Detoxification of Reactive Oxygen Species


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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

17/11/2022
Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 82

This document contains 1 pathway and 34 reactions (see Table of Contents)
Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-3299685

Compartments: cytosol, endoplasmic reticulum lumen, extracellular region, mitochondrial inner membrane, mitochondrial intermembrane space, mitochondrial matrix, peroxisomal matrix

Reactive oxygen species such as superoxide (O2⁻⁻), peroxides (ROOR), singlet oxygen, peroxynitrite (ONOO⁻⁻), and hydroxyl radical (OH⁻) are generated by cellular processes such as respiration (reviewed in Murphy 2009, Brand 2010) and redox enzymes and are required for signaling yet they are damaging due to their high reactivity (reviewed in Imlay 2008, Buettner 2011, Kavdia 2011, Birben et al. 2012, Ray et al. 2012). Aerobic cells have defenses that detoxify reactive oxygen species by converting them to less reactive products. Superoxide dismutases convert superoxide to hydrogen peroxide and oxygen (reviewed in Fukai and Ushio-Fukai 2011). Catalase and peroxidases then convert hydrogen peroxide to water.

Humans contain 3 superoxide dismutases: SOD1 is located in the cytosol and mitochondrial intermembrane space, SOD2 is located in the mitochondrial matrix, and SOD3 is located in the extracellular region. Superoxide, a negative ion, is unable to easily cross membranes and tends to remain in the compartment where it was produced. Hydrogen peroxide, one of the products of superoxide dismutase, is able to diffuse across membranes and pass through aquaporin channels. In most cells the primary source of hydrogen peroxide is mitochondria and, once in the cytosol, hydrogen peroxide serves as a signaling molecule to regulate redox-sensitive proteins such as transcription factors, kinases, phosphatases, ion channels, and others (reviewed in Veal and Day 2011, Ray et al. 2012). Hydrogen peroxide is decomposed to water by catalase, decomposed to water plus oxidized thioredoxin by peroxiredoxins, and decomposed to water plus oxidized glutathione by glutathione peroxidases (Presnell et al. 2013).

Literature references


### Editions

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**SOD1:Zn2+ apoenzyme binds CCS:Zn2+:2xCu1+**

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3697860

**Type:** binding

**Compartments:** cytosol


**Followed by:** 2xSOD1:CCS:Zn2+:2xCu1+ dimer dissociates

**Literature references**


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**Preceded by:** SOD1:Zn2+ apoenzyme binds CCS:Zn2+:2xCu1+

**Followed by:** CCS transfers Cu to SOD1 and oxidizes cysteine residues in SOD1

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Copper chaperone of superoxide dismutase (CCS) transfers a copper(I) atom to a SOD1 monomer that already contains a Zn atom. After initial heterodimerization between SOD1 and CCS, the copper atom is transferred, intramolecular cysteine disulfide bonds are formed in SOD1, and SOD1 dimerizes (Banci et al. 2012, Casareno et al. 1998, Culotta et al. 1997, Rae et al. 2001, Brown et al. 2004, Carroll et al. 2006, Kawamata and Manfredi 2008). The transfer of copper to SOD1 requires oxygen but it is unknown at which step the oxygen acts (Brown et al. 2004). There is also a CCS-independent, oxygen-independent pathway of maturation of SOD1 (Leitch et al. 2009) whose molecular details and physiological role are not well characterized.

**Preceded by:** 2xSOD1:CCS:Zn2+:2xCu1+ dimer dissociates

**Followed by:** SOD1 catalyzes 2H+ + 2O2.- => O2 + H2O2 (cytosol)

**Literature references**


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**SOD1:Zn2+ apoenzyme binds CCS:Cu1+ (mitochondrial)**

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3780958

**Type:** binding

**Compartments:** mitochondrial intermembrane space

**Inferred from:** SOD1:Zn2+ apoenzyme binds CCS:Zn2+:2xCu1+ (Homo sapiens), Sod1 apoenzyme binds Ccs (Mus musculus)

As inferred from the cytosolic reaction and from the mouse mitochondrial reaction, Copper chaperone of superoxide dismutase (CCS) transfers a copper(I) atom to a SOD1 monomer that already contains a Zn atom. The reaction proceeds by a two step mechanism in which SOD1 first forms heterodimers with CCS. The amounts of CCS and SOD1 in the intermembrane space appear to be regulated by the concentration of oxygen. Mutations in SOD1 are responsible for familial amyotrophic lateral sclerosis (fALS) and cause unregulated localization and aggregation of SOD1 in the intermembrane space (reviewed in Kawamata and Manfredi 2010).

