# Mammalian antioxidant enzymes

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## Research Field and Subjects

Oxidative stress is a major biological process involved in the development of a number of acute or chronic pathological situations (inflammation, cancer, neurodegenerative diseases, atherosclerosis, lung diseases, aging). Our research is focused on identification and characterization of proteins that may play protective roles against cell death caused by oxidative stress (apoptosis and necrosis). After expression of these proteins in bacteria, in yeasts or in mammalian cells, their protective antioxidant activity is tested in different *in vitro* models such as animal and human cell lines exposed to oxidative or pro-apoptotic compounds. The yeast *Saccharomyces cerevisiae* is also used as model organism. Peroxide and peroxynitrite reductase activities of recombinant proteins are measured. Tridimensional structure is determined by X-ray crystallography.

One of the proteins currently under investigation is a novel mammalian thioredoxin peroxidase (PRDX5) which is a member of the recently identified peroxiredoxin family of antioxidant enzymes. We have solved crystal structure of PRDX5. Enzymatic activities of PRDX5 as well as its physiological implication in cellular protection against oxidative stress are also explored using *E. coli* recombinant proteins and cell transfection strategies. The deletion of the gene homologous to human *PRDX5* in *Saccharomyces cerevisiae* has been performed and revealed the importance of this protein in the defence against oxidative stress but also against heavy metal toxicity.

## Products and Services

- Gene cloning
- Recombinant proteins
- Transfection of mammalian cell lines
- Crystallography

## Main Equipment

- Cell culture equipment
- Confocal and electron microscopy
- Molecular biology equipment

## Representative References

- B. KNOOPS, A. CLIPPE, K. ARSALANE, R. WATTIEZ, C. HERMANS, E. DUCONSEILLE, P. FALMAGNE & A. BERNARD (**1999**) Cloning and characterization of AOEB166, a novel mammalian antioxidant enzyme of the peroxiredoxin family. J. Biol. Chem. 274, 30451-30458.
- J.-P. DECLERCQ, C. EVRARD, A. CLIPPE, D. VANDER STRICHT, A. BERNARD & B. KNOOPS (**2001**) Crystal structure of human peroxiredoxin 5, a novel type of mammalian peroxiredoxin at 1.5 A resolution. J. Mol. Biol. 311, 751-759.
- M.X. WANG, A. W., J. YAN, A. CLIPPE, A. BERNARD, B. KNOOPS & G.A. MURRELL (**2001**) Antioxidant enzyme peroxiredoxin 5 is upregulated in degenerative human tendon. Biochem. Biophys. Res. Commun., 284, 667-673.
- N.T. NGUYEN-NHU & B. KNOOPS (**2002**) Alkyl hydroperoxide reducatse 1 protects Saccharomyces cerevisiae against metal ion toxicity and glutathione depletion. Toxicol. Letters. 135, 219-226.
- M.X. WANG, A.WEI, J.YAN, A. TRICKETT, B. KNOOPS & G.A.C. MURRELL (**2002**) Expression and regulation of peroxiredoxin 5 in human osteoarthitis. FEBS Letters. 531, 359-362.
- F. PLAISANT, A. CLIPPE, D. VANDER STRICHT, B. KNOOPS & P. GRESSENS (**2003**) Recombinant peroxiredoxin 5 protects against excitotoxic brain lesions in newborn mice. Free Rad. Biol. Med. 34, 862-872.
- N.T. NGUYEN-NHU & B. KNOOPS (**2003**) Mitochondrial and cytosolic expression of human peroxiredoxin 5 in Saccharomyces cerevisiae protect yeast cells from oxidative stress induced by paraquat. FEBS Letters. 534, 148-152.
- G. LEYENS, I. DONNAY & B. KNOOPS (**2003**) Cloning of bovine peroxiredoxins: gene expression in bovine tissues and amino acid sequence comparison with rat, mouse and primate peroxiredoxins. Comp. Biol. Phys. In press.
- I. BANMEYER, C. MARCHAND, C. VERHAEGHE, B. VUCIC, J.-F. REES & B. KNOOPS (**2003**) Overexpression of human peroxiredoxin 5 in subcellular compartments of Chinese hamster ovary cells: effects on cytotoxicity and DNA damage caused by peroxides. Free Rad. Biol. Med. In press.

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## Patents

- B. KNOOPS, C. HERMANS, A. BERNARD, R. WATTIEZ & P. FALMAGNE (**1999**) Peroxisome-associated polypeptide, nucleotide sequence encoding said polypeptide and their uses in the diagnosis and/or the treatment of lung injuries and diseases, and of oxidative stress-related disorders. WO9909054.
- J.-P. DECLERCQ, C. EVRARD, A. CLIPPE, D. VANDER STRICHT, A. BERNARD & B. KNOOPS (**2001**) Crystal structure of PRDX5. European Patent Application n° 01870016.1.

## Partnership

- Member of the *Institut des Sciences de la Vie,* Louvain-la-Neuve, Belgium
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- Prof. J.P. BRION (ULB, BELGIUM)
- Dr. P. GRESSENS (INSERM 9935, Paris, FRANCE)
- Prof. G. MURRELL (St George Hospital Sydney, AUSTRALIA)
- Prof. L. POOLE (Wake Forest University School of Medicine, USA)
- Prof. W.H. KOPPENOL (ETH, Zurich, SWITZERLAND)
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Total: 16

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