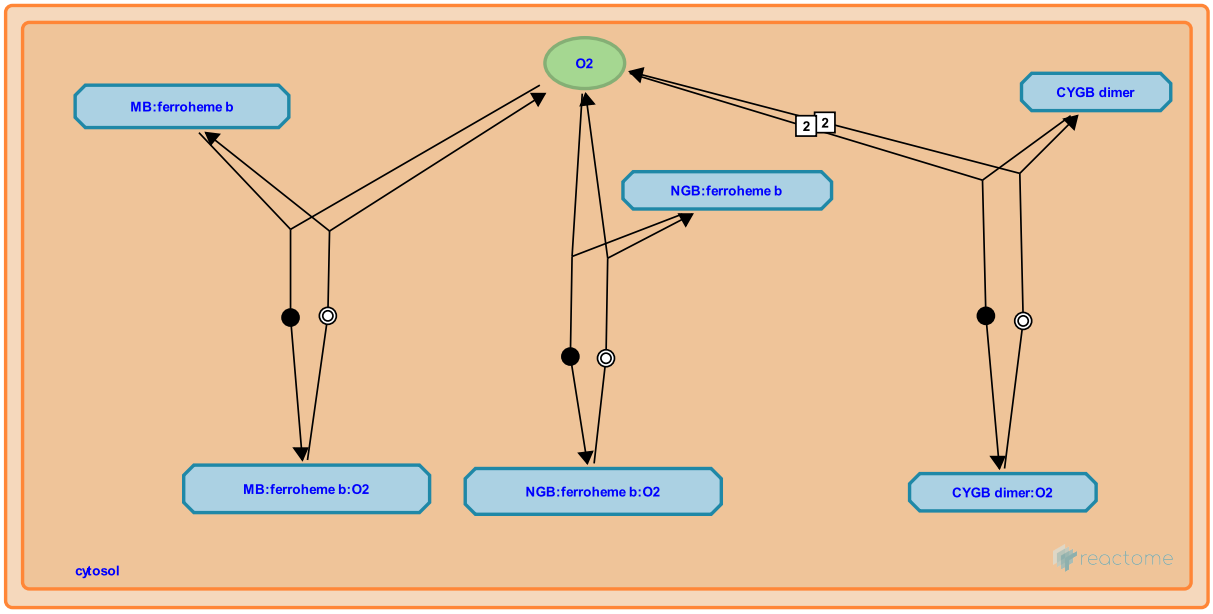
Intracellular oxygen transport



Burmester, T., D'Eustachio, P., Jassal, B., May, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

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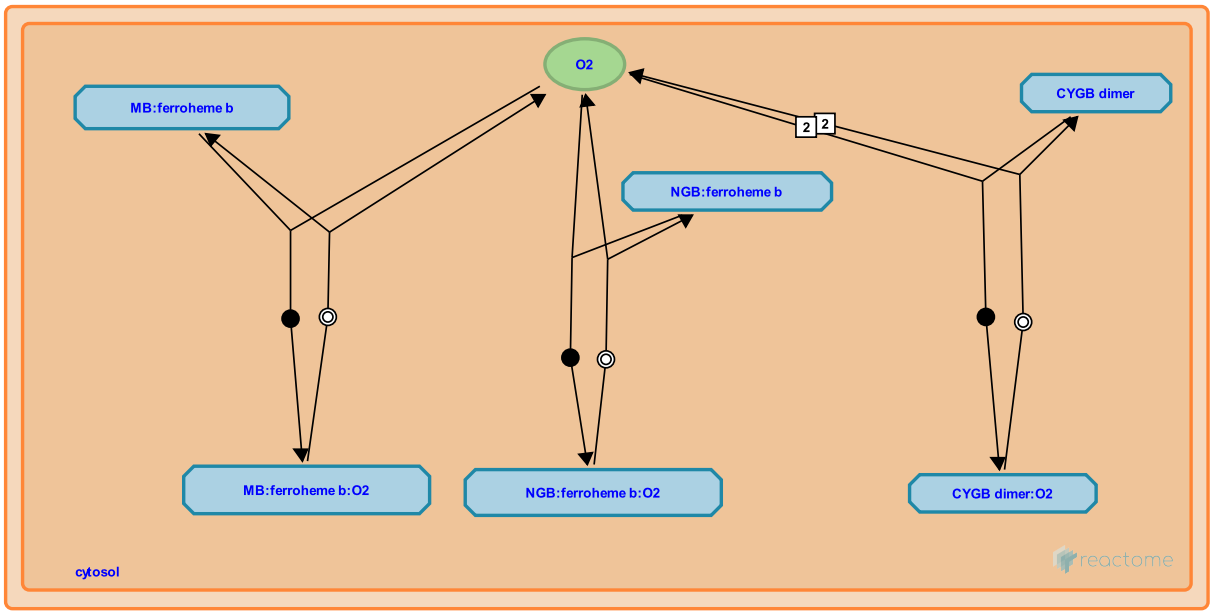
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Intracellular oxygen transport ↗