**Followed by:** CCS transfers Cu to SOD1 (mitochondrial)

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**CCS transfers Cu to SOD1 (mitochondrial)**

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3780979

**Type:** transition

**Compartments:** mitochondrial intermembrane space

**Inferred from:** Ccs transfers Cu to Sod1 (Mus musculus), CCS transfers Cu to SOD1 and oxidizes cysteine residues in SOD1 (Homo sapiens)

As inferred from the cytosolic reaction and from the mitochondrial reaction in mouse, Copper chaperone of superoxide dismutase (CCS) transfers a copper(I) atom to a SOD1 monomer that already contains a Zn atom. After initial heterodimerization between SOD1 and CCS, the copper atom is transferred, intramolecular cysteine disulfide bonds are formed in SOD1, and SOD1 dimerizes.

**Preceded by:** SOD1:Zn2+ apoenzyme binds CCS:Cu1+ (mitochondrial)

**Followed by:** SOD1 catalyzes 2H+ + O2.- => O2 + H2O2 (mitochondrial intermembrane space)

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ATP7A transfers Cu from ATOX1 to SOD3

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3697838

**Type:** omitted

**Compartments:** trans-Golgi network membrane, Golgi lumen, cytosol

**Inferred from:** Atp7a transfers Cu from Atox1 to Sod3 (Mus musculus)

As inferred from mouse, ATP7A (Menke's ATPase, MNK) transports copper from ATOX in the cytosol to SOD3 in the lumen of the trans golgi network. ATP7A and SOD3 directly interact. Mutations in ATP7A cause Menke's disease, a neurodegenerative condition.

**Followed by:** Secretion of SOD3

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Secretion of SOD3

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-4837364

Type: omitted

Compartments: Golgi lumen, extracellular region

SOD3 is secreted from cells into the extracellular region. Before secretion a portion of SOD3 molecules are cleaved near the C-terminus at glutamate-227 (glutamate-209 in the mature protein) (Olsen et al. 2004, Karlsson et al. 1993). Removal of the C-terminus prevents interaction with the extracellular matrix so cleaved molecules are soluble. Cleaved and uncleaved molecules are believed to be capable of forming mixed tetramers (Sandstrom et al. 1993).

Preceded by: ATP7A transfers Cu from ATOX1 to SOD3

Followed by: SOD3 catalyzes 2H⁺ + 2O₂⁻ → O₂ + H₂O₂ (extracellular)

Literature references


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NOX4, NOX5 reduce O2 to O2.-

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-6807557

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

NADPH oxidases 4 and 5 (NOX4, 5) are ER membrane-bound proteins that generates superoxide (O2.-) in endothelial cells (BelAiba et al. 2007). NOX4 functions in association with cytochrome b heterodimer (CYBA:CYBB) on the ER (and nuclear) membrane (Martyn et al. 2006).

Literature references


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Cu-Zn superoxide dismutase (SOD1), originally known as erythrocuprein, catalyzes the reaction of two molecules of superoxide (O2•-) to yield one molecule of hydrogen peroxide (H2O2) and one molecule of oxygen (O2) (McCord and Fridovich 1969 assayed both bovine and human Cu-Zn superoxide dismutase, the human sample provided by Carrico and Deutsch). Diffusion of hydrogen peroxide, the product of SOD1, across the cytosol is limited (Mishina et al. 2011)

