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STEM CELLS

Harnessing stem cell potential

To exploit the full potential of neural stem cells, it is essential to identify not only the factors that promote their differentiation, but also the factors that preserve the stem-cell state. In *Neuron*, Kim and colleagues report that the transcription factor Sox10 has a pivotal role in this delicate balancing act in neural crest stem cells (NCSCs) — an important class of progenitor cell for the peripheral nervous system.

NCSCs are migratory cells that emerge from the dorsal tip of the vertebrate neural tube. They give rise to autonomic neurons, Schwann cells and smooth muscle cells, both *in vivo* and *in vitro*. Sox10 is expressed in NCSCs, and also in NCSC progeny that have begun to express proneural factors such as Mash1 but that are still multipotent. Sox10 expression persists in differentiating glia, but not in cells that are committed to the neuronal lineage.

Bone morphogenetic protein 2 (BMP2) promotes the differentiation of NCSCs into neurons. At the same time, it extinguishes glial potential, in part by downregulating the expression of Erbb3, a receptor for Neuregulin-1. However, Kim *et al.* showed that if NCSCs were transfected with a viral vector that caused them to express Sox10 constitutively, BMP2 could no longer extinguish glial potential. Normally, transforming growth factor-β (TGFβ) causes NCSCs to default to the smooth muscle differentiation pathway, but the constitutive expression of Sox10 prevented TGFβ from extinguishing neuronal potential. Therefore, Sox10 seems to maintain both neurogenic and glial potential in NCSCs. The authors showed that Sox10 also negates another effect of TGFβ — the arrest of NCSC proliferation.

Sox10 allows the induction of two proneural factors, Mash1 and Phox2b, and this might be one mechanism by which it maintains neurogenic potential in NCSCs. However, Sox10 also acts as a brake to delay or prevent the terminal differentiation of neurons, an activity that is reflected in its ability to repress Phox2a, a close relative of Phox2b.

These new findings indicate that Sox10 prevents the extinction of two key stem cell properties — proliferation and multipotency — in NCSCs. It is pertinent to compare it to the closely related factor Sox2, which has recently been shown to be required for stem cell development in the early mouse embryo. Sox2 is a marker for stem cells in the central nervous system, and it will be interesting to explore whether its properties in the central nervous system parallel the newly identified role of Sox10 in the peripheral nervous system.

Heather Wood

References and links

ORIGINAL RESEARCH PAPER Kim, J. *et al.* SOX10 maintains multipotency and inhibits neuronal differentiation of neural crest stem cells. *Neuron* **38**, 17–31 (2003)

FURTHER READING Avilion, A. A. *et al.* Multipotent cell lineages in early mouse development depend on SOX2 function. *Genes Dev.* **17**, 126–140 (2003) | Bertrand, N. *et al.* Proneural genes and the specification of neural cell types. *Nature Rev. Neurosci.* **3**, 517–530 (2003)

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