Stable identifier: R-HSA-8981607

Compartments: cytosol



Globins are heme-containing proteins that reversibly bind molecular oxygen. Humans contain at least 5 types of globins: hemoglobins, myoglobin, cytoglobin, neuroglobin, and androglobin (reviewed in Burmester et al. 2014). Myoglobin, neuroglobin, and cytoglobin are cytosolic globins with similar affinities for oxygen (reviewed in Hankeln et al. 2005). Androglobin is a more distantly related globin of uncertain function that is expressed in testes (Hoogewijs et al. 2012). Myoglobin is predominantly expressed in muscle tissue (reviewed in Helbo et al. 2013), neuroglobin is expressed in neurons, and cytoglobin is expressed in connective tissue fibroblasts and smooth muscle cells (reviewed in Pesce et al. 2002, Hankeln et al. 2004, Ascenzi et al. 2016). Whereas myoglobin contains pentacoordinated heme iron, neuroglobin and cytoglobin contain hexacoordinated heme iron: the iron atom is bound by 4 nitrogen atoms of heme and 2 histidine residues of the globin. Binding by one of the histidines is reversible, which allows the iron atom to bind various ligands such as molecular oxygen, carbon monoxide, and nitric oxide (reviewed in Kakar et al. 2010). Neuroglobin may function in oxygen homeostasis, however the importance of its oxygen-binding activity is unclear (reviewed in Pesce et al. 2002, Hankeln et al. 2005). Cytoglobin may function in nitric oxide metabolism (Thuy et al. 2016, Liu et al. 2017). Globins can also regulate oxygen homeostasis via reactions with nitric oxide (NO), a vasodilator. Oxygenated globins scavenge NO by oxidation while deoxygenated globins can act as a nitrite reductase to produce NO (reviewed in Hendgen-Cotta et al. 2014, Tejero and Gladwin 2014).

Literature references

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Editions

2015-02-11	Reviewed	D'Eustachio, P.
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2017-05-11	Reviewed	Burmester, T.

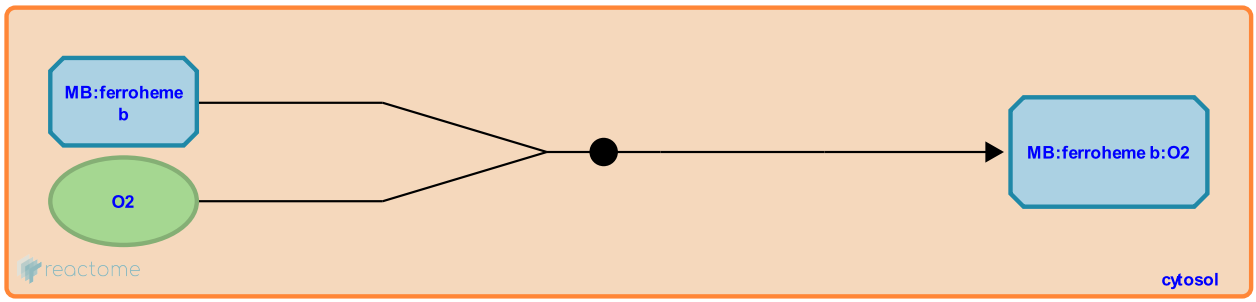
Myoglobin binds oxygen ↗

Location: Intracellular oxygen transport

Stable identifier: R-HSA-8981606

Type: binding

Compartments: cytosol



Myoglobin binds molecular oxygen (O2) in the cells of muscle tissue (Rossi-Fanelli and Antonini 1958, Boulton and Huntsman 1972, Wang et al. 2004). The dissociation constant of Myoglobin-oxygen is about 1 micromole per liter. The myoglobin:oxygen complex stores oxygen and also transports oxygen from the sarcolemma to the mitochondria. Myoglobin binds other small molecules such as nitric oxide and carbon monoxide. The ligands of myoglobin appear to migrate from the surface of the protein through pores (pockets) in the protein structure to reach the embedded heme group (reviewed in Tomita et al. 2010).