**Preceded by:** CCS transfers Cu to SOD1 and oxidizes cysteine residues in SOD1

**Followed by:** GPX1 catalyzes reaction of reduced glutathione and H2O2 to form oxidized glutathione and H2O, GPX2 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O, PRDX1,2,5 catalyze TXN reduced + H2O2 => TXN oxidized + 2H2O, PRDX6:GSTP1 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O

**Literature references**


SOD1 catalyzes \(2H^+ + O_2^- \rightarrow O_2 + H_2O_2\) (mitochondrial intermembrane space)

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-3777112

Type: transition

Compartments: mitochondrial intermembrane space

A portion of SOD1 is located in the mitochondrial intermembrane space (IMS) where it catalyzes the formation of oxygen (O2) and hydrogen peroxide (H2O2) from superoxide (O2^-) (He et al. 2011, Higgins et al. 2002, inferred from rat in Okado-Matsumoto and Fridovich 2001).

Preceded by: CCS transfers Cu to SOD1 (mitochondrial)

Literature references


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Mn superoxide dismutase (SOD2) is located in the mitochondrial matrix where it catalyzes the reaction of two molecules of superoxide (O2−) to form one molecule of oxygen (O2) and one molecule of hydrogen peroxide (H2O2). Data from mouse liver indicate that respiratory complex I leaks superoxide into the matrix and respiratory complex III leaks superoxide into both the matrix and the intermembrane space (Muller et al. 2004). Because of its negative charge superoxide is unable to cross membranes, however hydrogen peroxide, a product of SOD2, is released from mitochondria to the cytosol in proportion to the proton potential (inferred from rat heart mitochondria in Boveris et al. 2006, Korshunov et al. 1997). Followed by: H2O2 diffuses from the mitochondrial matrix to the cytosol, PRDX3,5 catalyze TXN2 reduced + H2O2 => TXN2 oxidized + 2H2O, GPX1 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O

Literature references


SOD3 catalyzes $2\text{H}^+ + 2\text{O}_2.- \to \text{O}_2 + \text{H}_2\text{O}_2$ (extracellular)

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-3299682

Type: transition

Compartments: extracellular region

Extracellular Cu-Zn superoxide dismutase (SOD3) catalyzes the reaction of two molecules of superoxide ($\text{O}_2.-$) to form one molecule of oxygen ($\text{O}_2$) and one molecule of hydrogen peroxide ($\text{H}_2\text{O}_2$) (Marklund et al. 1982, Marklund 1982)

Preceded by: Secretion of SOD3

Followed by: GPX3 catalyzes $2$ glutathione, reduced $+$ $\text{H}_2\text{O}_2 \to$ glutathione, oxidized $+$ $2$ $\text{H}_2\text{O}$

Literature references


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H2O2 diffuses from the mitochondrial matrix to the cytosol

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3779381

**Type:** transition

**Compartments:** mitochondrial inner membrane, mitochondrial matrix, cytosol

**Inferred from:** H2O2 diffuses from the mitochondrial matrix to the cytosol (Rattus norvegicus)

As inferred from rat heart mitochondria, hydrogen peroxide is released from mitochondria at a rate that is dependent on the membrane potential. Knockdown of Aquaporin-8 (AQP8) in human cells indicates that hydrogen peroxide is able to transit through the water channel of AQP8 located in the inner mitochondrial membrane (Marchissio et al. 2012). The resulting level of cytosolic hydrogen peroxide is hypothesized to signal the state of the mitochondria to regulatory molecules in the cytosol and nucleus (reviewed in Antico Arciuch et al. 2012).

**Preceded by:** SOD2 catalyzes 2H+ + 2O2.- => O2 + H2O2 (mitochondrial matrix)

**Literature references**


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[https://reactome.org](https://reactome.org)
H2O2 → O2 + 2 H2O

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-76031

Type: transition

Compartments: peroxisomal matrix

Hydrogen peroxide is generated in the course of peroxisomal fatty acid oxidation and purine catabolism, and is rapidly converted to water and molecular oxygen by the enzyme catalase. This enzyme is widely distributed in the body, but is especially abundant in liver, kidney, and red blood cells.

