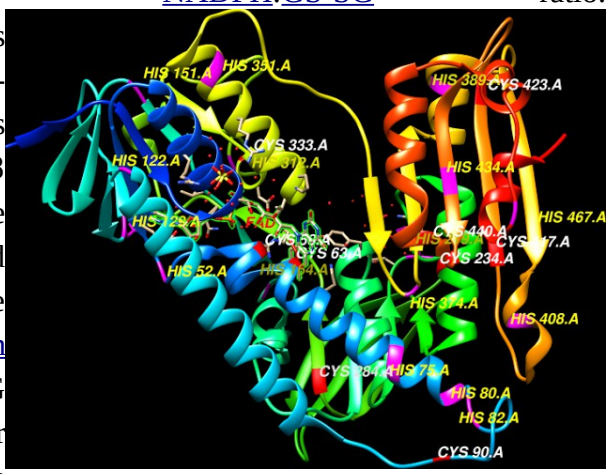
**CHANGES IN GLUTATHIONE AND GLUTATHIONE REDUCTASE POSITIONING GLUTATHIONE-S-TRANSFERASE AS A FUNCTION OF CELL CONCENTRATION WITH ENZYME ACTIVITIES FOUND TO INFLUENCE BEHAVIOR.**

Glutathione reductase (GSR, GR) locus in the chromosomal region 8p21.1, (EC 1.8.1.7)-(§, ‡) is a protein-S-glutathionylation, as a (human) Mitochondrial localization of hGSR and its associated enzymes cellular thiol/disulfides S-Glutathione reductase (GSR) which is the importance of significance in reversible thiol modifications which regenerates reduced glutathione (GSH) and GSSG to the reduced form found in the obvious structural properties of glutathione reductase. The redox regulating enzymes relationship with TTase (thioltransferase) activity with the ratio of the activities of G3PD, as the mechanism (of cellular repair) 'differs' (gssg-g6pg) according to the type of reducing glutathionylated mixed disulfide, including protein-S-S-glutathione (PSSG), GSR reduces (PSSG) modified by thiolation to a normal level in human lens epithelial (HLE) cells. This may have implications in stress- and aging-related pathologies in astrocytes and granule cells, demonstrated by comparable mitochondria/cytosolic concentrations of its thiol proteins, where a mitochondrial leader sequence (cDNA) is present in the gene structure of human GSR and may be the Cytoplasmic Isoform (derivative or inhibitor formed) of mitochondrial dysfunction that contains the catalytic cysteine revealing a possible therapeutic strategy/target, also indicating transiently accumulated inhibitor proteins modified by thiolation (cysteine catalytic subunits) compounds that inhibit these (re)activation processes (hGSR) with its structure-based prosthetic group (FAD) cofactor is common because of the levels of cysteine available; are mitochondria/cytosolic concentrations that the Glutathione reductases reversible thiol modifications which catalyzes the reduction of GSSG to GSH the natural GR substrate is dependent on the NADPH:GS-SG ratio.




Cys58 and Cys63 represent the enzyme's results seen as the reductive (GSH) Cys-58 and oxidative (GSSG) Cys-63 is the relationship of these two enzymes, His467' is seen to interact with Cys63 more optimally and Cys-58 produces the second GSH intermediate molecule of the reaction is the reduced glutathione-to-oxidized glutathione ratio (GSH/GS-SG) when compared to the substrate free form correlated with (FAD) the flavin compounds, flow from NADPH to the substrate GSSG via flavin. The reducing equivalents needed for regeneration of GSH are provided by NADPH. The enzyme has affinity for flavin adenine dinucleotide (FAD) the prosthetic group of GR, and maintains high levels of reduced glutathione (Cytoplasmic Isoform: Produced by alternative initiation of isoform Mitochondrial homodimer, derivative or inhibitor formed from the GSR Pyridine, dimerisation

