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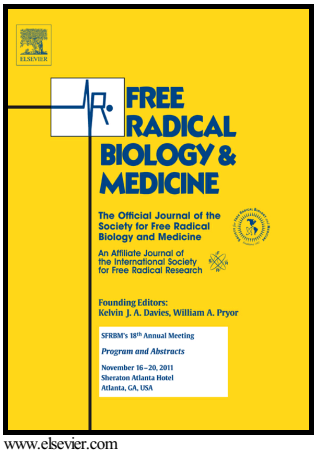

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NADPH-dependent and -independent Disulfide Reductase Systems

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Summary

Over the past seven decades, research on autotrophic and heterotrophic model organisms has defined how the flow of electrons ("reducing power") from high-energy inorganic sources, through biological systems, to low-energy inorganic products like water, powers all of Life's processes. Universally, an initial major biological recipient of these electrons is nicotinamide adenine dinucleotide-phosphate, which thereby transits from an oxidized state ($NADP^+$) to a reduced state (NADPH). A portion of this reducing power is then distributed *via* the cellular NADPH-dependent disulfide reductase systems as sequential reductions of disulfide bonds. Along the disulfide reduction pathways, some enzymes have active sites that use the selenium-containing amino acid, selenocysteine, in place of the common but less reactive sulfur-containing cysteine. In particular, the mammalian/metazoan thioredoxin systems are usually selenium-dependent as, across metazoan phyla, most thioredoxin reductases are selenoproteins. Among the roles of the NADPH-dependent disulfide reductase systems, the most universal is that they provide the reducing power for the production of DNA precursors by ribonucleotide reductase (RNR). Some studies, however, have uncovered examples of NADPH-independent disulfide reductase systems that can also support RNR. These systems are summarized here and their implications are discussed.

Abbreviations

Ahp, alkyl hydroperoxide reductase; APS, 5'-adenylylsulfate; BSO, buthionine sulfoximine ; CoA, coenzyme A; Cys, cysteine; EGFR, epidermal growth factor receptor; ER, endoplasmic reticulum; FTR, ferredoxin-thioredoxin reductase; Gpx, glutathione peroxidase; Grx, glutaredoxin; GSH, reduced glutathione; Gsr, glutathione reductase; GSSG, oxidized glutathione, glutathione-disulfide; Hcy, homocysteine; LA, lipoic Acid; Lpd, lipoic acid dehydrogenase; Met, methionine ; Msr, methionine-sulfoxide reductase; NAD^+, nicotinamide adenine dinucleotide, oxidized; NADH, nicotinamide adenine dinucleotide, reduced; $NADP^+$, nicotinamide adenine dinucleotide phosphate, oxidized; NADPH, nicotinamide