Literature references

Boulton, FE., Huntsman, RG. (1972). Variants of human myoglobin: their oxygen dissociation curves. *Br. J. Haematol. , 22*, 636-7. ↗

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Editions

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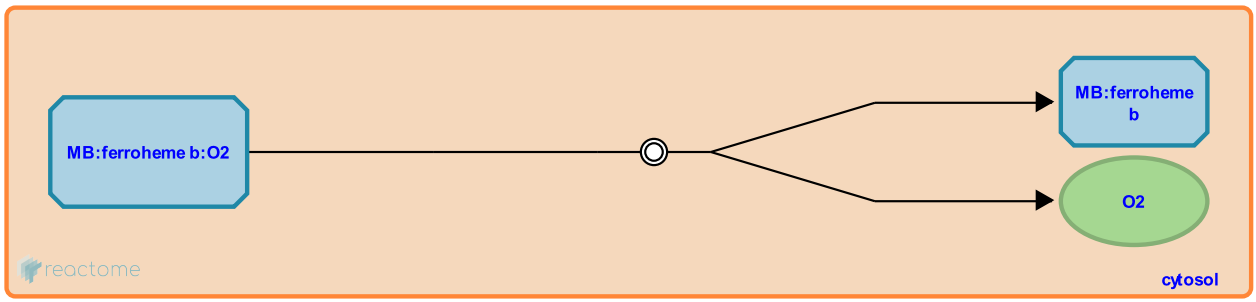
Myoglobin:oxygen dissociates ↗

Location: Intracellular oxygen transport

Stable identifier: R-HSA-8981622

Type: dissociation

Compartments: cytosol



When the concentration of oxygen is low myoglobin:oxygen dissociates to yield free oxygen (Rossi-Fanelli and Antonini 1958, Boulton and Huntsman 1972, Wang et al. 2004). The dissociation constant is about 1 micromole per liter. Myoglobin:oxygen may also transfer oxygen directly to cytochrome oxidase of mitochondria (inferred from rat homologs in Yamada et al. 2013).

Literature references

Boulton, FE., Huntsman, RG. (1972). Variants of human myoglobin: their oxygen dissociation curves. *Br. J. Haematol. , 22*, 636-7. ↗

Baskin, JS., Zewail, AH., Xia, T., Wang, Y. (2004). Human myoglobin recognition of oxygen: dynamics of the energy landscape. *Proc. Natl. Acad. Sci. U.S.A., 101*, 18000-5. ↗

ROSSI-FANELLI, A., ANTONINI, E. (1958). Studies on the oxygen and carbon monoxide equilibria of human myoglobin. *Arch. Biochem. Biophys., 77*, 478-92. ↗

Hashimoto, T., Takakura, H., Hanai, Y., Furuichi, Y., Jue, T., Masuda, K. et al. (2013). Interaction between myoglobin and mitochondria in rat skeletal muscle. *J. Appl. Physiol., 114*, 490-7. ↗

Editions

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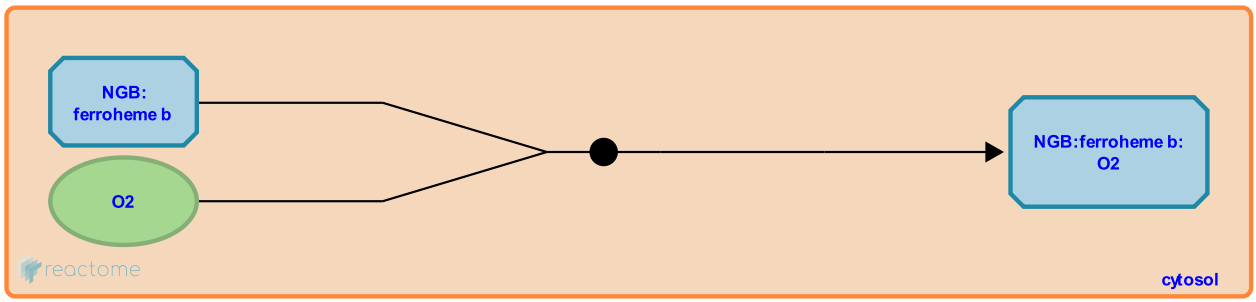
Neuroglobin binds oxygen ↗

Location: Intracellular oxygen transport

Stable identifier: R-HSA-8981610

Type: binding

Compartments: cytosol



Neuroglobin binds molecular oxygen (O2) in neurons of the central nervous system and peripheral nervous system (Burmester et al. 2000, Dewilde et al. 2001, Trent et al. 2001, Orlowski and Nowak 2008, Bocahut et al. 2009, Watanabe et al. 2012, Hundahl et al. 2013). An elongated cavity in the protein may facilitate the diffusion of oxygen to the heme (Pesce et al. 2003).

