

communicate directly with the pre-optic area.

Next the team showed that cold-responsive neurons in the parabrachial nucleus play a functional role in modulating thermoregulatory responses in the pre-optic area. The authors measured physiological parameters that are known to increase in response to skin cooling. This included measurements of metabolic activity in heat-generating brown adipose tissue, expired carbon dioxide, heart rate and blood pressure. They then used pharmacological inhibitors of neurotransmission within the parabrachial nucleus to see whether switching off the pathway affected the animal's physiological response to cold. They found that in response to cooling there was no longer an increase in these measured parameters. This implies that neurons in the lateral parabrachial nucleus play a crucial role in mediating the thermoregulatory response to a cold challenge.

Finally, the authors investigated whether the pathway responsible for the conscious perception of temperature, the spinothalamocortical pathway, which is relayed through the thalamus to the cortex, is also involved in the unconscious thermoregulatory response. By preventing neuronal signalling in areas of the thalamus that receive an abundance of spinothalamic projections, and measuring the same parameters as above, the authors established that the temperature perception and the thermoregulatory signalling pathways are distinct.

While cold-blooded organisms must acquire heat from the sun, an internal thermoregulatory response is a fundamental characteristic of warm-blooded animals. However, there are days when sunbathing seems a pleasant alternative even for the most warm blooded.

10.1242/jeb.011627

**Nakamura, K. and Morrison, S. F.** (2008). A thermosensory pathway that controls body temperature. *Nat. Neurosci.* **11**, 62-71.

**Sarah A. Hewitt**  
University of Calgary  
sahewitt@ucalgary.ca

## EVOLUTION



### HAEMOGLOBIN EVOLUTION IN MAMMALS

Haemoglobin is one of the most studied proteins in biology. It binds and transports oxygen in our blood, and releases it at our cells to fuel metabolism. Adult haemoglobin is composed of four subunits, two  $\alpha$ -globin subunits and two  $\beta$ -globin subunits, and the interaction between these subunits dictates many oxygen binding characteristics of the protein. Unlike adults, however, embryos and fetuses cannot breathe for themselves, and so have very different oxygen transport requirements. To accommodate this, the haemoglobin of placental mammals has a high affinity for oxygen before birth, which is helpful for loading oxygen into the blood. After birth and the development of the cardiorespiratory system, haemoglobin oxygen affinity decreases. This change in haemoglobin function occurs because there are different forms of the haemoglobin subunits, which arose from duplications of ancestral genes, and their expression changes throughout development. Early and late expression  $\beta$ -globins exist in all mammalian groups, not just in placental mammals, so Juan Opazo and colleagues from the University of Nebraska wondered how these genes evolved.

The authors used phylogenetic techniques to determine the evolutionary relationships between 168  $\beta$ -globin genes from across the vertebrates. This approach takes advantage of the fact that closely related genes are often more similar in DNA sequence than more distantly related genes. The authors were particularly interested in comparing the three mammalian subclasses: placental mammals, which includes humans, elephants and mice; marsupials, which includes kangaroos and opossums; and monotremes, which includes platypuses and echidnas. Their simplest prediction was that the  $\beta$ -globin gene was duplicated in the common ancestor of all mammals, and if this were so, the early and

late expressed  $\beta$ -globins would form separate clades in the phylogeny. In other words, all of the early expressed genes would be more closely related to each other than to any of the late expressed genes, and *vice versa*.

However, the researchers did not see two separate clades, but observed something very different: early and late  $\beta$ -globins from monotremes were more similar to each other than to any of the  $\beta$ -globins from other mammals. This observation made Opazo and colleagues suspect that the early and late forms of monotreme  $\beta$ -globins arose from a gene duplication that occurred after this subclass split from other mammals. The presence of different  $\beta$ -globins in multiple mammalian lineages therefore seemed to arise from two distinct duplication events.

But the coding sequence of duplicated genes can sometimes evolve in concert if they have similar functions, and thus become similar in sequence. The  $\beta$ -globin genes of monotremes could therefore appear to be more closely related than they actually are, so Opazo and colleagues decided to test this possibility and analysed the non-coding DNA sequences flanking each gene. In doing so they found that the flanking regions of the early and late genes in monotremes were also more similar to each other than to the  $\beta$ -globins from other mammals. In addition, when they looked at all the DNA sequence around the globin genes, they saw that monotremes had a unique arrangement of duplicated DNA sequences, different from other mammals. These observations affirmed the authors' conclusion that independent duplication events in monotremes and other mammals led to the occurrence of both early and late  $\beta$ -globin genes in all mammals. These probably evolved later in both lineages to deal with the differing oxygen transport requirements before and after birth.

Despite being one of the best studied proteins in biology, studies of haemoglobin are still providing insight into how physiological systems evolve. Natural selection has formed complex physiological systems, and Opazo and colleagues have brought us one step closer to understanding how the evolution of genes can make this happen.

10.1242/jeb.011601

**Opazo, J. C., Hoffmann, F. G. and Storz, J. F.** (2008). Genomic evidence for independent origins of  $\beta$ -like globin genes in monotremes and therian mammals. *Proc. Natl. Acad. Sci. USA* **105**, 1590-1595.

**Graham R. Scott**  
University of British Columbia  
scott@zoology.ubc.ca