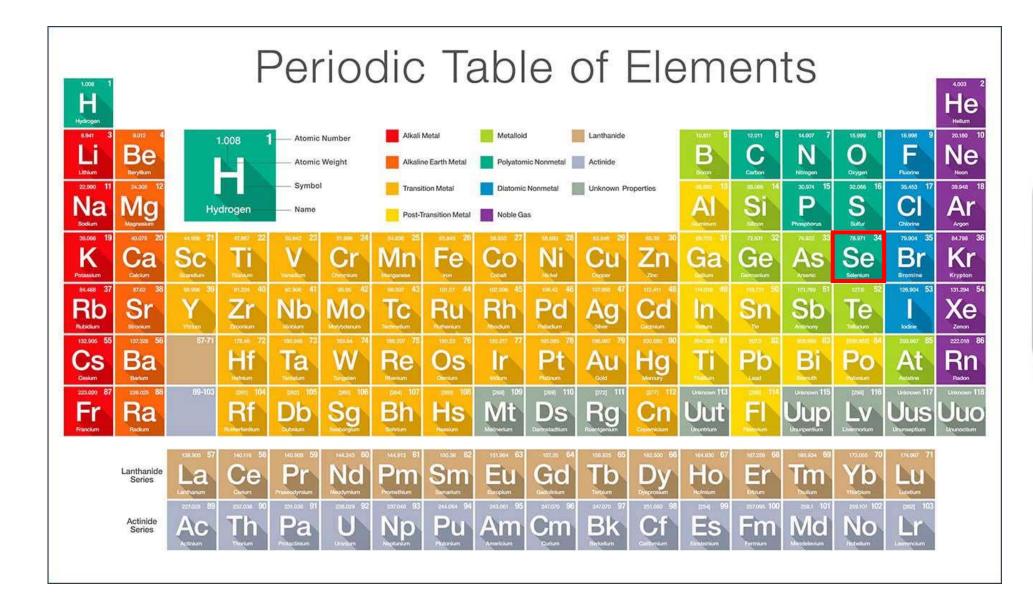
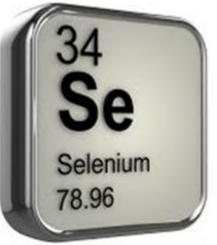




Speaker: M. Zaghari Available at www.minatoyoor.com





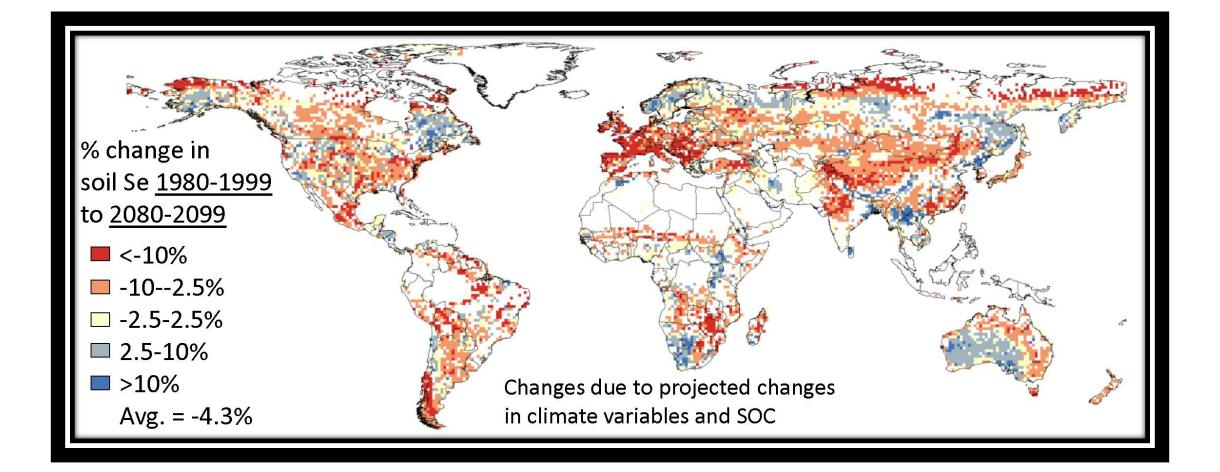


Jöns Jacob Berzelius (1779–1848)			
Born	20 August 1779		
	Väversunda, Östergötland,		
	Sweden		
Died	7 August 1848 (aged 68)		
	Stockholm, Sweden		
Nationality	Sweden		
Alma mater	Uppsala University		
Known for	r Atomic weights		
	Chemical notation		
	catalysis		
	Silicon		
	Selenium Thorium		
	Cerium		
Awards	Copley medal (1836)		
	Scientific career		
Fields	Chemistry		
Institutions	Karolinska Institute		
Doctoral	Johann Afzelius		
advisor			
Doctoral	James Finlay Weir Johnston		
students	Heinrich Rose		

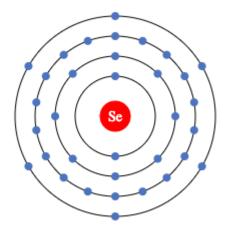






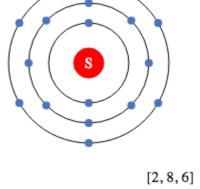


34: Selenium



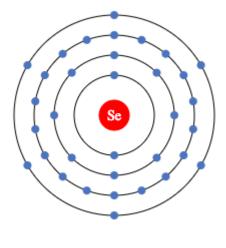


16: Sulfur

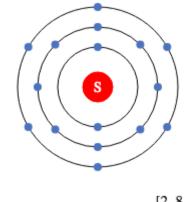


[2, 8, 18, 6] .

34: Selenium

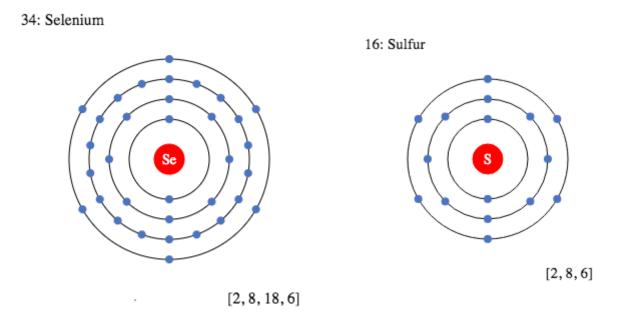


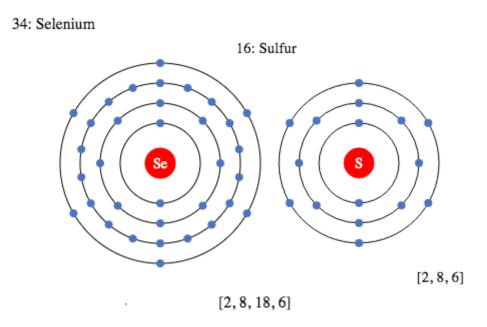


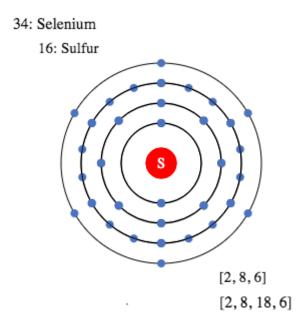




[2, 8, 18, 6]









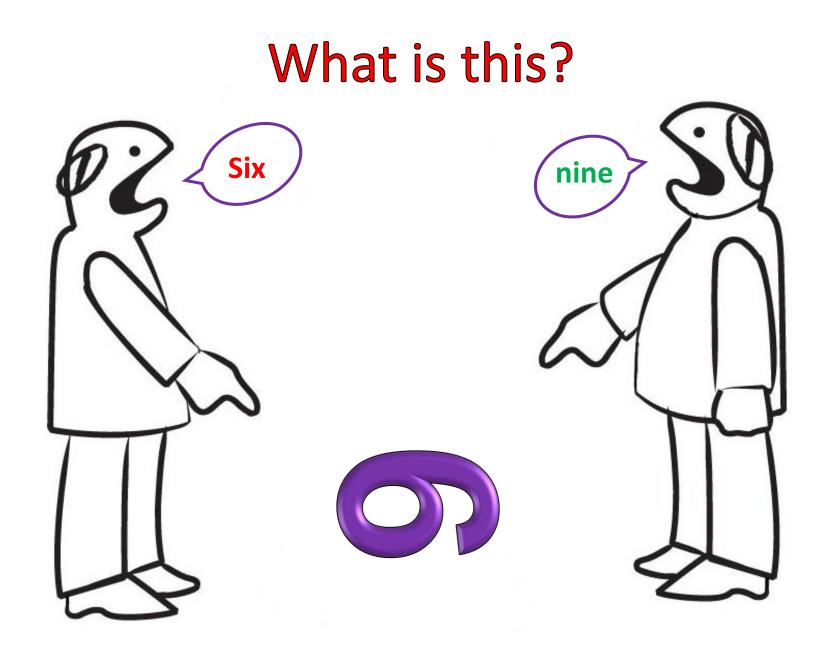
The discovery of Se essentiality in early 1960s.

The discovery in 1973 that glutathione peroxidase is a selenoprotein.

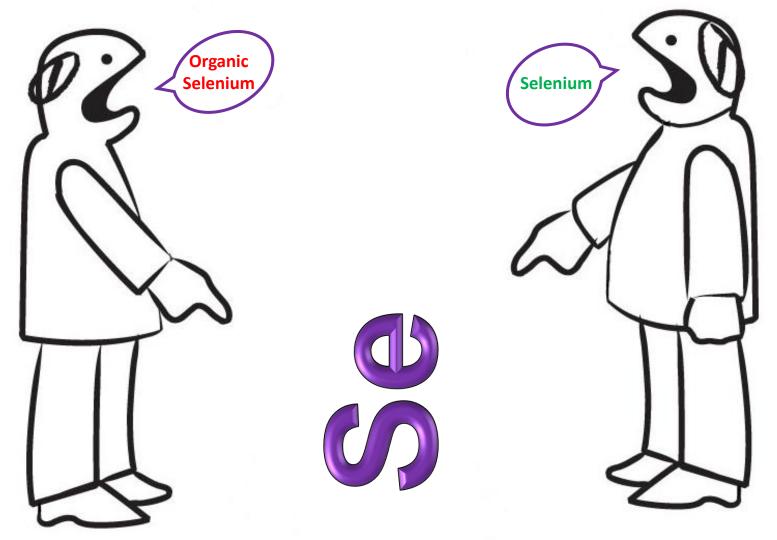
Characterisation of main selenoproteins in nutrition and health in 2003.

New insight

The role of free radicals as signalling molecules, understanding the role of nutrients in gene expression and maternal programming, tremendous progress in human and animal genome.

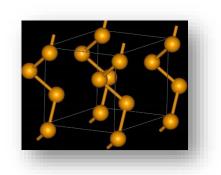


What is this?