Literature references

Watts, RA., Hargrove, MS., Trent, JT. (2001). Human neuroglobin, a hexacoordinate hemoglobin that reversibly binds oxygen. *J. Biol. Chem., 276*, 30106-10. ↗

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Reinhardt, S., Weich, B., Hankeln, T., Burmester, T. (2000). A vertebrate globin expressed in the brain. *Nature, 407*, 520-3. ↗

Wakasugi, K., Watanabe, S., Uchida, H., Takahashi, N. (2012). Human neuroglobin functions as an oxidative stress-responsive sensor for neuroprotection. *J. Biol. Chem., 287*, 30128-38. ↗

Orlowski, S., Nowak, W. (2008). Topology and thermodynamics of gaseous ligands diffusion paths in human neuroglobin. *BioSystems, 94*, 263-6. ↗

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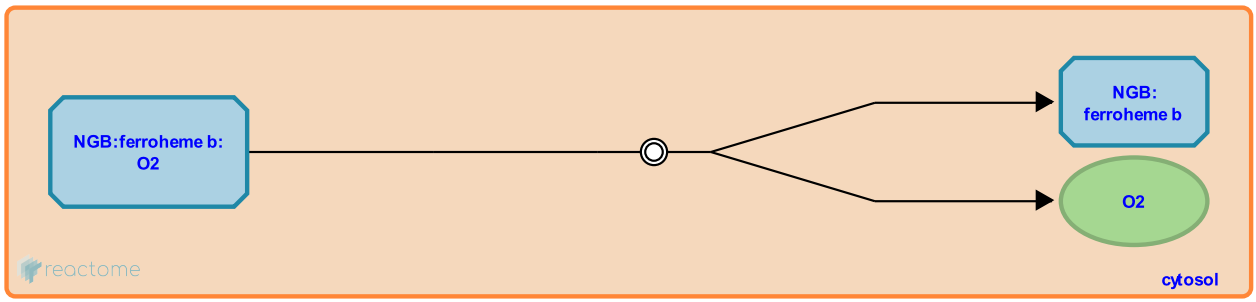
Neuroglobin:oxygen dissociates ↗

Location: Intracellular oxygen transport

Stable identifier: R-HSA-8981621

Type: dissociation

Compartments: cytosol



When the concentration of oxygen is low, neuroglobin:oxygen dissociates to yield free oxygen (Burmester et al. 2000, Dewilde et al. 2001, Trent et al. 2001).

Literature references

Watts, RA., Hargrove, MS., Trent, JT. (2001). Human neuroglobin, a hexacoordinate hemoglobin that reversibly binds oxygen. *J. Biol. Chem., 276*, 30106-10. ↗

Reinhardt, S., Weich, B., Hankeln, T., Burmester, T. (2000). A vertebrate globin expressed in the brain. *Nature, 407*, 520-3. ↗

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Editions

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2017-05-11	Reviewed	Burmester, T.

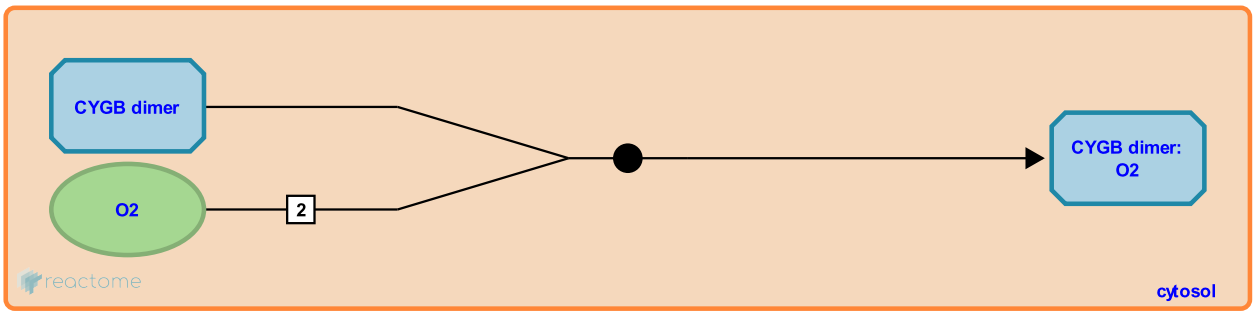
CYGB binds O2 ↗

Location: Intracellular oxygen transport

Stable identifier: R-HSA-5340214

Type: binding

Compartments: cytosol



Vertebrates possess multiple respiratory globins that differ in structure, function, and tissue distribution. Three different globins have been described so far: hemoglobin facilitates oxygen transport in blood, myoglobin mediates oxygen transport and storage in the muscle and neuroglobin has a yet unidentified function in nerve cells. A fourth globin has been identified in mouse, human and zebrafish. It is ubiquitously expressed in human tissue and therefore called cytoglobin (CYGB) (Burmester et al. 2002, Trent & Hargrove 2002). Unlike the specific expression patterns of Hb and Mb, CYGB is found in vascular smooth muscle, fibroblasts and cardiomyocytes. CYGB functions as a homodimer (Hamdane et al. 2003) and is localised to the cytosol of these cells where its O2 loading and unloading ability within a narrow O2 tension range makes it an ideal protein for O2 storage, especially during hypoxia (Fago et al. 2004).

