

In the news

'SKIN DEEP' GOES TO A NEW DEPTH

Mice can sense the level of O₂ in their surroundings through their skin and can thereby regulate the ability of their blood to carry O₂, report Randall Johnson of the University of California, San Diego, USA, and colleagues, in *Cell*. Although it is well known that amphibians can breathe in part through their skin, this paper shows for the first time that epidermal gas exchange is also important for mammalian physiology. Moreover, this finding, which flies in the face of the general notion that the skin is merely a protective envelope, “brings home in spades the theme of whole-body physiology,” says Franklin Bunn, a Harvard University professor who was not involved in this study (*The Scientist*, 17 April 2008).

The transcription factor hypoxia-inducible factor-1 α (HIF-1 α) has previously been linked to the mammalian response to low levels of O₂. Specifically, HIF-1 α activity initiates a cascade that increases production of erythropoietin (EPO) in the kidney and liver, causing increased production of red blood cells and increased ability of the blood to carry O₂. To examine this pathway in greater detail, the authors knocked out the *Hif-1 α* gene in the skin of a mouse line, exposed the mice to low levels of O₂ and measured EPO levels. “When we knock out *Hif-1 α* , the net result is that the animal’s response to a hypoxic environment is basically blunted almost to the point of not happening,” says Johnson (*The Scientist*, 17 April 2008). Conversely, knockout of the von Hippel-Lindau (VHL) factor in the skin, which has opposing activity to HIF-1 α , resulted in increased EPO production.

Notably, this finding may have important therapeutic implications, especially if human skin also senses environmental O₂ levels. “EPO administration is a multi-billion dollar drug market for the treatment of all sorts of diseases involving low red blood cell counts,” says Johnson (*ScienceDaily*, 22 April 2008).

Asher Mullard