Elemental selenium

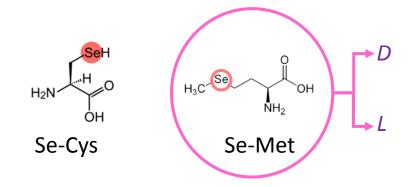
Se⁰

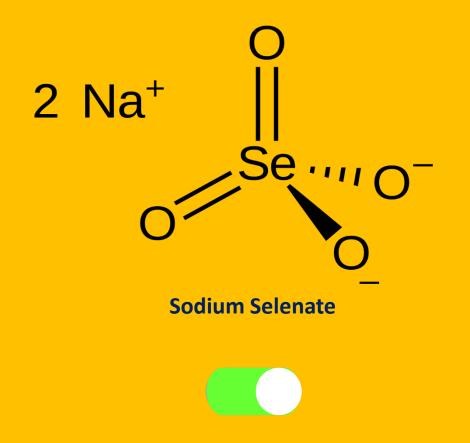


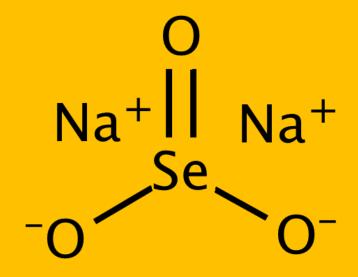
Inorganic selenium compounds

Selenite (SeO₃⁻⁻), Selenate (SeO₄⁻⁻), Selenide (Se⁻⁻)

Organic selenium compounds

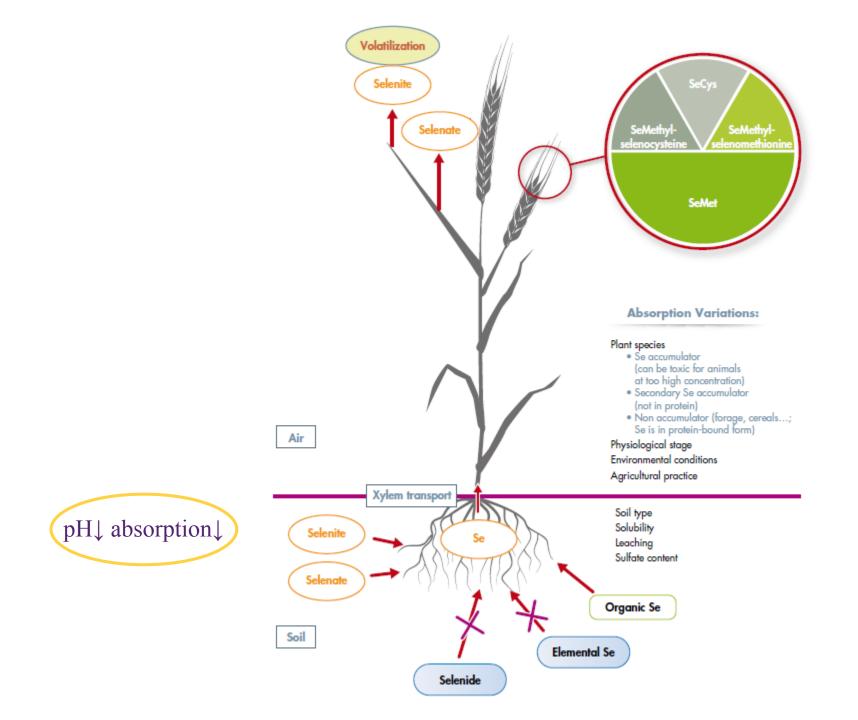






Sodium Selenite





Plants differ markedly in their ability to incorporate selenium from soil into tissues; and based on this ability, plants are divided into three major categories:

Selenium accumulators

1

3

2

Astragalus, Stanleya, Morinda, Neptunia, Oonopsis, and Xylorhiza

Secondary Se accumulators

Aster, Astragalus, Atriplex, Castilleja, Comandra, Grayia, Grindelia, Gutierrezia, Machaeranthera and Brassica

Non-accumulator plants

forage, cereal, oilmeal and crop plants

Selenium concentrations in various feed ingredients, mg/kg

Ingredient	USA	Canada
Alfalfa meal	0.01-2.00	0.02-0.27
Barley	0.05-0.5	0.02-0.99
Brewer's grains	0.15-1.00	0.29-1.10
Corn	0.01-1.00	0.01-0.33
Fish meal	1.0-5.0	1.3-3.4
Linseed meal	0.5-1.2	0.7-1.5
Meat meal	0.08-0.5	0.2-0.81
Oats	0.01-1.00	0.01-1.10
Poultry by-product	0.5-0.10	-
Soybean meal	0.06-1.00	0.04-0.78
Wheat	0.1-3.00	0.02-1.5
Wheat bran	0.1-3.0	0.24-1.3
Wheat middling	0.15-1.0	0.41-0.89
Whole soybeans	0.07-0.90	-

Feedstuff	Biological availability, %	
Dehydrated alfalfa meal	210	
Brewer's yeast	89	
Cottonseed meal	86	
Corn	86	
Brewer's grains	80	
Wheat	71	
Distiller's dried grains and solubles	65	
Soybean meal	60	
Herring meal	25	
Tuna meal	22	
Poultry by-product meal	18	
Menhaden fish meal	16	
Meat and bone meal	15	
Fish solubles	9	

Bioavailability of Se in feedstuffs (adapted from Cantor, 1997).

	Grains	SeMet proportion, % total Se	References
Wheat	wheat grain	56-83	Whanger, 2002
	wheat	50.4-81.4	Yang et al., 1997
	wheat grain	72-85	Cubadda et al., 2010
	spring wheat grains, Australia	90	Stadlober et al., 2001
	spring wheat grain, India	66	Cubadda et al., 2010
	durum wheat, Austria	62	Stadlober et al., 2001
	winter wheat grain, India	58	Cubadda et al., 2010
	wheat flour, Belgium	52	Moreno et al., 2004
Barley	summer barley grains, Austria	77	Stadlober et al., 2001
Maize	maize	61-64	Whanger, 2002
	maize	45.5-82.0	Yang et al., 1997
Soybeans	soybeans	>80	Whanger, 2002
	soybeans	62.9-71.8	Yang et al., 1997
Rice	rice	68-81	Whanger, 2002
	rice	54.9-86.5	Yang et al., 1997
	basmati rice, India	93	Mar et al., 2009
	jasmine rice, Thailand	96	Mar et al., 2009
	white rice, USA	94	Mar et al., 2009

Major differences

Absorption	similar to methionine with active transport in the gut	similar to other mineral with passive transport in the gut
Accumulation	building Se reserves by non-specific incorporation of SeMet into the proteins	not accumulated in the body
Toxicity	at least 3 times less toxic than selenite	highly toxic, can penetrate via skin causing problems
Bioavailability	higher bioavailability in comparison to selenite to animals/poultry	lower bioavailability in comparison to SeMet
Antioxidant activity	possesses antioxidant properties per se and could scavenge NO and other radicals	possesses prooxidant properties and could stimulate free radical production when reacting with GS
Effect on DNA	stimulate DNA-repair enzymes	causes DNA damage
Transfer to eggs and muscles	transferred to egg and muscles giving an opportunity to produce Se-eggs and Se-meat	poorly transferred to eggs and muse
Reactions with other elements	neutral, ascorbic acid promotes SeMet assimilation from the diet	highly reactive, reduced to metallic, unavailable selenium by ascorbic acid
Protective effect in stress conditions	provide additional protection due to Se reserves in the body	cannot provide additional protection due to absence Se reserves in the body
Effect on drip loss	decrease drip loss	does not affect drip loss
Environmental issues	better retention in tissues, less released with faeces and urine	low retention in tissues and high release with faeces and urine
Stability	stable	stable
Classification based on the mode of action	feed additive	drug

Selenite

Organic selenium





Selenium acid > selenite > selenate > selenocysteine > methylated selenium compounds

Molecular mode of action of toxic interaction

- Toxicity occurs from a flaw in protein synthesis.
- Recall that sulfur is a key component of proteins.
 - Sulfur disulfide bonds required for proper folding of protein (tertiary structure)
 - Disulfide bonds are between strands of amino acids
 - Structure=Function

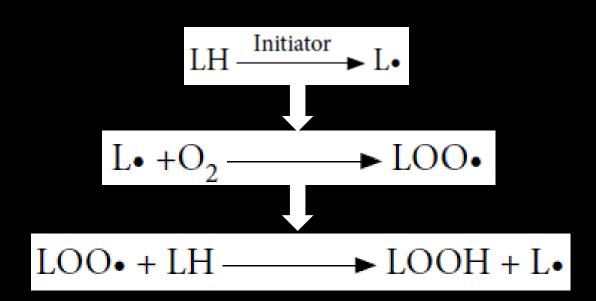
Cells do not discriminate well between Se and Sulfur during protein synthesis Formation of triselenium linkage (SE-SE-SE) or a selenotrisulfide linkage (S-Se-S)

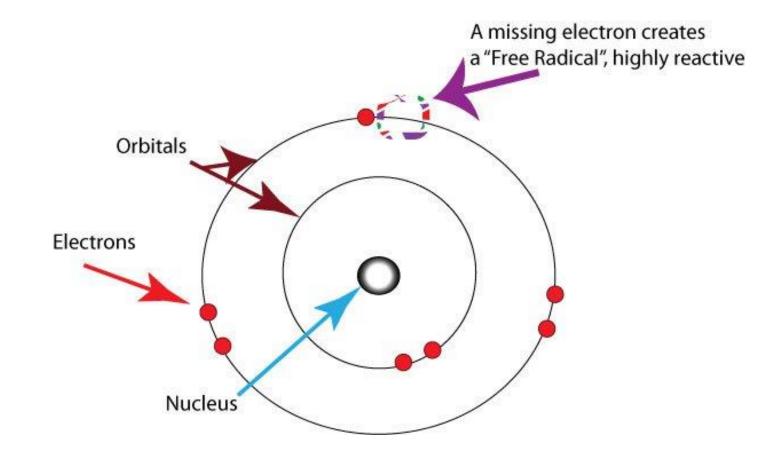
Functions

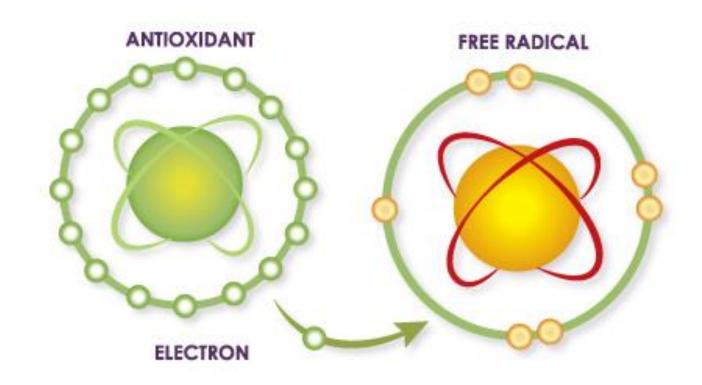
- Selenium dependent enzymes Glutathione peroxidase Deiodinases
- Other functions
 - Immune response
 - Complex with heavy metals (Cd, Hg & Ag)

