

Characterization of human thioredoxin system and the potential cellular responses encoded to observe the Thioredoxin-Trx1 reversibly regulated redox sites.

Thioredoxin: human TXN, is a oxidoreductase enzyme in the status of a [12 kDa](#) cellular [redox](#)-reductase reaction ([70-kDa](#) in bacteria, fungi and plants), a [cellular](#) defense mechanisms against oxidative stress of the cell, and numerous cytosolic processes in [all cells](#). Txn1 is a [pleiotropic](#) cellular causative gene factor which has [numerous](#) functions. Chromosome [3p12-p11](#) shares homology with human thioredoxin gene Trx1, Trx80: 9q31.3; ([§](#), [±](#)). Here the following reaction is the possible mechanisms of the thioredoxin-catalyzed reduction and re-oxidation of its characteristic cystine residues.

The TXN gene, consists of the first of 5 [exons](#) separated by 4 introns and is located [22 bp](#) downstream from the only known basal [TATA](#) box factor [TBP-2](#)/TXNIP vitamin [D\(3\)](#) up-regulated [protein](#) 1-[VDUP1](#), [negatively](#) regulating [TRX](#) function, and exhibiting [cellular](#) growth and [suppressive](#) (cancer) activity. [TRX](#) inhibited [Apoptosis](#) signal-regulating kinase-[ASK1](#) kinase ([MAP3K5](#)), activity, dependent on two [cysteine](#) residues in the N-terminal domain of [ASK1](#) on the redox ([regulation](#)) forming intramolecular disulfide between the status of TXN. Two cysteine residues (N-terminal [C32S](#) or Trx C-terminal [C35S](#) and/or a Trx-CS double [mutation](#)) remaining trapped with the Ask1 as a inactive high-[molecular-mass](#) complex, blocking its reduction to release Trx from ASK1 depends on intramolecular disulfide to catalyze the reduction of the [redox](#) regulation of [TRX](#). Trx and a thiol-specific antioxidant [thioredoxin peroxidase-2](#) orthologue ([Tpx](#)) in [various*](#) biological [phenomena](#) is involved in redox regulation ([NADPH](#)-the thioredoxin [system](#)) of the [dithiol-disulfide](#) active site.

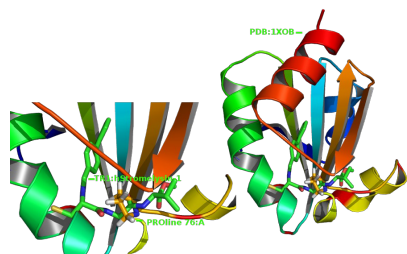
An [apoptosis](#) signal transduction pathway through stimulus-coupled [S-nitrosation](#) of [cysteine](#), has [two](#) critical ([almost identical](#)) cysteine residues in the Trx redox-active center. Where a [disulfide](#) exchange reaction between [oxidized](#) Txnip [thioredoxin-interacting protein; mouse [Vdup1](#)] and reduced TXN occurs. [Txnip](#) ([-when used](#) to investigate [cardiac](#) hypertrophy) is a regulator of [biomechanical](#) signaling. Hydrogen peroxide downregulated expression is the only [known](#) function associated with an [incomplete](#) TRX response through stimulus-coupled S-nitrosation of cysteine residues. Peroxiredoxin [PrxIII](#)-[Tpx1](#) serves as' a tandem (dimer) thioredoxin (Trx2) and [NADP](#)-linked thioredoxin reductase ([TRR2](#)-TxnR1), are Trx mechanisms of the [two electron](#) donor system.

Cytosolic [caspase-3](#) was maintained by S-nitrosation, consistent with [cytosolic](#) and

