **92**, 8749–8753
- Gasdaska, P. Y., Gasdaska, J. R., Cochran, S., and Powis, G. (1995) Cloning and sequencing of a human thioredoxin reductase. *FEBS Lett.* **373**, 5–9
- Gladyshev, V. N., Jeang, K. T., and Stadtman, T. C. (1996) Selenocysteine, identified as the penultimate C-terminal residue in human T-cell thioredoxin reductase, corresponds to TGA in the human placental gene. *Proc. Natl. Acad. Sci. U.S.A.* **93**, 6146–6151
- Rotruck, J. T., Pope, A. L., Ganther, H. E., Swanson, A. B., Hafeman, D. G., and Hoekstra, W. G. (1973) Selenium: biochemical role as a component of glutathione peroxidase. *Science* **179**, 588–590
- Flohe, L., Günzler, W. A., and Schock, H. H. (1973) Glutathione peroxidase: a selenoenzyme. *FEBS Lett.* **32**, 132–134
- Forstrom, J. W., Zakowski, J. J., and Tappel, A. L. (1978) Identification of the catalytic site of rat liver glutathione peroxidase as selenocysteine. *Biochemistry* **17**, 2639–2644
- Chambers, L., Frampton, J., Goldfarb, P., Affara, N., McBain, W., and Harrison, P. R. (1986) The structure of the mouse glutathione peroxidase gene: the selenocysteine in the active site is encoded by the “termination” codon, TGA. *EMBO J.* **5**, 1221–1227
- Mills, G. C. (1957) Hemoglobin catabolism: I. glutathione peroxidase, an erythrocyte enzyme which protects hemoglobin from oxidative breakdown. *J. Biol. Chem.* **229**, 189–197
- Günzler, W. A., Steffens, G. J., Grossmann, A., Kim, S. M., Otting, F., Wendel, A., and Flohé, L. (1984) The amino acid sequence of bovine glutathione peroxidase. *Hoppe-Seyler's Z. Physiol. Chem.* **365**, 195–212
- Chu, F. F., Doroshov, J. H., and Esworthy, R. S. (1993) Expression, characterization, and tissue distribution of a new cellular selenium-dependent glutathione peroxidase, GSHPx-GI. *J. Biol. Chem.* **268**, 2571–2576
- Takahashi, K., Akasaka, M., Yamamoto, Y., Kobayashi, C., Mizoguchi, J., and Koyama, J. (1990) Primary structure of human plasma glutathione peroxidase deduced from cDNA sequences. *J. Biochem.* **108**, 145–148