domain.) in the cytosol. Glutathione reductase (GR) plays a key role in maintaining either a thiol group or a nonprotein sulfhydryl group (NPS) form of GSH, and potential for thioredoxin and glutathione systems, as thioredoxin dose not require GSH and GR for catalytic activity. Glutathione reductase (GR) utilizes NADPH produced by G6PDH (glucose-6-phosphate dehydrogenase) enzyme activities, and enzyme glutathione reductase (GR) represents the erythrocyte glutathione-reducing system (GRS), of the GSH pathway to oxidation and inactivation in the activity of GSH peroxidase and GSH reductase. Expression of the regulatory subunit of gamma-glutamylcysteine synthetase/ligase (GCL) catalyzes the first and rate-limiting step in the production of the cellular (GSH) glutathione. Dietary riboflavin (Vitamin B2) intake produces its active essential coenzyme flavin forms, riboflavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) of glutathione reductase (GR), or the GR activity correlated with red-cell flavin compounds.When both GSSG and NADP(+) substrates and products are present, glutathione reductase (GR) is a enzyme required for the conversion in the presence and absence of flavin adenine dinucleotide (FAD), glutathione reductase (GR) is an obligatory FAD-containing homodimer. GSSG via glutathione reductase (GR) regenerates reduced glutathione which is essential for antioxidant defense. The flavoenzyme glutathione reductase (GR) reduces 'oxidized glutathione' (GSSG) back to GSH, also involving glutamate-cysteine ligase and modulatory (GCL)-can be upregulated ∉ as the cellular GSH system, indicating short-term and heritable tolerance of exposure to oxidative stress from/via numerous reporting ∈ mechanisms. NADPH is used by glutathione reductase for the reduction of oxidized glutathione (glutathione disulphide) GSSG to GSH-dependent peroxide metabolism. 4-Hydroxynonenal (HNE) is one of the major end products of lipid peroxidation which may lead to enhanced action of the (GSR) oxygen radical, glutathione S-transferases (GSTs) are specifically suited to the detoxification and removal of 4-HNE (∋ or ∝) from cells which may provide a basis for selective cellular and/or subcellular distribution of mitochondrial and cytosolic to individual detoxifying gene inducer activities of glutathione reductase (GR), the cellular (GSH) glutathione. It was evident the enzyme glutathione reductase (GR) represents the erythrocyte glutathione-reducing system (GRS), of the GSH pathway to oxidation and the (∉ or ∝) inhibition constant for reversible inactivation in the activity of glutathione related antioxidant enzymes. And GSH reductase may be one of the factors that remained in focus that suggests its effects on the antioxidant system related to glutathione synthesis (GCL), degradation, and functions.

Biological Xenobiotics, Extracts, Applications of note In the presence of Glutathione reductase.:

Schisandrin (Schisandra chinensis), used in traditional Chinese medicine. PMID:21328628

Transketolase (TK) and transaldolase (TA)

Melatonin PMID:15571523, 19475625

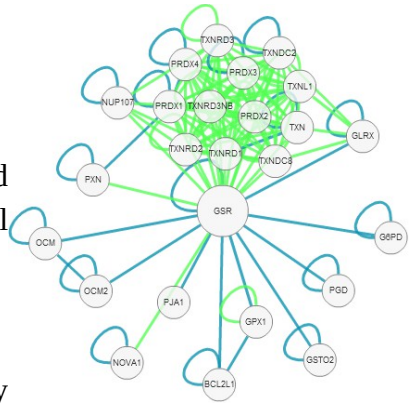
Blackberry (Rubus sp.) cultivars, The 'Hull Thornless', PMID:11087537

Glutathione dehydrogenase (ascorbate)-[dehydroascorbate reductase (DHAR), and glutathione reductase (GR). This enzyme participates in the glutathione metabolism the active metabolite of

vitamin D3 increases glutathione levels.] PMID:11087537, 23770363

3H-1,2-dithiole-3-thione nutraceutical D3T potently induces the cellular GSH system, Anethole trithione is a drug used in the treatment of dry mouth, the Anethole trithione isomer is related to anethole (anise camphor) used as a flavoring substance. PMID:17206382*, 19408115, 19176875*, 15896789, 18408143*,

