NEUROGENESIS

VEGF — a route to new neurons

Vascular endothelial growth factor (VEGF) is an important common component in the induction of hippocampal neurogenesis by various means, according to a study published in *Nature Genetics* by Cao *et al.* The study also shows that the effect is mediated through one of the receptors for VEGF, the kinase insert domain protein receptor (KDR).

In adult mammals, the subgranular zone of the hippocampus is one of the most active sites of continuing neurogenesis, and the rate of neurogenesis can be increased by various manipulations, including exercise, environmental enrichment and the performance of hippocampus-dependent tasks such as the Morris water maze. Peripheral VEGF has previously been implicated in the ability of exercise to drive neurogenesis, so Cao *et al.* investigated whether it, or other growth factors, might be produced in the hippocampus of rats and drive neurogenesis induced by hippocampal activity or environmental enrichment.

VEGF was the only growth factor tested that showed an increase in expression in the hippocampus of rats that had either been housed in an enriched environment or trained and tested on the Morris water maze. When the authors used recombinant adeno-associated viral vectors to induce overexpression of VEGF in the rat hippocampus, the rats performed better in learning and memory tests, and also showed increased angiogenesis and neurogenesis in the hippocampus. Overexpression of placental growth factor (PGF) also caused increased angiogenesis, but had no effect on learning or on neurogenesis, supporting the idea that VEGF acts directly on neuronal precursors as well as on vascular endothelial cells. The authors also showed that knocking down expression of VEGF using specific small hairpin RNAs (shRNAs) prevented the induction of neurogenesis by an enriched environment.

VEGF can act through several receptors, including KDR. When overexpression of VEGF in the hippocampus was accompanied by overexpression of a dominant-negative mutant KDR, the effects of VEGF were antagonized. This indicates that KDR is the main mediator of the effects of VEGF on neurogenesis.

These results point towards a common mechanism — involving VEGF signalling through KDR — that links environmental effects, such as learning or enrichment, with the induction of neurogenesis in the hippocampus and with improved cognitive performance.

Rachel Jones

References and links

ORIGINAL REFERENCE PAPER Cao, L. *et al.* VEGF links hippocampal acticity with neurogenesis, learning and memory. *Nature Genet.* **36**, 827–835 (2004)

FURTHER READING van Praag, H. *et al.* Neural consequences of environmental enrichment. *Nature Rev. Neurosci.* **1**, 191–198 (2000)

IN BRIEF

NEUROTRANSMISSION

Synaptotagmins are trafficked to distinct subcellular domains including the postsynaptic compartment.

Adolfsen, B. *et al. J Cell. Biol.* **166**, 249–260 (2004)

Synaptotagmin 1 (SYT1) is an abundant synaptic protein and has been implicated in neurotransmission. The authors characterized the subcellular localization of other SYT proteins. They show that SYT4 is localized at the post-synapstic compartment, SYT12 and SYT14 are expressed at low levels presynaptically, SYTα and SYTβ are present in some neurosecretory cells, and SYT7 is not detectable at synapses. Overexpression of SYT4 and SYT7 cannot rescue the defects in neurotransmission in SYT1-deficient neurons.

REGENERATION

P_2X_7 receptor inhibition improves recovery after spinal cord injury

Wang, X. *et al. Nature Med.* **10**, 821–827 (2004)

This study shows that high levels of ATP are released after spinal cord injury and can lead to secondary damage. ATP also acts as an excitatory neurotransmitter in spinal cord neurons and results in high-frequency spiking and cell death. The effects of ATP can be blocked by antagonists of the P2X7 receptors, oxidised-ATP (OxATP) and piridoxalphosphate-6-azophenyl-2'-4'-disulphonic acid (PPADS). OxATP and PPADS can reduce cell death and significantly improve functional recovery after spinal cord injury.

STEM CELLS

Telomere shortening and chromosomal instability abrogates proliferation of adult but not embryonic neural stem cells.

Ferrón, S. *et al. Development* **131**, 4059–4070 (2004)

Chromosome integrity is important for cell survival and proliferation. Ferrón *et al.* show that proliferation of adult neural stem cells (NSCs) from the subventricular zone of telomerase-deficient mice is impaired both *in vitro* and *in vivo*. By contrast, embryonic NSCs proliferate extensively despite their shortened telomeres, severe chromosome abnormalities and increased p53 expression.

MOTION DETECTION

Neurons compute internal models of the physical laws of motion.

Angelaki, D. E. *et al. Nature* **430**, 560–564 (2004)

The CNS needs to differentiate various types of motion that generate similar sensory signals. The authors proposed an equation of motion, which states that the neural estimate of the inertial acceleration along the y-axis can be approximated by a linear superposition of the net acceleration signal sensed by the otoliths and an internal estimate of the y-axis gravitational acceleration. The firing rates of the vestibular nuclei and the rostral fastigial nucleus were consistent with their predictions, indicating that these neurons might carry out the computations to detect motion and orientation.