Literature references

Hankeln, T., Burmester, T., Pesce, A., Hamdane, D., Bolognesi, M., Kiger, L. et al. (2003). The redox state of the cell regulates the ligand binding affinity of human neuroglobin and cytoglobin. *J. Biol. Chem., 278*, 51713-21. ↗

Hargrove, MS., Trent, JT. (2002). A ubiquitously expressed human hexacoordinate hemoglobin. *J. Biol. Chem., 277*, 19538-45. ↗

Gilany, K., Hundahl, C., Dewilde, S., Moens, L., Fago, A., Weber, RE. (2004). Allosteric regulation and temperature dependence of oxygen binding in human neuroglobin and cytoglobin. Molecular mechanisms and physiological significance. *J. Biol. Chem., 279*, 44417-26. ↗

Hankeln, T., Burmester, T., Ebner, B., Weich, B. (2002). Cytoglobin: a novel globin type ubiquitously expressed in vertebrate tissues. *Mol. Biol. Evol., 19*, 416-21. ↗

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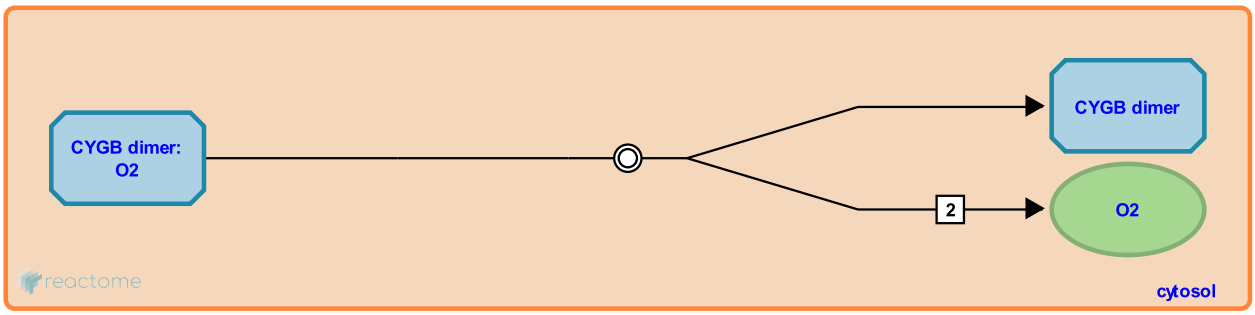
CYGB:O2 dissociates ↗

Location: Intracellular oxygen transport

Stable identifier: R-HSA-8982617

Type: dissociation

Compartments: cytosol



At low oxygen concentrations cytoglobin:oxygen dissociates to yield free oxygen (O2) (Burmester et al. 2002, Trent and Hargrove 2002, Hamdane et al. 2003, Fago et al. 2004). The affinity of cytoglobin for oxygen is similar to the affinity of myoglobin for oxygen therefore cytoglobin is postulated to act similarly to myoglobin in transporting oxygen from regions of high concentration to regions of low concentration.

Literature references

Hankeln, T., Burmester, T., Pesce, A., Hamdane, D., Bolognesi, M., Kiger, L. et al. (2003). The redox state of the cell regulates the ligand binding affinity of human neuroglobin and cytoglobin. *J. Biol. Chem., 278*, 51713-21. ↗

Hargrove, MS., Trent, JT. (2002). A ubiquitously expressed human hexacoordinate hemoglobin. *J. Biol. Chem., 277*, 19538-45. ↗

Gilany, K., Hundahl, C., Dewilde, S., Moens, L., Fago, A., Weber, RE. (2004). Allosteric regulation and temperature dependence of oxygen binding in human neuroglobin and cytoglobin. Molecular mechanisms and physiological significance. *J. Biol. Chem., 279*, 44417-26. ↗

Hankeln, T., Burmester, T., Ebner, B., Weich, B. (2002). Cytoglobin: a novel globin type ubiquitously expressed in vertebrate tissues. *Mol. Biol. Evol., 19*, 416-21. ↗

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Table of Contents