Literature references


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GPX1 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3323013

**Type:** transition

**Compartments:** mitochondrial matrix

Glutathione peroxidase 1 (GPX1) located in the mitochondrial matrix (Bera et al. 2014) uses glutathione to reduce hydrogen peroxide (H2O2) to yield oxidized glutathione and water (Legault et al. 2000, Li et al. 2000, Faucher et al. 2003, Lu et al. 2012). As inferred from rat mitochondria, GPX1 is the major determinant of steady-state hydrogen peroxide levels (Antunes et al. 2002).

**Preceded by:** SOD2 catalyzes 2H+ + 2O2.- => O2 + H2O2 (mitochondrial matrix)

**Followed by:** GSR catalyzes glutathione (oxidized) + NADPH + H+ => 2 glutathione (reduced) + NADP+

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GSR catalyzes glutathione (oxidized) + NADPH + H+ => 2 glutathione (reduced) + NADP+ ↗

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-3323079

Type: transition

Compartments: mitochondrial matrix

Glutathione reductase (GSR) in the mitochondrial matrix regenerates reduced glutathione from oxidized glutathione and NADPH (Berkholz et al. 2008).

Preceded by: GPX1 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O

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GPX1 catalyzes reaction of reduced glutathione and H2O2 to form oxidized glutathione and H2O

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-71676

**Type:** transition

**Compartments:** cytosol

Cytosolic glutathione peroxidase (GPX1) tetramer catalyzes the reaction of reduced glutathione and hydrogen peroxide to form reduced glutathione and water (Chu et al. 1993).

**Preceded by:** SOD1 catalyzes $2\text{H}^+ + 2\text{O}_2.- \Rightarrow \text{O}_2 + \text{H}_2\text{O}_2$ (cytosol), glutathione (oxidized) + NADPH + H+ $\Rightarrow$ 2 glutathione (reduced) + NADP+

**Literature references**


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https://reactome.org
glutathione (oxidized) + NADPH + H+ => 2 glutathione (reduced) + NADP+

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-71682

Type: transition

Compartments: cytosol

Cytosolic glutathione reductase catalyzes the reaction of glutathione (oxidized) and NADPH + H+ to form two molecules of glutathione (reduced) and NADP+ (Scott et al. 1963, Loos et al. 1976). Deficiency of glutathione reductase can cause hemolytic anemia.

Followed by: GPX1 catalyzes reaction of reduced glutathione and H2O2 to form oxidized glutathione and H2O

Literature references


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GPX2 catalyzes $2 \text{glutathione, reduced} + \text{H}_2\text{O}_2 \Rightarrow \text{glutathione, oxidized} + 2 \text{H}_2\text{O}$

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3341277

**Type:** transition

**Compartments:** cytosol

GPX2 (located in the gastrointestinal tract, also called GSHPx-GI, GPX-GI, and GI-GPx), like glutathione peroxidase 1 (GPX1, ubiquitous), reduces one molecule of hydrogen peroxide (H2O2) with two molecules of glutathione to yield one molecule of oxidized glutathione (glutathione disulfide, GSSG) and two molecules of water (Chu et al. 1998).

**Preceded by:** SOD1 catalyzes $2\text{H}^+ + 2\text{O}_2.- \Rightarrow \text{O}_2 + \text{H}_2\text{O}_2$ (cytosol)

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**GPX3 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O**

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3341397

**Type:** transition

**Compartments:** extracellular region

Glutathione peroxidase 3 (GPX3) in plasma reduces hydrogen peroxide (H2O2) with glutathione to yield oxidized glutathione and water (Maddipati and Marnett 1987, Takahashi et al. 1987, Chung et al. 2009, Ottaviano et al. 2009). Glutathione is synthesized in the liver and exported into the plasma.

**Preceded by:** SOD3 catalyzes 2H+ + 2O2.- => O2 + H2O2 (extracellular)

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Peroxiredoxin 3 (PRDX3) and PRDX5 in the mitochondrial matrix reduce hydrogen peroxide (H2O2) with thioredoxin to yield oxidized thioredoxin and water (Yamashita et al. 1999, Knoops et al. 1999, Cao et al. 2007, Nagy et al. 2011). Reduced PRDX5 is a monomer (Declercq et al. 2001) and oxidized PRDX5 is a dimer (Evrard et al. 2004) therefore the enzyme may cycle between states.

