tional channels can assemble from simpler building blocks. So, the identification of NaChBac supports the idea that gene duplications resulted in the appearance of eukaryotic sodium channels. But more importantly, the preference of NaChBac for sodium, despite its similarity to a calcium channel, should lead us to revise our views on the molecular determinants of ion selectivity. The discovery of this bacterial channel will foster a better understanding of sodium channels, in the same way that KcsA has aided in the study of potassium channels.

*Juan Carlos López*

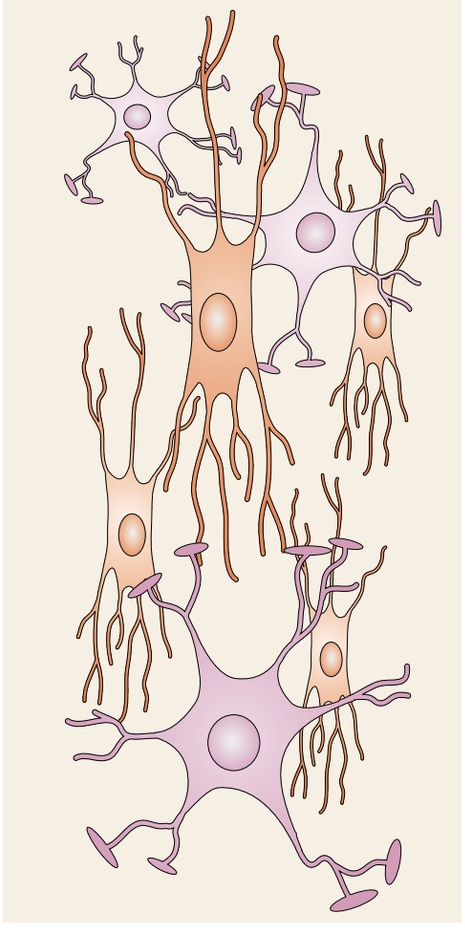

### References and links

**ORIGINAL RESEARCH PAPER** Ren, D. *et al.* A prokaryotic voltage-gated sodium channel. *Science* **294**, 2372–2375 (2001)

**FURTHER READING** Catterall, W. A. From ionic currents to molecular mechanisms: the structure and function of voltage-gated sodium channels. *Neuron* **26**, 13–25 (2000)

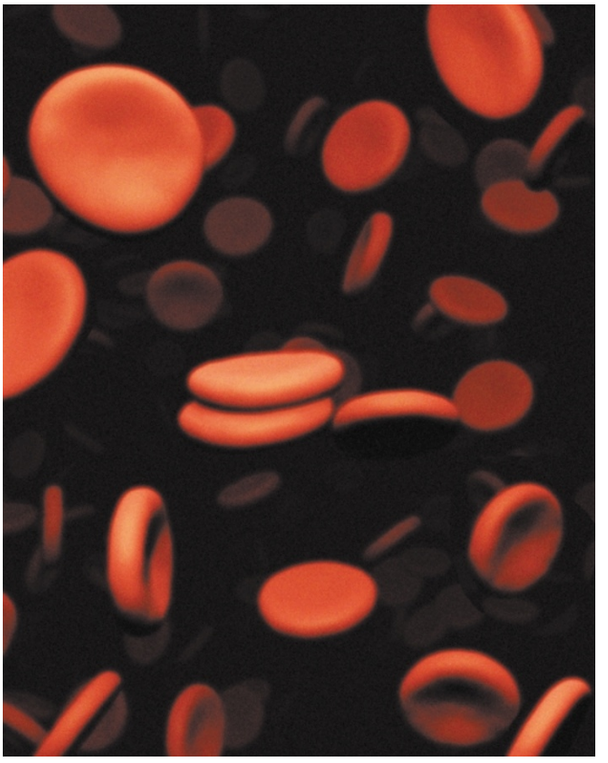
**WEB SITES**

**Encyclopedia of Life Sciences**
http://www.els.net/
ion channels | sodium channels | sodium, calcium and potassium channels

NEUROPROTECTION

# New blood in the globin family



**Most of us will have heard of haemoglobin and myoglobin; these porphyrin-containing proteins have a vital role in providing cells with an adequate supply of oxygen. They have been the focus of decades of study, which have taught us an enormous amount about the structure and function of proteins in general, and about the particular roles of globins in vertebrate physiology. By contrast, neuroglobin is a newcomer to the family of vertebrate globins, and clues to its function are only now beginning to emerge. In a report published recently in *Proceedings of the National Academy of Sciences*, Sun *et al.* show that this protein might serve to protect neurons against hypoxia.**

Owing to the relatively low solubility of oxygen in water, vertebrates rely on oxygen-carrying molecules to maintain aerobic respiration. The heterotetrameric haemoglobins carry oxygen in the blood, whereas myoglobin, a monomer, binds oxygen and facilitates its transport in muscle. Neuroglobin, a monomer with oxygen-binding properties comparable to those of myoglobin, is expressed chiefly in the brain. This fact led Sun and co-workers to examine the possibility that neuroglobin might be involved in neuronal responses to hypoxia and ischaemia.

Using an antibody raised against neuroglobin, Sun *et al.* showed that when cultures of mouse cortical neurons were deprived of oxygen, expression of the globin increased; the abundance of messenger RNA also increased, in keeping with the transcriptional induction of neuroglobin. Immunocytochemistry revealed that this protein was present in the cytoplasm of cells that expressed the neuronal nuclear antigen NeuN and were therefore likely to be neurons. And in immunostained sections of the cerebral cortex of rodents that had been subjected to focal cerebral ischaemia, Sun *et al.* showed that neuroglobin expression in the cytoplasm of cortical neurons was increased in the ischaemic compared with the non-ischaemic hemisphere.

But could neuroglobin protect neurons against hypoxia? Sun *et al.* transfected cultured neurons with an antisense oligodeoxynucleotide directed against the initial coding region of neuroglobin mRNA. As expected, the antisense-transfected cells, which expressed lower levels of neuroglobin than sense-transfected or untreated cells, were more susceptible to hypoxia. Conversely, overexpression of neuroglobin in an immortalized hippocampal neuronal cell line increased the viability of cells that were exposed to hypoxia.

So, one role of neuroglobin seems to be to promote neuronal survival after hypoxic-ischaemic insults. It remains to be seen how neuroglobin exerts its neuroprotective effect. Although globins are perhaps best known for their roles as oxygen carriers, these proteins have assumed a range of functions in evolution, including the scavenging and sensing of gases such as nitric oxide and carbon dioxide. So, for example, neuroglobin might act by facilitating the transport of oxygen to mitochondria, by scavenging the mediators of hypoxic-ischaemic injury, or by sensing hypoxia and activating protective mechanisms.

Neuroglobin has a long way to go to match the prominence of haemoglobin and myoglobin in the biosciences; nevertheless, Sun *et al.* have made a significant advance in defining a role for this protein. An important next step will be to determine whether neuroglobin has a neuroprotective effect *in vivo*; for example, by showing that cortical neurons are less sensitive to focal cerebral ischaemia in animals that overexpress this protein.

*Rebecca Craven*


### References and links

**ORIGINAL RESEARCH PAPER** Sun, Y. *et al.* Neuroglobin is up-regulated by and protects neurons from hypoxic-ischemic injury. *Proc. Natl Acad. Sci. USA* **98**, 15306–15311 (2001)

**FURTHER READING** Burmester, T. *et al.* A vertebrate globin expressed in the brain. *Nature* **407**, 520–523 (2000)

**WEB SITES**

**David Greenberg's lab:** http://www.buckinstitute.org/