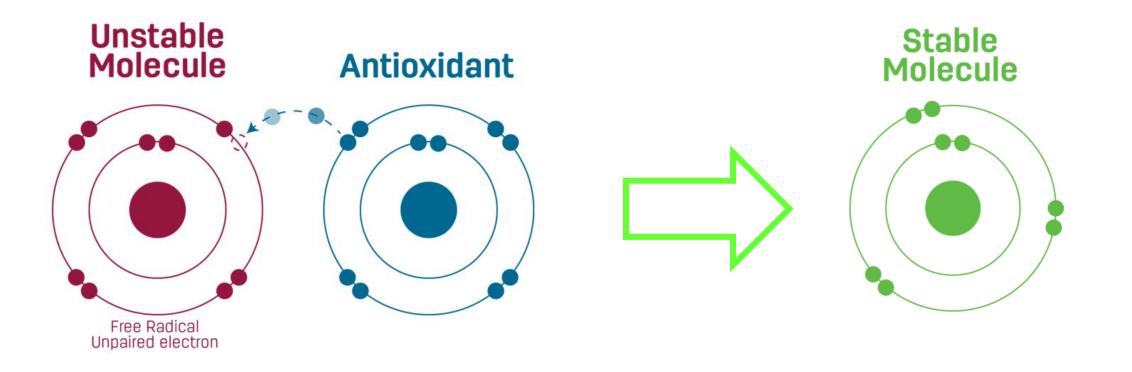


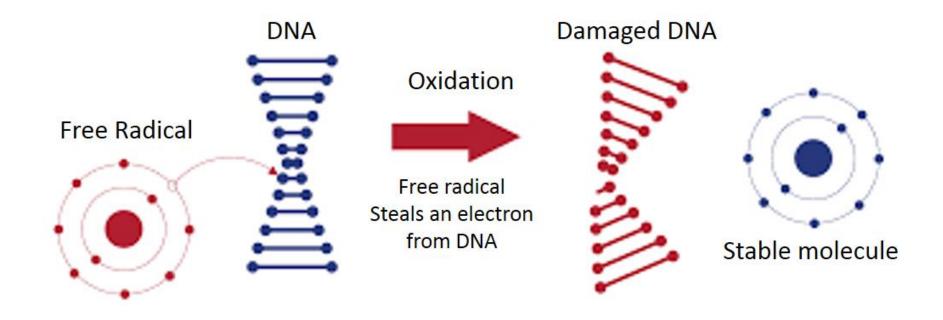
Self-preservation is the first law of nature