**Preceded by:** TXNRD2 catalyzes the reduction of TXN2 by NADPH, SOD2 catalyzes 2H+ + 2O2.- => O2 + H2O2 (mitochondrial matrix)

**Followed by:** TXNRD2 catalyzes the reduction of TXN2 by NADPH

**Literature references**


**Editions**

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https://reactome.org
Thioredoxin reductase 2 (TXNRD2) in the mitochondrial matrix regenerates reduced thioredoxin (TXN) by reacting oxidized thioredoxin with NADPH (Gasdaska et al. 1999, Cao et al. 2007).

**Preceded by:** PRDX3,5 catalyze TXN2 reduced + H2O2 => TXN2 oxidized + 2H2O

**Followed by:** PRDX5 reduces peroxynitrite to nitrite using TXN2, PRDX3,5 catalyze TXN2 reduced + H2O2 => TXN2 oxidized + 2H2O

**Literature references**


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https://reactome.org
Superoxide reduces cytochrome c

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-3341294

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial intermembrane space

Superoxide can reduce cytochrome c in the intermembrane space (Wegerich et al. 2013, and inferred from other mammals in Butler et al. 1975, Koppenol et al. 1976, Butler et al. 1982). Superoxide has been shown in rat and mouse mitochondria to be released into the intermembrane space by the complex III of the respiratory chain (Han et al. 2001, Muller et al. 2004).

Literature references


Editions

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**PRDX1,2,5 catalyze TXN reduced + H2O2 => TXN oxidized + 2H2O**

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3341343

**Type:** transition

**Compartments:** cytosol

Peroxiredoxin 1 (PRDX1), PRDX2, and PRDX5 in the cytosol reduce hydrogen peroxide (H2O2) with thioredoxin yielding oxidized thioredoxin and water (Yamashita et al. 1999, Lee et al. 2007, Nagy et al. 2011).

**Preceded by:** thioredoxin, oxidized + NADPH + H+ => thioredoxin, reduced + NADP+, SOD1 catalyzes 2H+ + 2O2.- => O2 + H2O2 (cytosol)

**Literature references**


**Editions**

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<td>Inga, A., Zaccara, S.</td>
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thioredoxin, oxidized + NADPH + H+ => thioredoxin, reduced + NADP+ ➤

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-73646

**Type:** transition

**Compartments:** cytosol

Cytosolic thioredoxin reductase catalyzes the reaction of thioredoxin, oxidized and NADPH + H+ to form thioredoxin, reduced and NADP+ (Urig et al. 2006).

Followed by: PRDX1,2,5 catalyze TXN reduced + H2O2 => TXN oxidized + 2H2O, PRDX5 reduces peroxynitrite to nitrite using TXN

**Literature references**


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| 2016-02-04 | Reviewed                | Inga, A., Zaccara, S.
GPX5,6 reduce H2O2 to H2O

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-6799695

**Type:** transition

**Compartments:** extracellular region

Epididymal secretory glutathione peroxidase (GPX5), a secreted and selenium-independent isoform of glutathione peroxidases, is present in very low levels in human sperm ejaculate. GPX5 has the potential to reduce hydrogen peroxide (H2O2) using glutathione (GSH), based on activity observed in rat and pig forms of the enzyme but its role in human epididymis is unknown (Hall et al. 1998). Glutathione peroxidase 6 (GPX6) is thought to have peroxidase activity based on sequence similarity to GPX5.

**Literature references**


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Glutathione peroxidase 7 (GPX7) and GPX8 are atypical glutathione peroxidases that catalyze the peroxidation of protein disulfide isomerases, such as PDI (P4HB) (Nguyen et al. 2011 and inferred from mouse in Bosello-Travain et al. 2013). GPX7 and GPX8 are each able to form heterodimers with the sulfhydryl oxidase ERO1alpha (ERO1L) in the endoplasmic reticulum lumen. It is hypothesized that GPX7 and GPX8 use hydrogen peroxide produced by ERO1L.