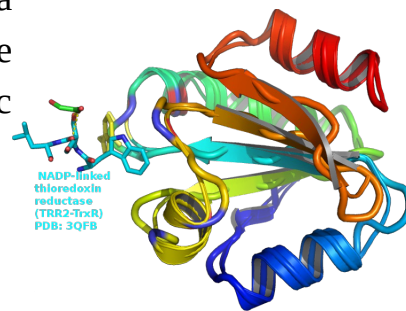
mitochondria, Trx-1 contain [equivalent](#) Trx [systems](#), which enabled identification of [caspase-3](#) substrates [where TXN](#) may regulate S-nitrosation with the redox center of TXN specific (C73S) to Nitric oxide-[NO](#) cellular signal [transduction](#) associated with inhibition of [apoptosis](#) or mutant Trx neurotoxicity. [EGCG](#)^o (epigallocatechin-3-gallate) may be useful in cell survival on caspase-(3-dependent)-[neuronal](#) apoptosis where a membrane reaction, a reduced [hormesis](#) consequently triggers the apoptosis effect and direct or indirectly numerous [protein-protein](#) interactions and basal [cofactor](#) substrates which occur between [caspase-3](#) and Trx. The effect of exercise [training](#) via activation of [caspase-3](#) has a decrease in [superoxide](#), and increase of Trx-1 levels in [brain](#). Protection from [mechanical](#) stress identified, NSF- [N-ethylmaleimide](#) transduced into a TRX [peroxidase](#) response via mechanical force of a typical transnitrosylated Casp3, attenuated Trx1 [2-cysteines](#) which directly transnitrosylates Peroxiredoxins. C32S ([redox potential](#)) was identified as thiol-[reducing system](#), which [lacks](#) reducing activity (non-active C69S and Cys(73) both monomeric) or a [reversible](#) regulating function in the presence of caspase 3 activity is a process found in the presence of NADP and TrxR. There are at least two [thioredoxin](#) reductive or [oxidative](#)** ([reductases](#) / [peroxiredoxin](#)) regulated systems. The mutant 32CXXC35' [motif](#) of thioredoxin [nitrosation](#) sites, where [two cysteines](#) are separated by two other amino acids, and [codes](#) for an additional [three](#) cysteines where the Cys 62/C73S ([not monomers](#)) sidechain the active site of [Cys 62](#) also can form several disulphides and be modified by the carbon-bonded [sulfhydryl](#), where the thiol [reducing](#) system, was evident. [Intracellular](#) TRX/[ADF](#) (Adult T cell [leukemia](#)-derived factor [HTLV-I](#)) can regulate cell [nuclei](#), protein-[nucleic](#) acid interactions. [Transnitrosylation](#) and [denitrosylation](#) is a reversible Post-translational ([PTM](#)) altered by redox [modification](#) of different cysteine residues (C32-73S) in Trx1, [S-nitrosation](#) or its interactions with [other](#) proteins and [DNA-dependent](#) nuclear processes. [NFKappaB](#) - [REF-1](#) redox factor 1 involving [Cys62](#), in the [two complexes](#), are correlated as N $\Leftrightarrow$ C-terminal responses with TRX-1 [nuclear migration](#) through the [reduction](#) of a pleiotropic cellular factor. TRX [redox](#) activities of protein-[protein](#) cysteine residues is identical to a [DNA repair](#) enzyme through various [cytoplasmic](#) aspects [mediating](#) cellular responses in the '[nucleus](#)'. The [DNA](#) binding [activity](#) and [transactivation](#) of '[AP-1](#)' activator proteins ([JUN-proto](#)* oncogen) depends on the [reduction](#) between the [sulfhydryl](#) of cysteines to keep Trx1 [reduced](#), is demonstrated in cells. [Selenium](#)-dependent [seleneocysteine](#) based peroxidase reductants, reduce [Lipoic](#) acid stereoselectively under the same TRX rather than [GSH-PX1](#)-glutathione peroxidase oxidative stress [conditions](#). [Sense-antisense](#) (TRX)

[antiapoptotic](#) interactions [nitrosylated](#) at Cys73 are [attenuated](#) and integrated into the host cell under oxidative [conditions](#), in which thioredoxin (TRX), and a cellular TRX reducing catalyst agent ([DTT](#)-redox reagent) to S-nitrosogluthathione ([GSNO](#)) intermediate [via](#) cysteine residues 'influences'-catalyst [mediated](#) (post-translational modifications) PTMs; and [possibly](#) 1,25D(3)-Calcitriol; NADPH:[oxygen](#) oxidoreductases correlated with ([Trx-1](#)) a protein [disulfide](#) oxidoreductase. [Peroxynitrite](#)** converts superoxide to hydrogen peroxide ([H2O2](#))-induced Trx [degradation](#), in concentrations that detoxify [reactive oxygen](#) species ([ROS](#)), demonstrated by superoxide dismutases (SOD)-[catalase](#): $\leftarrow$ and peroxidases, converting superoxide to hydrogen peroxide which is decomposed to water plus [oxidized](#) thioredoxin to maintain the [anti-apoptotic](#) (C62) function of thioredoxins additional [five](#) sulfhydryl group [thiols](#) in the fully reduced state, in a [Trx-dependent](#) manner. Reactive oxygen species ([ROS](#)) can cause DNA damage, and uncontrolled cellular [proliferation](#) or apoptotic death of [cancer](#) cells. The [NADPH](#) ([Trx system](#)) oxidizing [substrate](#)-dependent [reduction](#) of Thioredoxin reductase-[TrxR](#) has a [reversibly](#) modulated role in restoration of [GR](#) (glucocorticoid [receptor](#)) function, and [DNA](#) binding domain.

