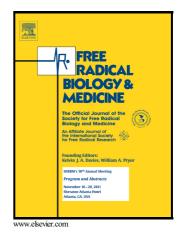
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Jianqiang Xu, Qing Cheng, Elias S.J. Arnér



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ACCEPTED MANUSCRIPT

Details in the Catalytic Mechanism of Mammalian Thioredoxin Reductase 1 Revealed Using Point Mutations and Juglone-Coupled Enzyme Activities

Jianqiang $Xu^{*,\dagger}$, Qing Cheng[†] and Elias S.J. Arnér^{†,‡}

* School of Life Science and Medicine, Dalian University of Technology, Panjin 124221, China.
† Division of Biochemistry, Department of Medical Biochemistry and Biophysics, Karolinska Institutet, SE-171 77, Stockholm, Sweden.

[‡] To whom correspondence should be addressed. Tel.: 46-8-5248-69-83; Fax: 46-8-31-15-51; E-mail: Elias.Arner@ki.se.

§ Abbreviations used are: Trx, thioredoxin; TrxR, thioredoxin reductase; TrxR1, thioredoxin reductase 1; Sec or U, selenocysteine; Cys or C, cysteine; Trp or W, tryptophan; Ser or S, serine; Asn or N, asparagine; Ala or A, alanine; Gly or G, glycine; juglone, 5-hydroxy-1,4-naphthoquinone; DNCB, 1-chloro-2, 4-dinitrobenzene; DTNB, 5, 5'-dithiobis (2-nitrobenzoic acid); DTT, dithiothreitol; FAD, flavin adenine dinucleotide; NADPH, nicotinamide adenine dinucleotide phosphate, reduced form; SecTRAPs, selenium-compromised thioredoxin reductase-derived apoptotic proteins; ROS, reactive oxygen species; -GCUG, wild-type TrxR1; -GCCG, the Sec-to-Cys variants of TrxR1; -GC or Δ 2, the Sec-truncation of TrxR1 which is missing the last two amino acid residues –Sec-Gly-COOH; -G or Δ 3, the further truncation of TrxR1 which is missing the last three amino acid residues –Cys-Sec-Gly-COOH.

ABSTRACT

The mammalian selenoprotein thioredoxin reductase 1 (TrxR1) is a key enzyme in redox regulation, antioxidant defense, and cellular growth. TrxR1 can catalyze efficient reduction of juglone (5-hydroxy-1,4-naphthoquinone; walnut toxin) in a reaction which, in contrast to reduction of most other substrates

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