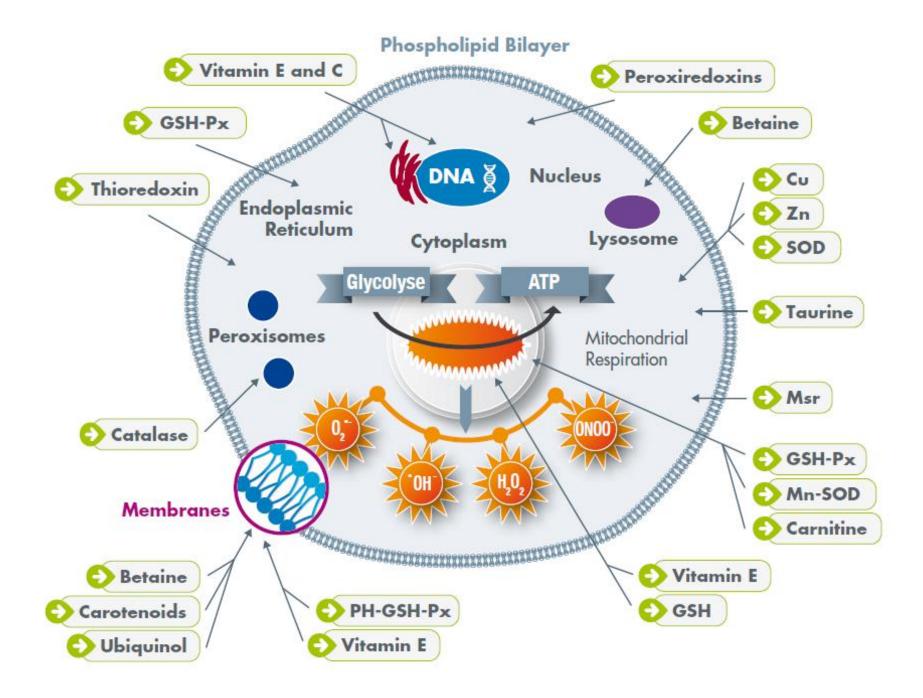


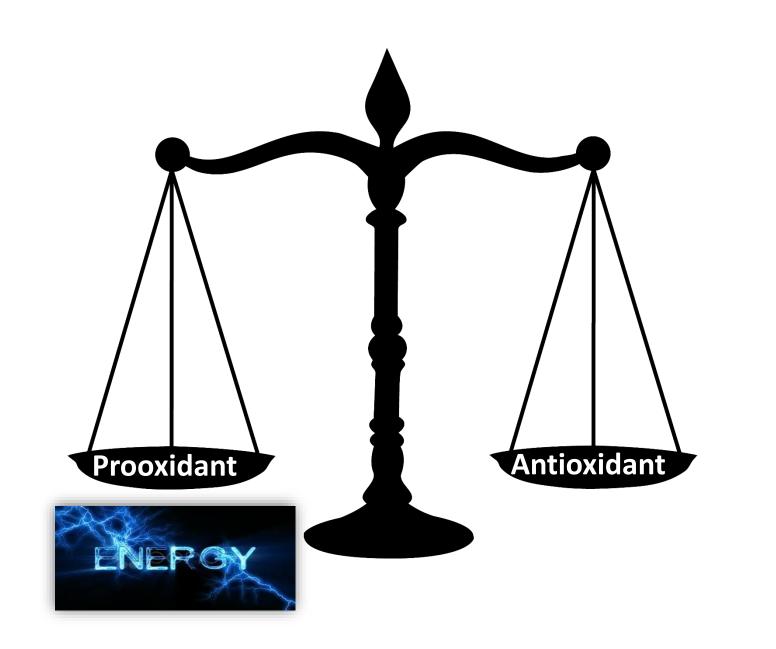


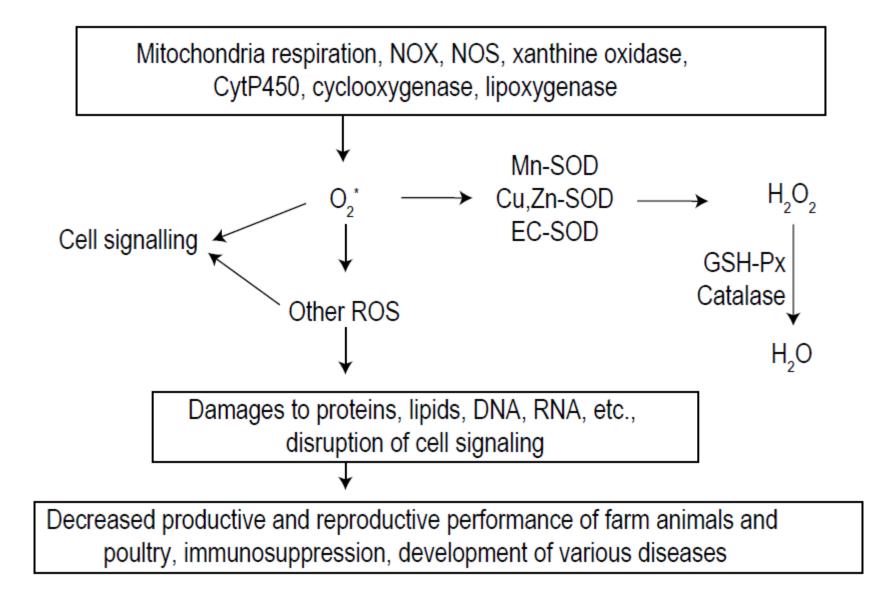






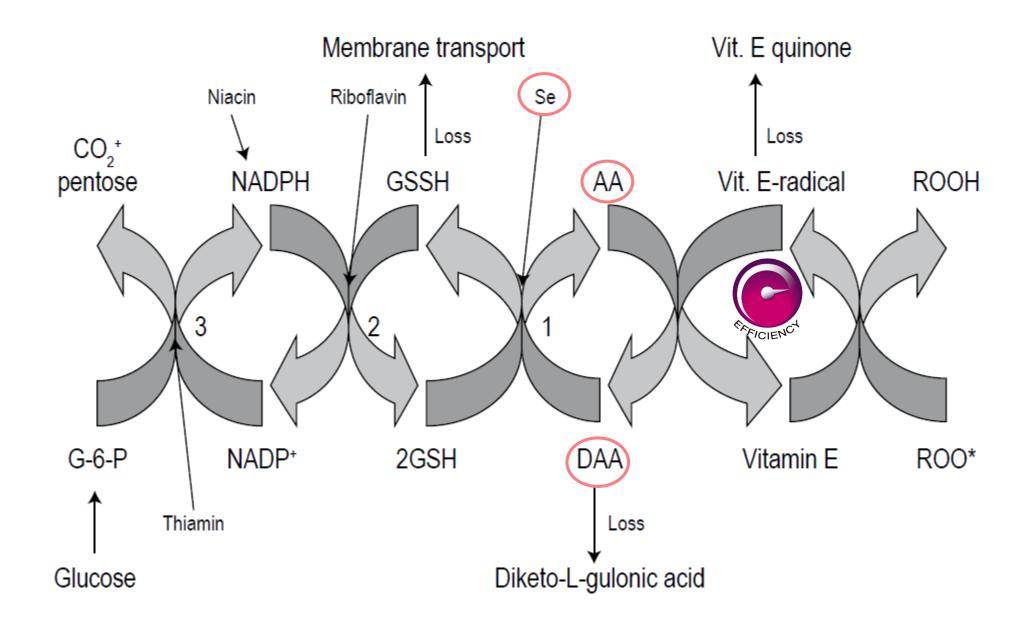


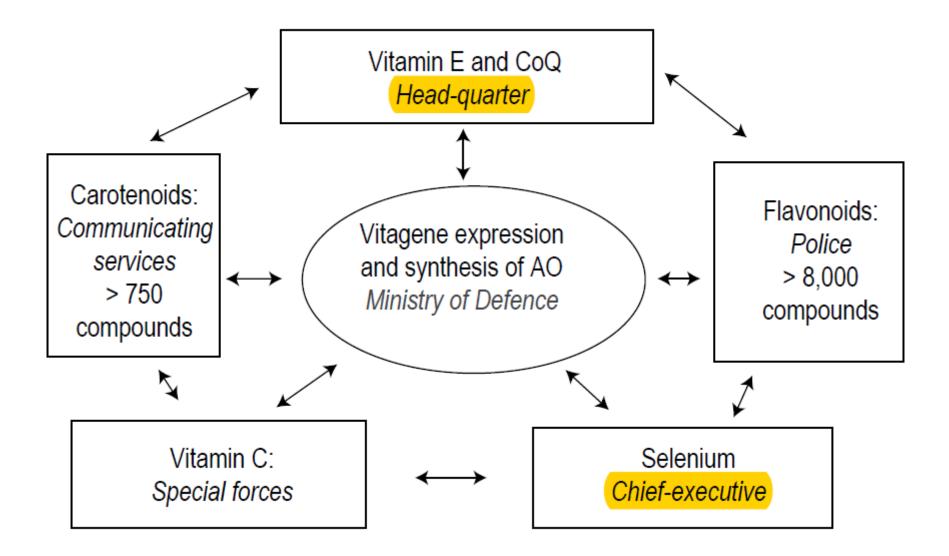




LOO• + Toc → Toc• + LOOH

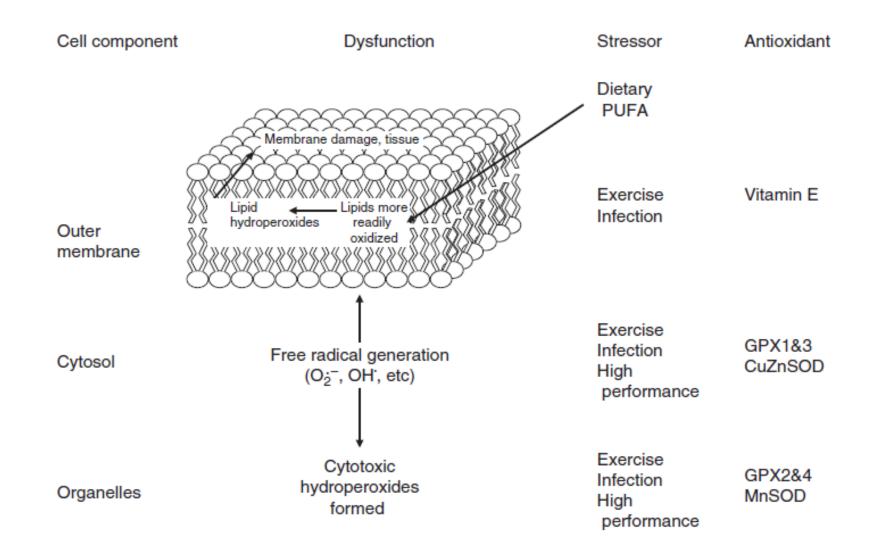
$ROOH + 2GSH \xrightarrow{GSH-Px} ROH (non-toxic) + H_2O + GSSG$





Nomenclature	Selenoprotein	Principal location	Function
GPX1	Cytosolic glutathione peroxidases (GPX)	Tissue cytosol, red blood cells	Storage, antioxidant
GPX2	Phospholipid hyperoxide GPX	Intracellular membranes, particularly testes	Intracellular antioxidant
GPX3	Plasma GPX	Plasma, kidney, lung	Extracellular antioxidant
GPX4	Gastrointestinal GPX	Intestinal mucosa	Mucosal antioxidant
GPX5	Epididymal GPX	Epididymis	Weak antioxidant
SPS-2	Selenophosphate synthetase 2	Ubiquitous	SeCys biosynthesis
ID1 or ORD1	Iodothyronine 5'-deiodinase type I	Liver, kidney, muscleª	Conversion of T4 to T3
ID2 or ORD2	Iodothyronine 5'-deiodinase type II	BAT	Conversion of T4 to T3
D3 or ORD3	Iodothyronine 5'-deiodinase type III	Placenta	Conversion of T4 to rT3
TR1 and 2	Thioredoxin reductase 1 and 2	Kidney, brain	Redox cycling
SePN	Selenoprotein N	Muscle	Cell proliferation
SePP	Selenoprotein P	Plasma	Transport, metal detoxifier
SePR	Selenoprotein R	Liver, kidney	Methionine sulfoxide reductase
SePW	Selenoprotein W	Muscle	Antioxidant, calcium-binding
MCSeP	Mitochondrial capsular selenoprotein	Sperm mitochondrial capsule	Store for GPX4

Selenoproteins that have been purified and/or cloned, their location and possible functions (after Beckett and Arthur, 2005).



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	Thilakarathna WPDW, Rupasinghe HPV. Food Chem Toxicol. 2019 Feb 5. pii: S0278-6915(19)30060-2. doi: 10.1016/j.fct.2019.02.010. [Epub ahead of print]	Glutathione peroxidase-1 overexpressing transgenic mice are protec [Neurochem Int. 2019]
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Characteristics of human selenoproteins

Protein	Protein Iength	SeCys position	Cellular distribution/tissues/species	Functions
Cytosolic GSH-Px (GSH-Px1)	201	47	cytosol	AO protection
GI-GSH-Px (GSH-Px2)	190	40	gastrointestinal tract	AO protection
pGSH-Px (GSH-Px3)	226	73	extracellular space and plasma	maintenance of cellular redox status
PH-GSH-Px (GSH-Px4)	197	73	cell membrane, many other tissues	detoxification of lipid hydroperoxides
Cytosolic TrxR1 (TrxR1)	499	498	cytosol, liver, kidney, heart	part of the Trx system, AO defence, redox regulation, cell signalling
Mitochondrial TrxR2 (TrxR2)	523	522	mitochondria, liver kidney	part of the Trx system, AO defence, redox regulation, cell signalling
TR3 (testicular) (TGR, TrxR3)	656	655	Testes	part of the Trx system, AO defence, redox regulation, cell signalling
lodothyronine deiodinase 1 (Dio1)	249	126	many tissues like liver, kidney, thyroid	conversion of T4 to T3 and T4 to reverse T3
lodothyronine deiodinase 2 (Dio2)	265	133	liver, kidney, thyroid, brown adipose tissue	conversion of T4 to T3
lodothyronine deiodinase 3 (Dio3)	278	144	placenta, brain, skin, (not in pituitary, thyroid, adult liver)	conversion T4 to reverse T3
Selenoprotein H (SepH, SelH)	122	44	widely distributed	upregulation of genes involved in GSH synthesis
Selenoprotein I (Sell,Sepl)	397	387	widely distributed	lipid metabolism
Selenoprotein K (Selke, SepK)	94	92	cardiomyocytes	possible AO protection in cardiomyocytes
Selenoprotein M (SelM, SepM)	145	48	brain and other tissues	distantly related to Sel15.
Selenoprotein N (SelN, SepN)	556	428	endoplasmatic reticulum	it is linked with rigid spine syndrome
Selenoprotein O (SelO, SepO)	669	667	widely distributed	unknown
Selenoprotein P (SepP, SepP1)	381	59 ^a	plasma, other tissues	involved in Se transport, AO defence
Selenoprotein Pb			plasma, other tissues	unknown
Methionine-R-sulfoxide reductase 1a	116	95	cytosol, nucleus	reduction of oxidised methionine residues in damaged proteins
(MsrB1, SelR, SelX)				
Selenoprotein S (SelS, SepS)	189	188	endoplasmatic reticulum	cellular redox balance, possible influence of inflammatory response
Selenophosphate synthetase 2a (SPS, SPS2, SPS2a)	448	60	testes, many other tissues	synthesis of selenophosphate
Selenoprotein T (SelT, SepT)	182	36	ubiquitous	role in regulation of Ca ²⁺ homeostasis and neuroendocrine secretion
Selenoprotein U (SelU, SepU1)			, fish and chicken, but not higher eukaryotes	unknown
Selenoprotein W (SelW, SepW1)	87	13	muscle, heart and other tissues	antioxidant protection
15-kDa Selenoprotein (Sel15, Sep15)	162	93	endoplasmatic reticulum	antioxidant protection

^a All positions of SeCys in SeP: 59, 300, 318, 330, 345, 352 367, 369, 376, 378.

^b AO = anti-oxidant; GSH = glutathione; TrxR = thioredoxin reductase.

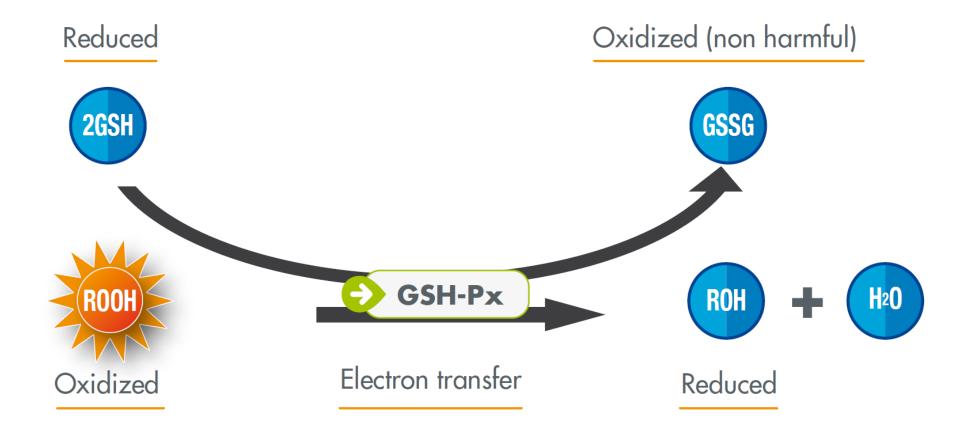
Se-dependent glutathione peroxidase characteristics

Glutathione peroxidase	Nomenclature	Localisation	Subunit size (kDa)	Substrates	Electron donors	Other characteristics
Cytosolic GSH-Px	GSH-Px1	intracellular, cytosolic, partly mitochondria	21.9	H ₂ O ₂ , t-BHP	GSH	Erythrocytes, kidney and liver
Gastrointestinal GSH-Px	GSH-Px2	intracellular, cytosolic	21.9	H ₂ O ₂ , t-BHP	GSH	mucosal epithelial cells in GIT
Extracellular (plasma) GSH-Px	GSH-Px3	plasma	25.5	H ₂ O ₂ , t-BHP, phospholipid hydroperoxides	GSH, thioredoxin, gluta-redoxin	expressed in kidney
Phospholipid hydroperoxide GSH-Px	GSH-Px4	intracellular, partly cytosolic, mitochondrial, membrane-bound	22.1	H ₂ O ₂ , phospholipid hydroperoxides	GSH, DTT, 2-ME, L-cys	renal epithelial cells and testes

¹ t-BHP = tret-butylhydroperoxide; DTT = 1,4-ditiothreitol; 2-ME = 2-mercaptoethanol; L-cys = L-cysteine.; GIT = gastrointestinal tract; GSH = glutathione.