**Literature references**


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PRDX6:GSTP1 catalyzes 2 glutathione, reduced + H2O2 => glutathione, oxidized + 2 H2O

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-3343700

Type: transition

Compartments: cytosol

Peroxiredoxin 6 (PRDX6) forms a heterodimer with GSTP1 (Pi Glutathione transferase) and catalyzes the reduction of hydrogen peroxide (H2O2) by glutathione to yield oxidized glutathione and water (Ralat et al. 2006, Ralat et al. 2008, Zhou et al. 2013).

Preceded by: SOD1 catalyzes 2H+ + 2O2.- => O2 + H2O2 (cytosol)

Literature references


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https://reactome.org
Peroxiredoxin 5 (PRDX5) very efficiently reduces peroxynitrite using thioredoxin to yield nitrite (NO2-), water, and oxidized thioredoxin (Dubuisson et al. 2004). The N-terminal cysteine (Cys 47) of PRDX5 attacks the O-O peroxide bond of peroxynitrite.

**Preceded by:** thioredoxin, oxidized + NADPH + H+ => thioredoxin, reduced + NADP+, Superoxide and nitric oxide react to peroxynitrite

**Literature references**

**PRDX5 reduces peroxynitrite to nitrite using TXN2**

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3697894

**Type:** transition

**Compartments:** mitochondrial matrix

Peroxiredoxin 5 (PRDX5) very efficiently reduces peroxynitrite using TXN2 in mitochondria to yield nitrite (NO2-), water, and oxidized TXN2 (Dubuisson et al. 2004). The N-terminal cysteine (Cys 47) of PRDX5 attacks the O-O peroxide bond of peroxynitrite.

**Preceded by:** TXNRD2 catalyzes the reduction of TXN2 by NADPH, Superoxide and nitric oxide react to form peroxynitrite in mitochondria

**Literature references**


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https://reactome.org
NUDT2 hydrolyses GP4G to GTP, GMP

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-5696197

**Type:** transition

**Compartments:** mitochondrial matrix

Bis(5'-nucleosyl)-tetraphosphatase (asymmetrical) (NUDT2) mediates the asymmetrical hydrolysis of P(1),P(4)-bis(5'-guanosyl) tetraphosphate (GP4G) to yield AMP and ATP. GP4G is implicated in the regulation of cellular responses to stress and its hydrolysis could serve as a mechanism by which homeostasis is maintained by preventing its build-up (Thorne et al. 1995, Swarbrick et al. 2005).

**Literature references**


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NOX2 generates superoxide from oxygen

Location: Detoxification of Reactive Oxygen Species

Stable identifier: R-HSA-1222376

Type: transition

Compartments: phagocytic vesicle membrane, cytosol

Macrophage NOX2 is a membrane complex that generates superoxide anions by reduction of oxygen with NADPH (Babior 1999, Dinauer et al. 1991).

Followed by: Superoxide and nitric oxide react to peroxynitrite

Literature references


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Superoxide and nitric oxide react to peroxynitrite

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-1222407

**Type:** transition

**Compartments:** cytosol

Nitric oxide and superoxide rapidly combine to form peroxynitrite (Pryor & Squadrito 1995).

**Preceded by:** NOX2 generates superoxide from oxygen

**Followed by:** PRDX5 reduces peroxynitrite to nitrite using TXN

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https://reactome.org
Superoxide and nitric oxide react to form peroxynitrite in mitochondria

**Location:** Detoxification of Reactive Oxygen Species

**Stable identifier:** R-HSA-3697855

**Type:** transition

**Compartments:** mitochondrial matrix

Superoxide and nitric oxide react to form peroxynitrite within mitochondria (Huie and Padmaja 1993, Packer et al. 1996, reviewed in Radi et al. 2002).

**Followed by:** PRDX5 reduces peroxynitrite to nitrite using TXN2

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https://reactome.org
Superoxide and nitric oxide react to peroxynitrite

Superoxide and nitric oxide react to form peroxynitrite in mitochondria

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