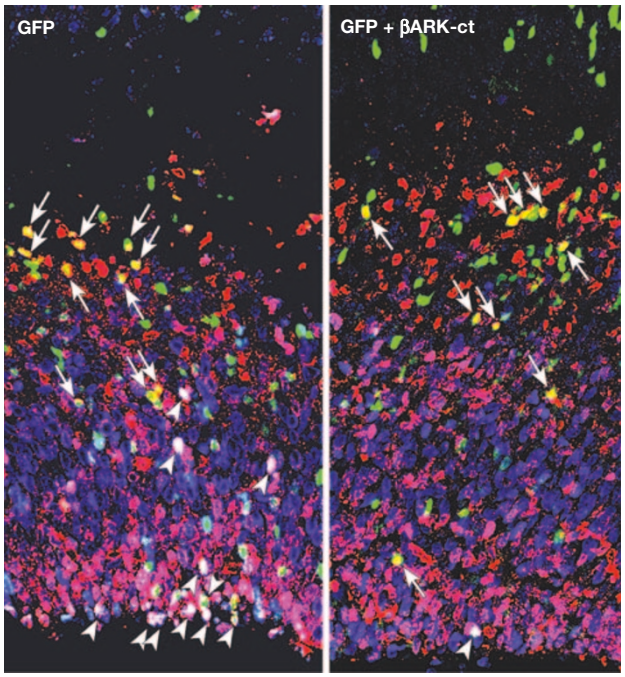
NEUROGENESIS

Lining up with destiny



Brain sections stained with antibodies against the DNA synthesis marker BrdU (red), the cell cycle marker Ki67 (blue) and green fluorescent protein (GFP; green). GFP-positive cells labelled with both BrdU and Ki67 (white; arrowheads) are active in the cell cycle, whereas GFP-positive cells labelled with BrdU but not Ki67 (yellow; arrows) have exited the cell cycle. Image courtesy of L.-H. Tsai, Howard Hughes Medical Institute, Harvard Medical School, Massachusetts, USA.

Orientation of cell-cleavage planes relative to the ventricular zone in the mammalian neocortex is important for the differentiation of progenitor cells into projection neurons, but little is known about how it is regulated. Reporting in *Cell*, Sanada and Tsai show that G protein βγ subunits (Gβγ) are important for regulating mitotic spindle orientation and cell fate determination during neurogenesis in the cerebral cortex.

Progenitor cells at the ventricular zone are highly polarized along the basal–apical axis, and it is thought that determinants of neuronal fate might be asymmetrically located at the basal side. When progenitors divide with the cleavage plane perpendicular to the ventricular surface (vertical cleavage plane), the two daughter cells have the same cellular determinants. Before neurogenesis, this symmetrical division produces two progenitors and expands the pool of cells that will ultimately give rise to neurons. However, when progenitors divide with the cleavage plane parallel to the ventricular surface (horizontal cleavage plane), the determinants are predominantly segregated into the basal daughter cells, and thereby induce asymmetric cell fates.

In this study, the researchers first established that about 50% of the dividing cells in the neocortex of mouse embryos had the vertical cleavage plane. This percentage increased to 72% when an inhibitor of Gβγ, the carboxy-terminal region of β-adrenergic receptor kinase (βARK-ct), was overexpressed. Overexpression of $G_{\alpha i}$, which is known to sequester free Gβγ and thereby inhibit its signalling, had a similar effect.

Interestingly, overexpression of either βARK-ct or $G_{\alpha i}$ resulted in a significant increase in the number of differentiated cortical neurons, which indicates that altered orientation in cleavage planes led to changes in cell fate. Further analysis showed that there was an increase in the percentage of progenitors that exited the cell cycle, which was correlated with a decrease in the number of mitotic cells.

Which G-protein activators are responsible for mitotic spindle orientation? Classically, ligands that bind to G-protein coupled receptors (GPCRs) initiate the cascade

SENSORY SYSTEMS

Bittersweet symphony

The neuropeptide cholecystokinin (CCK) is thought to be involved in mediating the sensation of bitter taste. Now, a research team led by Herness has shown that neuropeptide Y (NPY) is also expressed by most of the CCK-expressing cells in taste buds and has the opposite physiological effects to those of CCK. These findings might shed new light on the intricate orchestration of chemical signals that are important for the tongue's ability to differentiate bitter and sweet tastes.

Taste buds are clusters of 50–100 differentiated epithelial cells. Sensory afferent nerve fibres connect each bud to the brain to transmit signals about taste. Only a minority of cells in each bud form synaptic contacts with these fibres, and how other cells send signals to the brain has been the focus of intense academic curiosity.

The researchers believe that neuropeptides might be part of the answer. Having established the role of CCK in taste transduction, they moved on to study other neuropeptides and found that NPY was also expressed in a subset of taste bud cells at both the mRNA and protein levels. This prompted them to test the physiological effects of NPY on taste bud cells isolated from rat tongues.

In contrast to CCK, NPY enhances inwardly rectifying potassium currents (Kir) in some taste bud cells and has no effect on intracellular calcium concentrations. The NPY-mediated Kir enhancement can be mimicked by NPY1 receptor agonists and is blocked when the cells are treated with NPY1 receptor antagonists, indicating that the effect of NPY might be mediated by the NPY1 receptor subtype.

If CCK and NPY have contrasting physiological effects, one simple hypothesis could be that they are expressed by non-overlapping subsets of taste bud cells and are responsible for transducing bitter and sweet tastes, respectively. However, the researchers found that 68% of cells that expressed CCK also expressed NPY, and 95% of cells that expressed NPY expressed CCK. In other words, a subset of taste bud cells releases both neuropeptides.

Therefore, the brain might sense bitter and sweet tastes as a result of two competing signalling pathways: CCK and NPY might excite the transduction of one taste and, at the same time, suppress that of another. Alternatively, the same subset of taste bud cells might release only one neuropeptide in response to either bitter or sweet tastes, despite being able to release both.

Jane Qiu

References and links

ORIGINAL RESEARCH PAPER Zhao, F. *et al.* Expression, physiological action, and coexpression patterns of neuropeptide Y in rat taste-bud cells. *Proc. Natl Acad. Sci. USA* 22 July 2005 (doi:10.1073/pnas.0501988102)
FURTHER READING Mombaerts, P. Genes and ligands for odorant, vomeronasal and taste receptors. *Nature Rev. Neurosci.* **5**, 263–278 (2004)
WEB SITE
Herness' laboratory: http://ctoc.osu.edu/herness.htm