Total glutathione peroxidase (GSH-Px) activity in the liver of various animals, U/mg protein

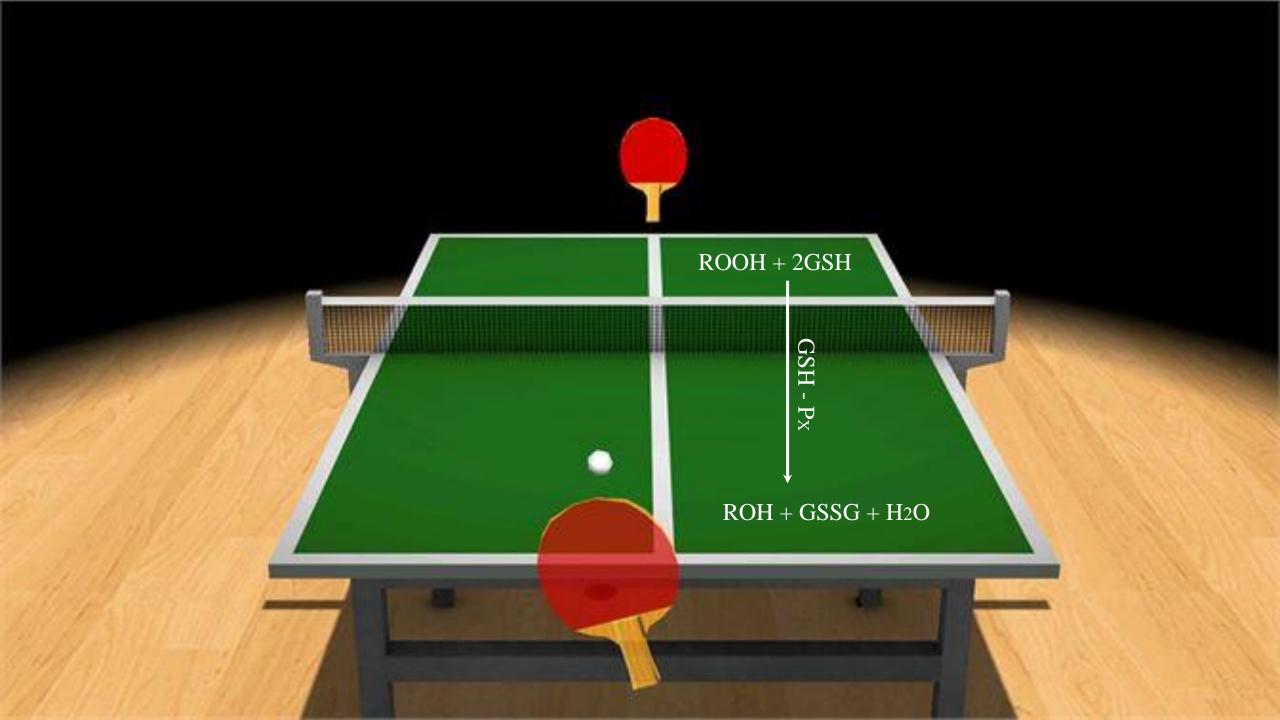
Animal	GSH-Px activity	Animal	GSH-Px activity
Chicken	33	White mouse	468
Cattle	70	Ground squirrel	49
Sheep	64	Cat	67
Rat	245	Dog	20
Mouse	476	Rainbow trout	0.9
Guinea pig	12	Blue gill sunfish	3.4
Hamster	920	Carp	143
Rabbit	496	Fence lizard	22
Gerbil	683	American toad	2
Wild house mice	446	Western newt	1.5

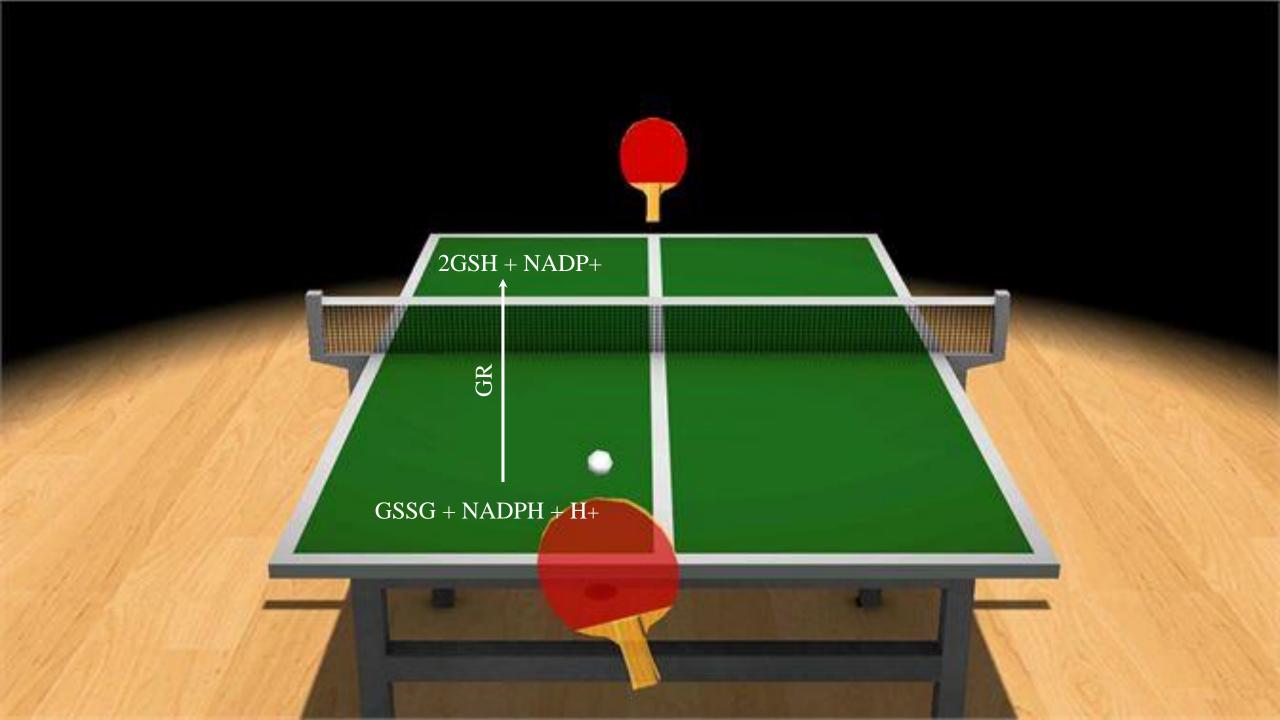


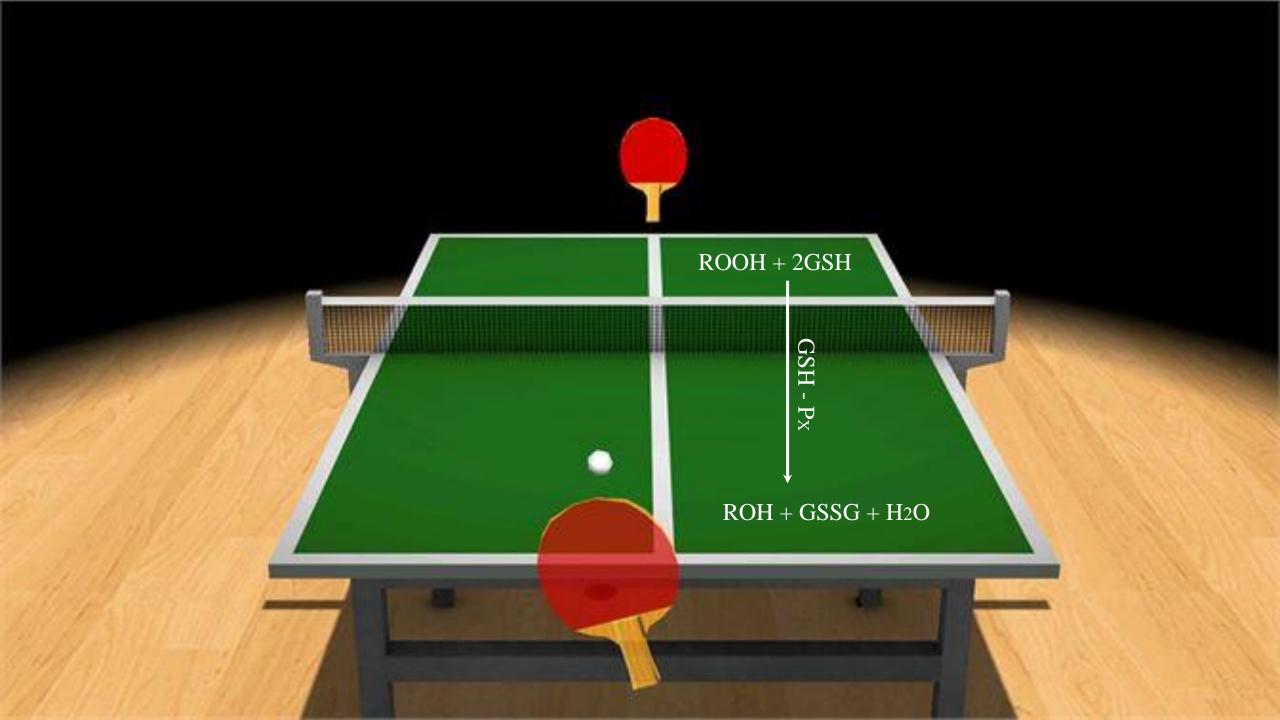
- 4 different GSH-Px in avian species
- Selenium feed supplementation / GSH-Px activity

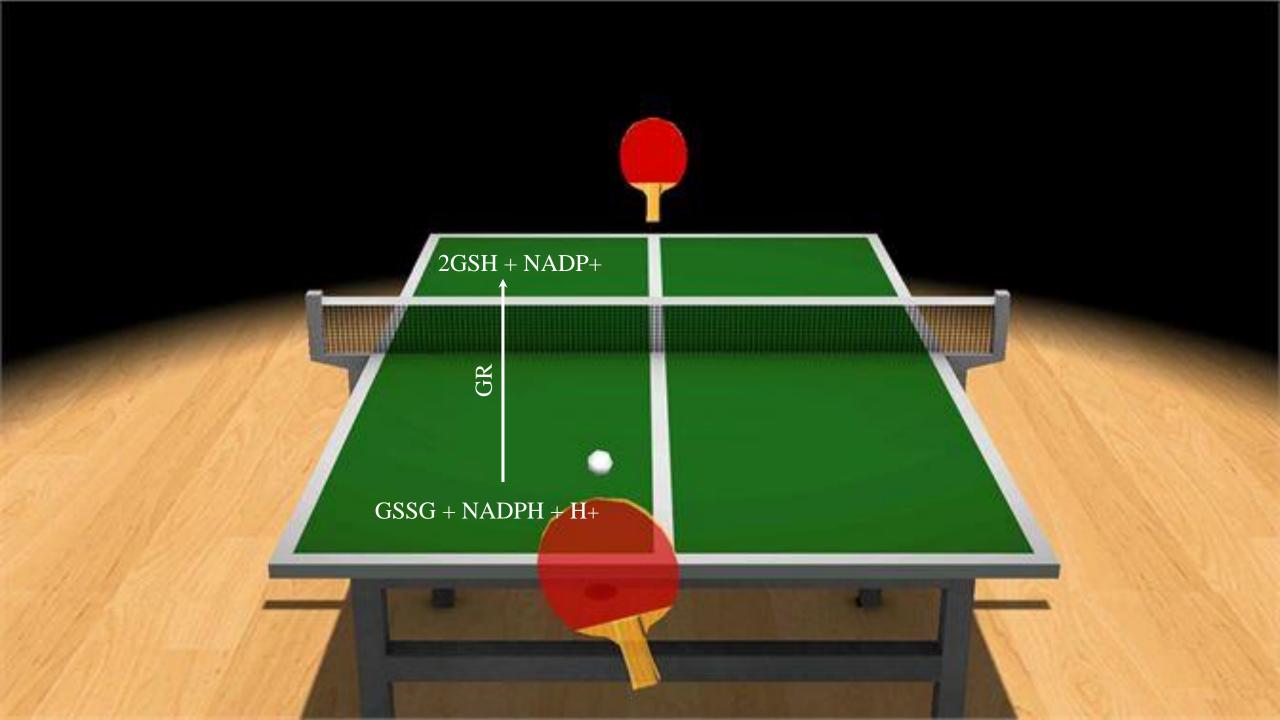
Different biological roles:

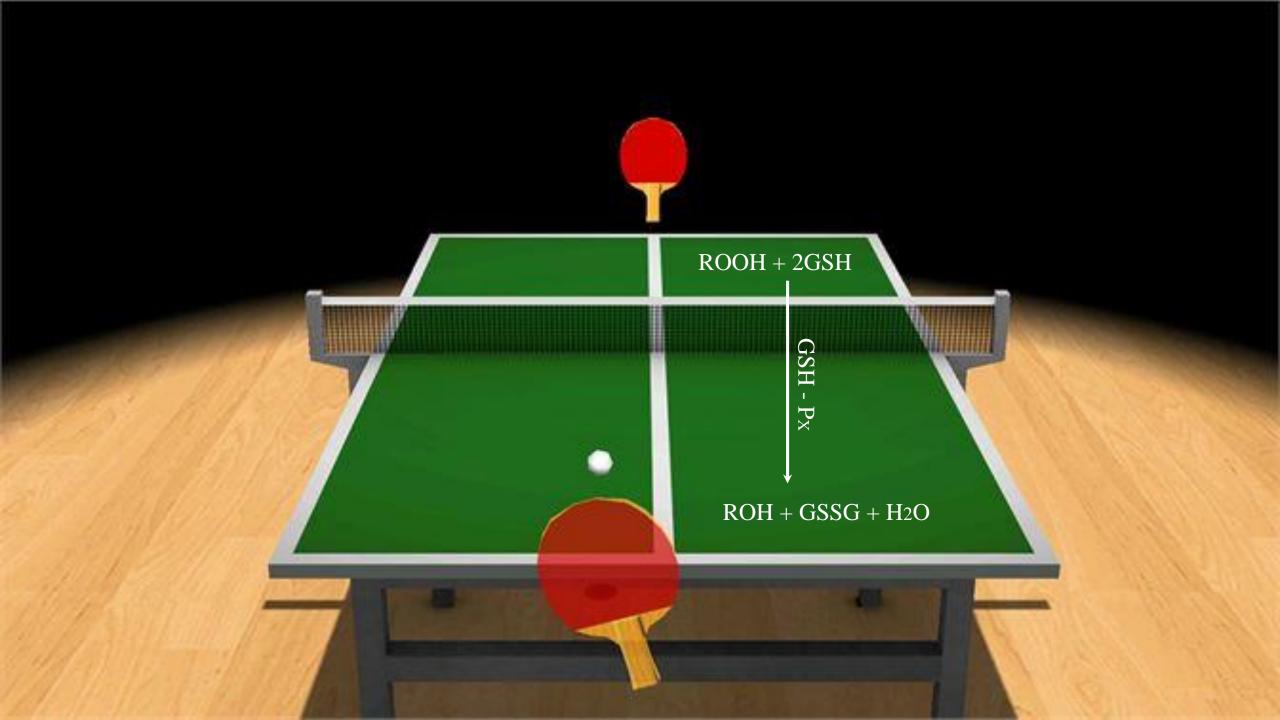
- Prevention of lipid peroxidation
- ROS detoxification
- Specific role of GSH-Px 4 in male fertility

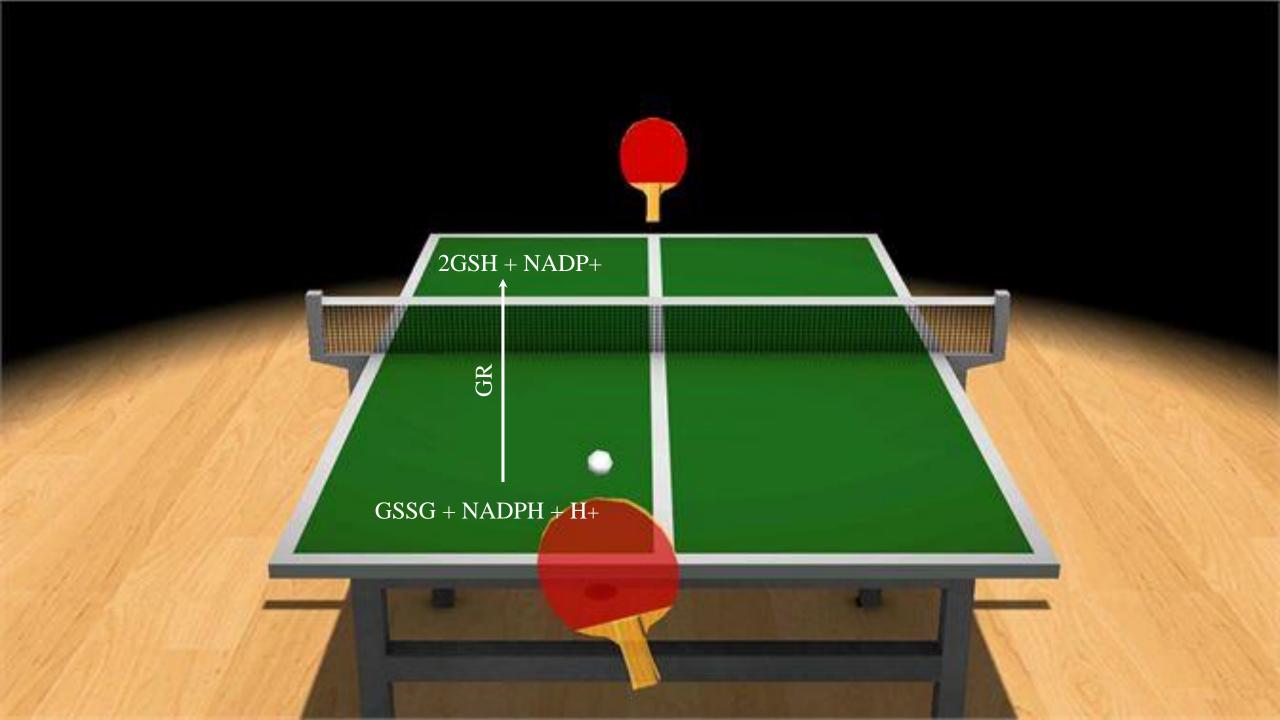


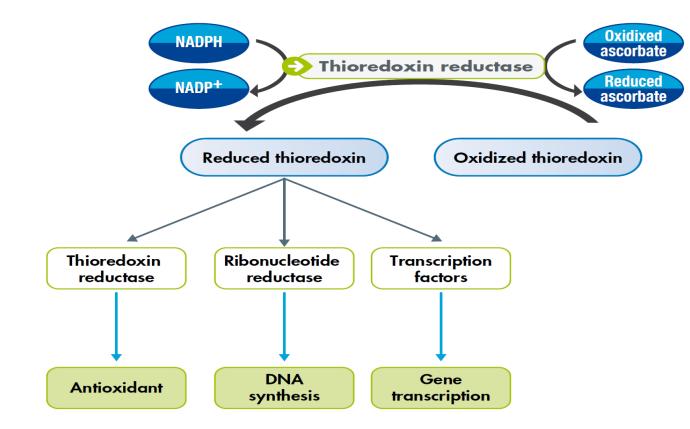












TrxR plays a role in:

- Cell growth
- Inhibition of apoptosis
- Cellular sensitivity to glucocorticoids
- Immunomodulation
- Pregnancy and birth
- Neuronal survival

Thioredoxin, (Peroxidase, Reductase)

Glutathione, (Peroxidase, Reductase)

Supply electrons for:

- Deoxyribonucleotide formation
 Antioxidant defence
- Protein and DNA synthesis and repair
- Redox regulation of signal transduction
- Transcription
- Cell growth, differentiation and apoptosis

Other selenoproteins

- I. Iodothyronine deiodinases
- II. Selenophosphate synthetase-2
- III. 15-kDa selenoprotein
- IV. Selenoprotein H
- V. Selenoprotein I
- VI. Selenoprotein K
- VII. Selenoprotein M
- VIII. Selenoprotein N
- IX. Selenoprotein O
- X. Selenoprotein P
- XI. Selenoprotein Pb
- XII. Selenoprotein R
- XIII. Selenoprotein S
- XIV. Selenoprotein T
- XV. Selenoprotein U
- XVI. Selenoprotein W

Selenoprotein location in chicken

Location/feature	Selenoproteins
Inside the cell	GSH-Px1, GSH-Px2, GSH-Px4, DIO1, DIO2, DIO3, TrxR1, TrxR2, TrxR3, Sep15, SelH, SelI, SelK, SelM, SelN, SelO, SelT, SelU, SelW, MsrB1, SPS2
Outside the cell/secreted	SelPa, SelPb and GSH-Px3
Endoplasmic reticulum	DIO1, DIO2, DIO3, Sep15, Sell, SelK, SelM, SelN SelS and SelT
Mitochondria	GSH-Px1, GSH-Px2, GSH-Px4, TrxR1, TrxR2, TrxR3, SelM, SelO and SelU
Cytoplasm	GSH-Px1, GSH-Px2, GSH-Px4, TrxR1, TrxR2, TrxR3 and SelW
Nucleus	GSH-Px4, MsrB1 and SelH
Golgi apparatus	SelT
Membrane	Sell
Membrane-bound	Sell, SelK, SelS, SelT, DIO1 and DIO3
Zn-containing	Sep15, MsrB1, SelW and SelM
POP-containing	GSH-Px1, GSH-Px2, GSH-Px3 and GSH-Px4
Thioredoxin-like fold-containing	GSH-Px1, GSH-Px2, GSH-Px3, GSH-Px4, DIO1, DIO2, DIO3, TrxR3, SeIT, SeIH, SeIW, Sep15, SeIM, SeIU and SeIO
Flavin adenine dinucleotide-interacting	TrxR1, TrxR2 and TrxR