16946404*




Cassia fistula used in herbal medicine. PMID:19088944

Sanguinarine is extracted from some plants, including bloodroot and Mexican prickly poppy (Argemone mexicana) where argimone oil causes Epidemic dropsy. PMID:11260782

Vitamin E, PMID: 15672860

Tocotrienols are natural compounds members of the vitamin E family found in select vegetable oils are an essential nutrient for the body. PMID:21845802

Pyrrolizidine alkaloids are produced by plants as a defense mechanism against insect herbivores consumption of PAs is known as pyrrolizidine alkaloidosis. PMID:20144959

Apple extract (AE) PMID:20401791

Lipoic Acid an organic compound, forming a disulfide bond, available as a dietary supplement PMID:15246746, 21073761

Carnitine PMID:15246746, 10581232

Vitamin D upregulated expression of GCLC and GR. PMID:23770363

Vitamin D3_ PMID:12416023

Vitamin E_ PMID:10459841, 8360018, 18296478, 21845802, 15490422, 16885600, 7062348, 20729758, 21086752

Shidagonglao roots Mahonia fortunei (十大功劳 shi da gong lao) species contains the alkaloid berberine PMID:199382 18

Coenzyme Q10 (CoQ10) PMID:16621054

Trigonella foenum graecum seed powder (TSP) PMID:15026271

Boschniakia rossica, a Traditional Chinese medicine. PMID:19352025

Aegle marmelos commonly known as bael is a species of tree. PMID:18830880

Scoparia dulcis A medicinal plant, dulcis. PMID:21905284

Fenugreek (Trigonella foenum-graecum) is used as a herb. PMID:15026271

L-arginine (L-Arg) semiessential supplementation common natural amino acid. PMID:16038634

Hypericum perforatum (St. John's Wort) PMID:18754092

Urtica dioica often called common nettle PMID:12834006

Usnea longissima, a medicinal lichen. PMID:16169175

Capparis decidua, a fruting tree also used in folk medicine and herbalism. PMID:22272107

Indole-3-carbinol found at relatively high levels in cruciferous vegetables such as broccoli

PMID:9512722, 14512388

Ascorbate Vitamin C. PMID:14512388

Sulforaphane It is obtained from cruciferous vegetables such as broccoli. PMID:12628444, 18607771*, 22303412

Andrographis paniculata, may shorten the duration and lessen the symptoms of common cold. PMID:11507728

Vitamin B-1 (thiamine) PMID:1132146, 10450194, 21308351*, 11514662*, 1270885

Vitamin B2 (riboflavin) PMID: 5822598, 5550591, 1201246, 5794396, 237845, 3677785, 3582603, 12194936, 2721660, 1261528, 5721130, 14608016, 4400882, 7883462, 844948, 7337797, 5881,12641409, 4393763, 3497609, 16883966...(№ 1244, OMIM.138300)

Vitamin B-6 (Pyridoxine) PMID:2721660, 3582603, 10450194, 15490422, 1270885, 7417521, 7337797, 7814235

Vitamin B9 (Folic acid)  PMID: 844947, 1270885

Aspartate transaminase (AST) or glutamic oxaloacetic transaminase (GOT) catalyzes the interconversion of aspartate an important enzyme in amino acid metabolism. PMID:1132146, 10450194, 1253408

β-Carotene is a strongly colored red-orange pigment abundant in plants and fruits. PMID:19957244

3-Hydroxykynurenine (3OHKyn) a metabolite of tryptophan. PMID:11273669

Ajoene ((E,Z)-4,5,9-trithiadodeca-1,6,11-triene 9-oxide), a garlic-derived natural compound. PMID:9986706 PDB: 1BWC

Propolis a product made by bees. PMID:19394397

Resveratrol produced naturally by several plants PMID:12797471