Selenoprotein Gene Nomenclature

38. Ursini, F., Maiorino, M., and Gregolin, C. (1985) The selenoenzyme phospholipid hydroperoxide glutathione peroxidase. *Biochim. Biophys. Acta* **839**, 62–70
39. Brigelius-Flohé, R., Aumann, K. D., Blöcker, H., Gross, G., Kiess, M., Klöppel, K. D., Maiorino, M., Roveri, A., Schuckelt, R., Ursini, F., Wingender, E., and Flohé, L. (1994) Phospholipid hydroperoxide glutathione peroxidase: genomic DNA, cDNA and deduced amino acid sequence. *J. Biol. Chem.* **269**, 7342–7348
40. Berry, M. J., Banu, L., and Larsen, P. R. (1991) Type I iodothyronine deiodinase is a selenocysteine-containing enzyme. *Nature* **349**, 438–440
41. Behne, D., Kyriakopoulos, A., Meinhold, H., and Köhrle, J. (1990) Identification of type I iodothyronine 5'-deiodinase as a selenoenzyme. *Biochem. Biophys. Res. Commun.* **173**, 1143–1149
42. Davey, J. C., Becker, K. B., Schneider, M. J., St Germain, D. L., and Galton, V. A. (1995) Cloning of a cDNA for the type II iodothyronine deiodinase. *J. Biol. Chem.* **270**, 26786–26789
43. St Germain, D. L., Schwartzman, R. A., Croteau, W., Kanamori, A., Wang, Z., Brown, D. D., and Galton, V. A. (1994) A thyroid hormone-regulated gene in *Xenopus laevis* encodes a type III iodothyronine 5-deiodinase. *Proc. Natl. Acad. Sci. U.S.A.* **91**, 7767–7771
44. Guimarães, M. J., Peterson, D., Vicari, A., Cocks, B. G., Copeland, N. G., Gilbert, D. J., Jenkins, N. A., Ferrick, D. A., Kastelein, R. A., Bazan, J. F., and Zlotnik, A. (1996) Identification of a novel selD homolog from eukaryotes, bacteria, and archaea: is there an autoregulatory mechanism in selenocysteine metabolism? *Proc. Natl. Acad. Sci. U.S.A.* **93**, 15086–15091
45. Castellano, S., Lobanov, A. V., Chapple, C., Novoselov, S. V., Albrecht, M., Hua, D., Lescure, A., Lengauer, T., Krol, A., Gladyshev, V. N., and Guigó, R. (2005) Diversity and functional plasticity of eukaryotic selenoproteins: identification and characterization of the SelJ family. *Proc. Natl. Acad. Sci. U.S.A.* **102**, 16188–16193
46. Castellano, S., Novoselov, S. V., Kryukov, G. V., Lescure, A., Blanco, E., Krol, A., Gladyshev, V. N., and Guigó, R. (2004) Reconsidering the evolution of eukaryotic selenoproteins: a novel nonmammalian family with scattered phylogenetic distribution. *EMBO Rep.* **5**, 71–77
47. Shchedrina, V. A., Novoselov, S. V., Malinouski, M. Y., and Gladyshev, V. N. (2007) Identification and characterization of a selenoprotein family containing a diselenide bond in a redox motif. *Proc. Natl. Acad. Sci. U.S.A.* **104**, 13919–13924
48. Novoselov, S. V., Hua, D., Lobanov, A. V., and Gladyshev, V. N. (2006) Identification and characterization of Fep15, a new selenocysteine-containing member of the Sep15 protein family. *Biochem. J.* **394**, 575–579
49. Kryukov, G. V., and Gladyshev, V. N. (2000) Selenium metabolism in zebrafish: multiplicity of selenoprotein genes and expression of a protein containing 17 selenocysteine residues. *Genes Cells* **5**, 1049–1060

Selenoprotein Gene Nomenclature

Vadim N. Gladyshev, Elias S. Arnér, Marla J. Berry, Regina Brigelius-Flohé, Elspeth A. Bruford, Raymond F. Burk, Bradley A. Carlson, Sergi Castellano, Laurent Chavatte, Marcus Conrad, Paul R. Copeland, Alan M. Diamond, Donna M. Driscoll, Ana Ferreiro, Leopold Flohé, Fiona R. Green, Roderic Guigó, Diane E. Handy, Dolph L. Hatfield, John Hesketh, Peter R. Hoffmann, Arne Holmgren, Robert J. Hondal, Michael T. Howard, Kaixun Huang, Hwa-Young Kim, Ick Young Kim, Josef Köhrle, Alain Krol, Gregory V. Kryukov, Byeong Jae Lee, Byung Cheon Lee, Xin Gen Lei, Qiong Liu, Alain Lescure, Alexei V. Lobanov, Joseph Loscalzo, Matilde Maiorino, Marco Mariotti, K. Sandeep Prabhu, Margaret P. Rayman, Sharon Rozovsky, Gustavo Salinas, Edward E. Schmidt, Lutz Schomburg, Ulrich Schweizer, Miljan Simonovic, Roger A. Sunde, Petra A. Tsuji, Susan Tweedie, Fulvio Ursini, Philip D. Whanger and Yan Zhang

J. Biol. Chem. 2016, 291:24036-24040.

doi: 10.1074/jbc.M116.756155 originally published online September 19, 2016

Access the most updated version of this article at doi: [10.1074/jbc.M116.756155](https://doi.org/10.1074/jbc.M116.756155)

Alerts:

- [When this article is cited](#)
- [When a correction for this article is posted](#)

[Click here](#) to choose from all of JBC's e-mail alerts

This article cites 48 references, 30 of which can be accessed free at <http://www.jbc.org/content/291/46/24036.full.html#ref-list-1>