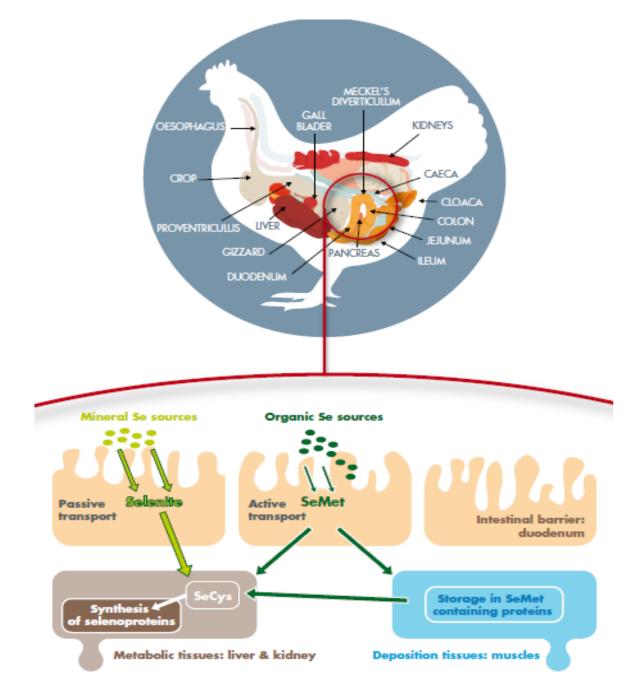
- AO defence Cell proliferation
- DNA-repair systems Cell differentiation
- Transfer of genetic information Stability of cell membrane
- Stress protein synthesis Stability of intracellular milieu
- Proteosomal function Macromolecular turnover
- Neutralisation and removing toxic chemicals Stress response
- Tissue regeneration and wound healing Hormonal response
- Tumour suppression Immune response
- Cell death and cell replacement Thermoregulation
- Neuronal response

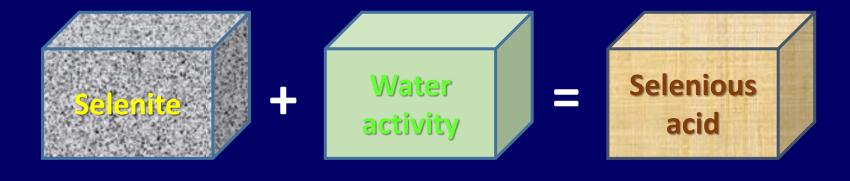
In particular, it was proven in an university-conducted trial that inclusion of antistress composition (PerforMax) into the drinking water improved chicken growth and feed conversion ratio (FCR; Fotina et al., 2011, 2014). Using the same anti-stress composition under commercial conditions improved FCR during a 39 day broiler growth trial. The improvement in FCR due to the anti-stress composition during the first three days post-hatch, as well as before and after vaccination was highly significant (Velichko and Surai, 2014; Velichko et al., 2013). The importance and efficacy of the anti-stress composition for rearing birds and adult egg type parent stock (Hy-Line) at one of the biggest egg producing farms in Russia (Borovskaya poultry farm, Tumen region) have been recently reviewed (Shatskich et al., 2015).



Selenium absorption and metabolism

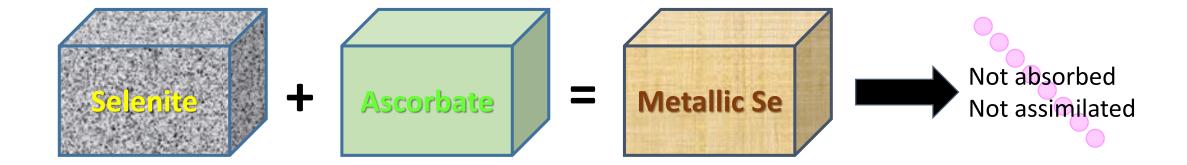
- Chemical form of Se
- Other dietary components
- ✓ Selenium status
- Physiological status
- ✓ Species



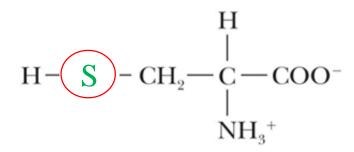




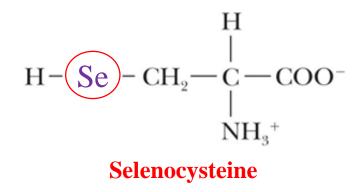




Synthesis Mechanism of 21st Amino Acid Selenocysteine

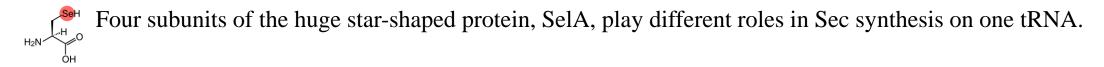


Cysteine

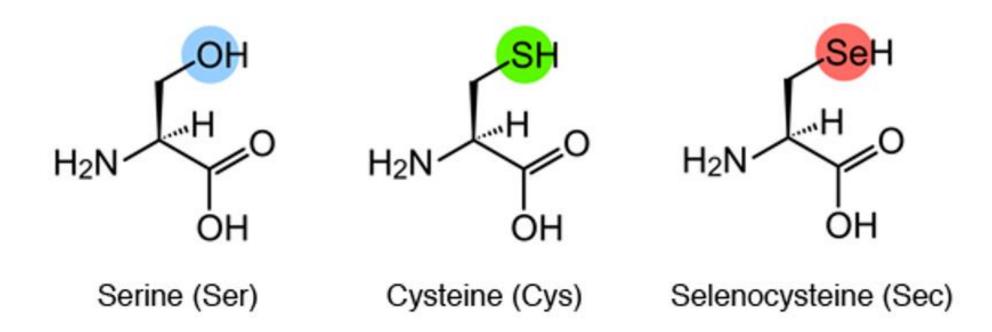


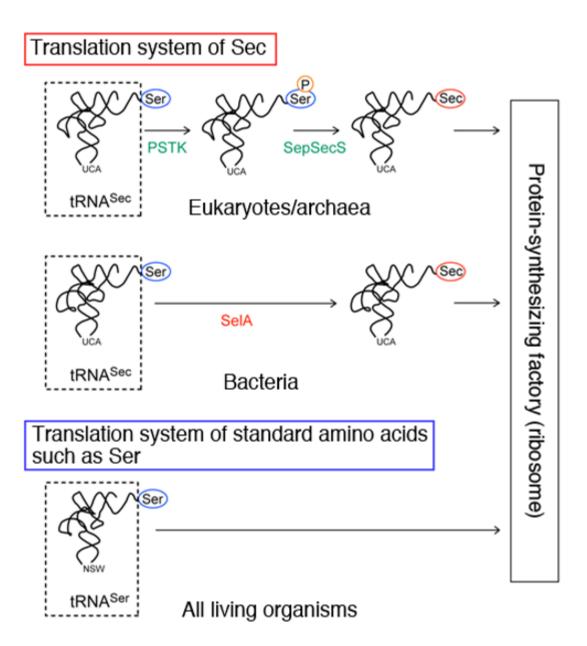
Key points

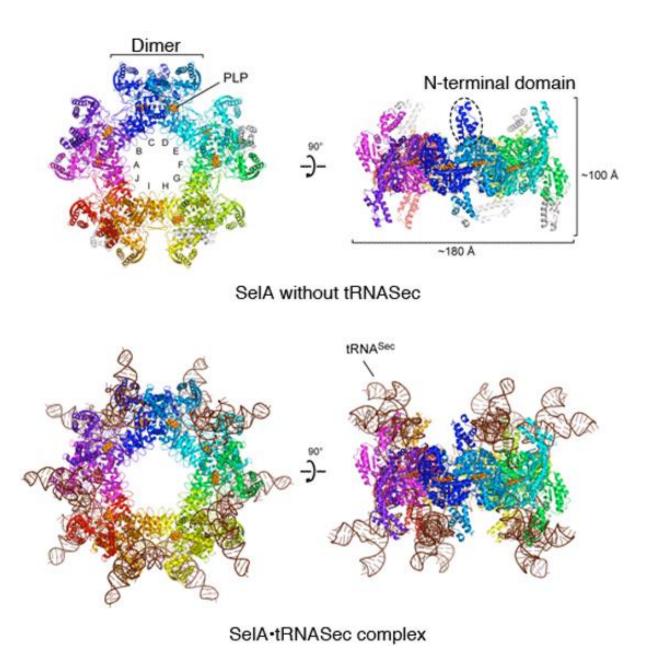
The three-dimensional structure of SelA, the enzyme required for selenocysteine (Sec) synthesis, is determined.

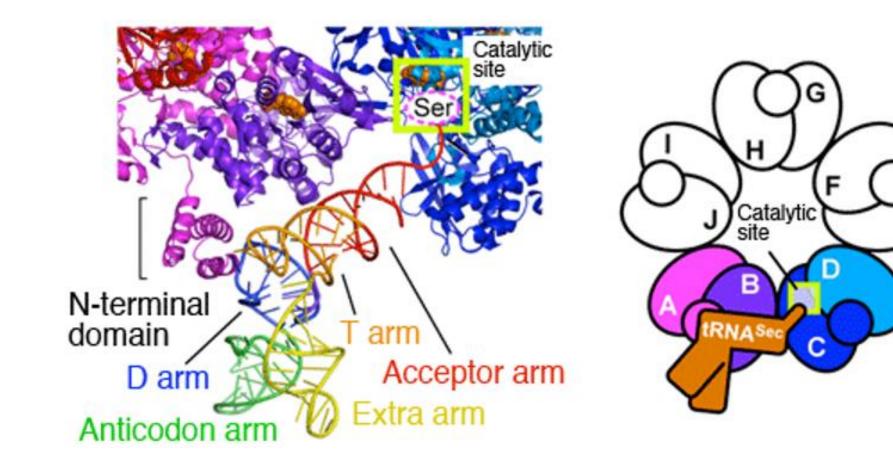


The findings will contribute to the development of super-enzymes by facilitating introduction of selenium (Se) into enzymes.

