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Regulating the hypoxia response

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Hypoxia-inducible transcription factors (HIFs) control the changes in gene expression that are critical for allowing cells to adapt to limited oxygen levels. In the November 29 Nature, Makino *et al.* describe the cloning of a new inhibitor of the transcriptional response to hypoxic conditions (*Nature* 2001, **414:**550-554). They mined mouse EST databases in search of HIF homologues and identified a new gene, *IPAS*, encoding a protein containing a motif (bHLH PAS) that is found in other HIF family members. The IPAS protein lacks the carboxy-terminal activation domains present in HIF proteins, and IPAS expression reduced the hypoxia-induced activation response (including induction of the *VEGF* gene). High IPAS levels also reduced tumour growth and angiogenesis. IPAS expression is predominantly restricted to the Purkinje cells in the cerebellum and corneal epithelium in the eye, where it may play an important role in negatively regulating levels of the vascular endothelial growth factor, VEGF. Thus, IPAS appears to regulate the response to hypoxia by acting as a dominant-negative HIF.

References

1. Mammalian oxygen sensing, signaling and gene regulation.

2. *Nature*, [http://www.nature.com]