(Click on image to Zoom)

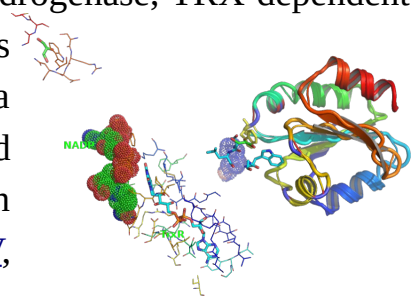
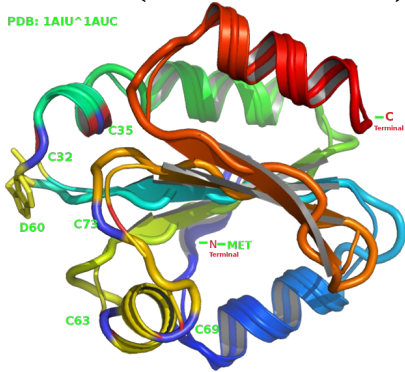


Secreted Trx may participate in removing inhibitors of collagen-degrading metalloproteinases. PMID: [14503974](#) the molecular mechanisms underlying functional the TR1-Trx1 redox pair and structure determination of an active site of the ligand mini-stromelysin-1 TR-1 augmentation composed of TR (Trx reductase activities) the main function of [TR1](#) here is to reduce Trx1 also validated as a ligand PMID; [23105116](#), have been characterized between ligand bound and free structures PMID; [20661909](#), for specific isolation of C35S selenocysteine (SeCys)-containing protein shows the best docking position found, consists of one strand at position [PROline]76:A.side chain: from the four-stranded antiparallel beta sheet was with wild-type TrxA C32-35S located in the Thioredoxin_fold (PDB accession code 1XOB: PMID: [15987909](#)) , TR1 as a single hybrid PDB (Cys32 and Cys35 for Trx1, and for TR1) pubmed/[20536427](#) investigate the possible mechanism. {{{During this reduction, the thiol-disulfide oxidoreductase thioredoxin-1 (Trx1) linked thioredoxin reductase (TRR2) a working model suggesting that deregulation of the thioredoxin reductase TXNRD1 and}}}} its characteristic



substrate thioredoxin (TR [1]), concomitant with diminution of their Trx reductase cellular contents is highly related to glutamate excitotoxicity PMID: [20620191](#); TR1: hStromelysin-1

An ET (electron transfer) mechanism from NADPH and another enzyme thioredoxin reductase pubmed/[17369362](#) the charged residue aspartate D60 (Fig.2) pubmed/[9369469](#)/ plays a role in the degradation of proteins and in apoptotic processes induced by oxidative stress PMID: [16263712](#) to determine the effect of [zerumbone](#) ZSD1 (from shampoo ginger; Name: [Alpha-humulene](#)) on NADP-malate dehydrogenase, TRX dependent oxidoreductase, that NADPH does not contain. Monomeric Thioredoxin is present across phyla from humans to plants PMID: [20661909](#), [11012661](#) mediated in vivo by thioredoxin-catalyzed reduction and re-oxidation of cystine residues PubMed id: [10196131](#) (Fig.3-PDB: [1CIV](#), NADP). Trx is able to activate vegetal NADP-malate dehydrogenase PMID: [3170595](#) (excluding the initial methionine) Met is located at the N-terminal - PMID: [11807942](#), [2684271](#). A relatively rigid local configuration for the TRX-aspartate residue D60 is found but which implies that the (NADP-TrxR) protein fluctuates among the numerous protein models and mutations over the time scales fluctuations.



- Trx (thioredoxin) a redox-regulating protein also controls the antioxidant enzyme activity of the main cellular antioxidant enzymes (AOE) superoxide dismutase (SOD) and catalase. [[↔](#)]
- (Reference: 1-189)

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