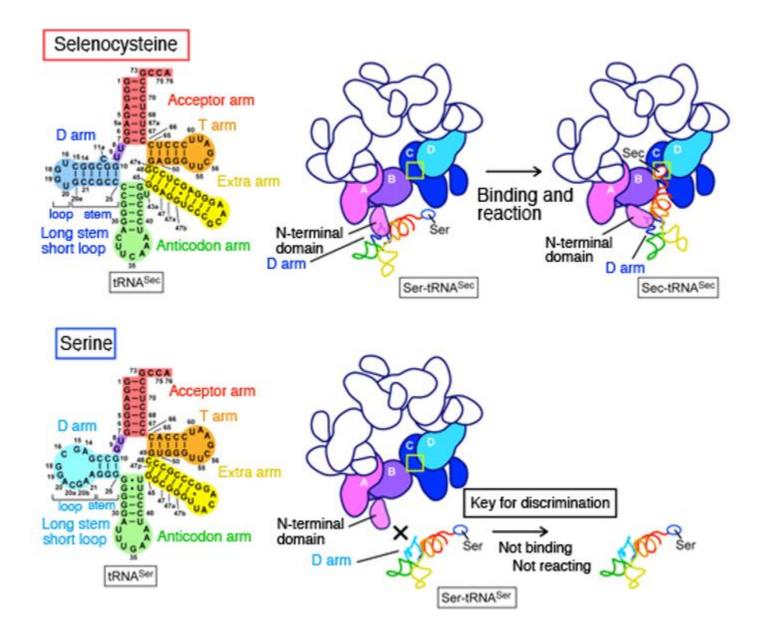


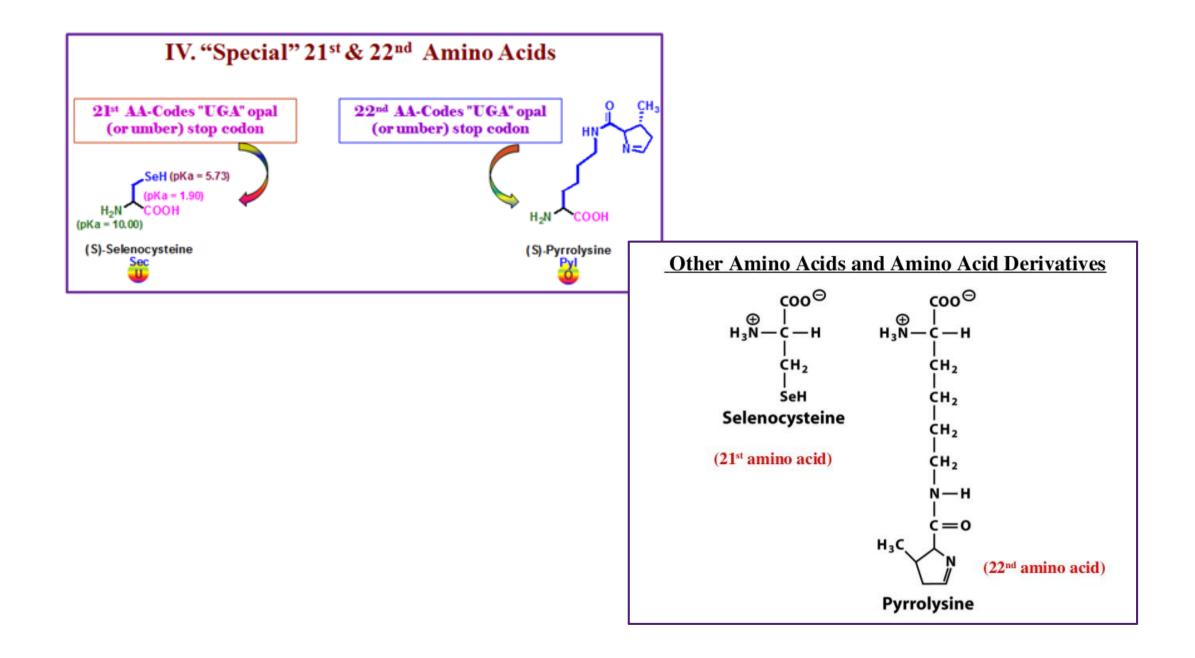


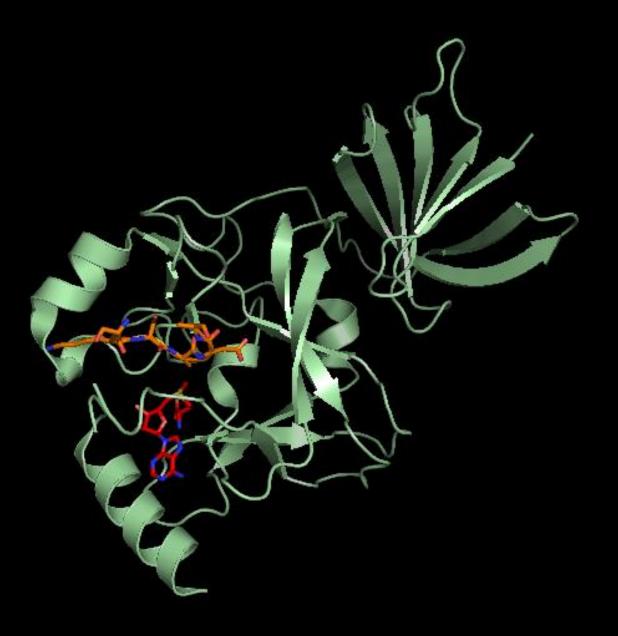




F





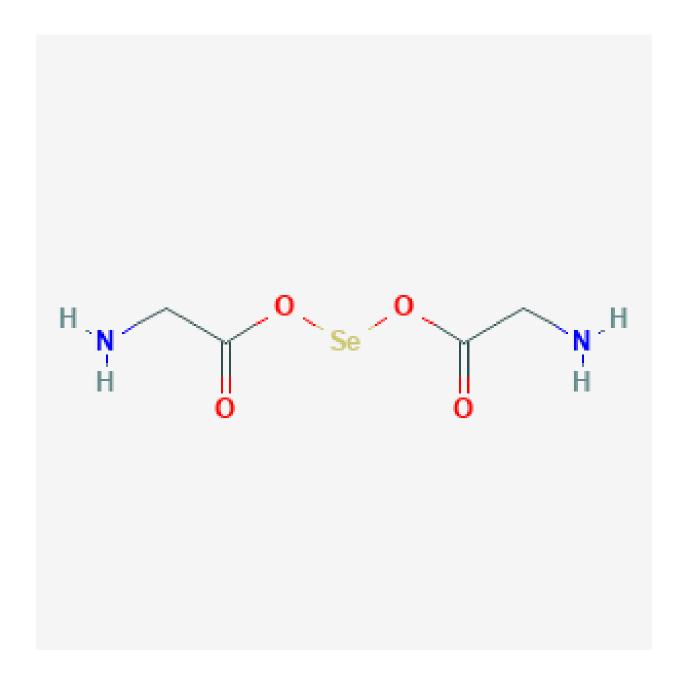


Chelated Selenium products

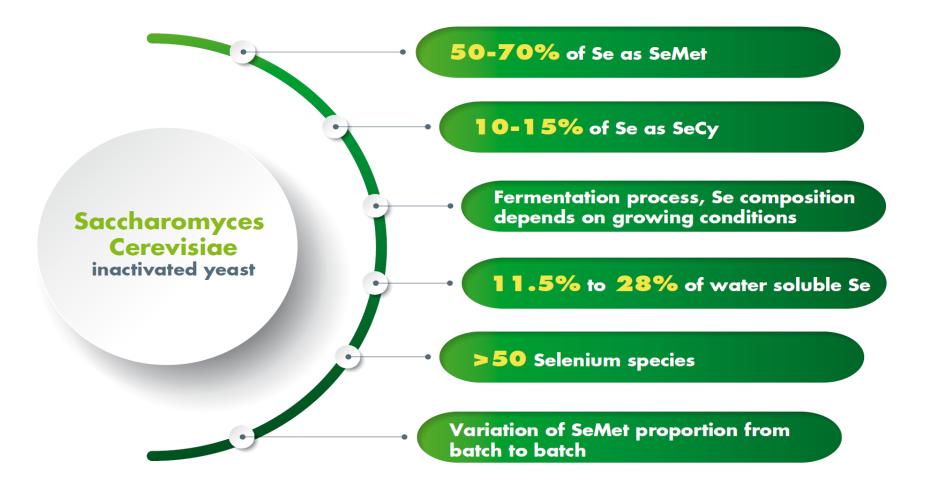
Se-glycinates Se-proteinates Se-amino acids complexes

The chemical position of Se in the periodic table of elements indicates that Se is not a true metal, and therefore its chelating ability is in question.

Chelated Se products are not related to SeMet or SeCys and, probably, should not be included into the organic Se category.



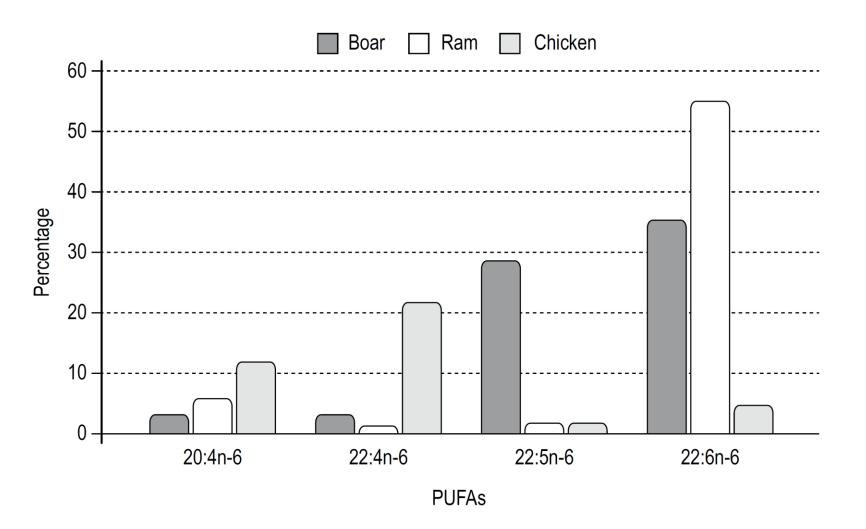
Selenium-enriched yeast



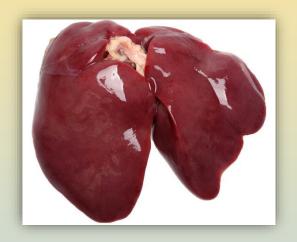
The legal definition of Se-yeast is as follows:

Selenium yeast is a dried, non-viable yeast (*Saccharomyce vervisiae*) weivated in a fedbatch fermentation which provides incremental amounts of the selenium salts (to the growth rate of the yeast and allows for optimal incorporation of inorganic selenium into cells (ar organic material. Residual inorganic selenium is eliminated in a rigorous Washing proce 6 and must not exceed **2%** of the total selenium content in the final selenium yeast product (LII, 2015).



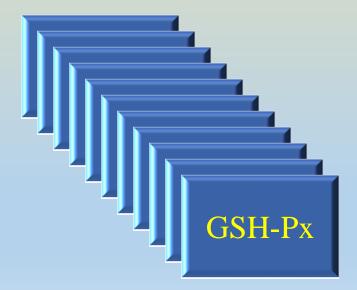


Polyunsaturated fatty acids (PUFAs) in spermatozoa phospholipids, % (adapted from Surai, 2002). 20:4n-6 = arachidonic acid; 22:4n-6 = docosatetraenoic acid; 22:5n-6 = docosapentaenoic acid; 22:6n = 3 docosahexaenoic acid.









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An improvement in productive and reproductive performance of aged broiler breeder hens by dietary supplementation of organic selenium

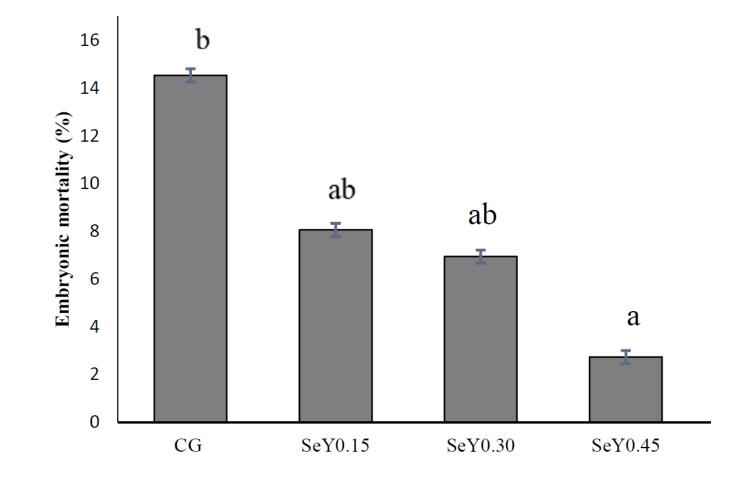


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DIET CURES, MORE THAN THE LANCET