DEVELOPMENT

# Get Wise to Wnt

The Wnt family of signalling molecules is involved in various aspects of neural development, including the patterning of the nervous system along the anteroposterior (AP) axis. Writing in *Development*, Itasaki and colleagues report on the identification of a new factor that regulates Wnt signalling, and they show how the consequences of its actions vary for different developmental processes.

The authors carried out a screen to identify factors that can change the AP identity of neural tissue. They 'neuralized' frog animal caps (explants of naive ectoderm) with Noggin, which is an inhibitor of bone morphogenetic protein (BMP) signalling. By default, tissue that is neuralized in this way adopts an anterior character. The authors then looked for factors that are secreted by tissues — such as somites, surface ectoderm or endoderm — that have a posteriorizing effect on neural tissue. A new posteriorizing factor, which they named Wise (Wnt modulator in surface ectoderm), emerged from this screen.

Wise is a secreted molecule that is related to the CCN (Cef10/Cyr61, CTGF and Nov) family of extracellular matrix-associated signalling molecules. When Itasaki *et al.* overexpressed Wise in animal caps, they found that the tissue acquired a posterior character, as shown by the activation of progressively more posterior markers with increased amounts of Wise. This posteriorizing effect requires Dishevelled and β-catenin, which are components of the canonical Wnt signalling pathway.

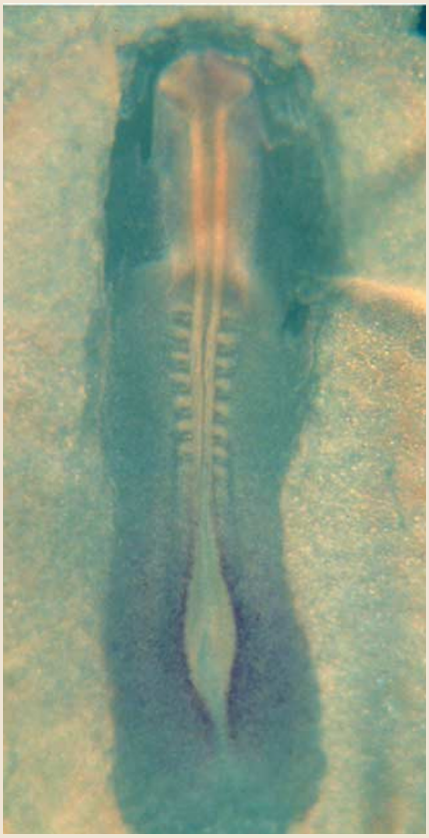
The authors then investigated the effects of Wise on another aspect of Wnt function — induction of the neuroaxis. Normally, Wnt8 can induce an entire secondary axis if its RNA is injected into a ventral cell of a 4–8-cell stage frog embryo, but surprisingly, if Wise RNA was injected into the same cell simultaneously, the axis-inducing activity of Wnt8 was inhibited. Interestingly, Wise seems to compete with Wnt8 to bind to lipoprotein receptor-related protein 6 (LRP6), which is a canonical mediator of Wnt signalling.

So, Wise seems to be able to act as an agonist or an inhibitor of Wnt signalling, depending on the cellular context. The next step will be to identify the factors that determine the effects of Wise on the Wnt pathway in these different situations.

*Heather Wood*

**References and links**

**ORIGINAL RESEARCH PAPER** Itasaki, N. *et al.* Wise, a context-dependent activator and inhibitor of Wnt signalling. *Development* **130**, 4295–4305 (2003)

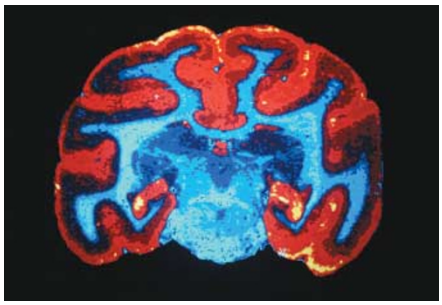


At embryonic stage 10 in the chick, Wise RNA (dark punctate staining) is expressed in the surface ectoderm from the level of the presomitic mesoderm to the posterior end of the embryo. Image courtesy of Nobue Itasaki, National Institute for Medical Research, Mill Hill, London, UK.

BRAIN IMAGING

# Closer to the source

A growing trend in neuroimaging research is to combine standard imaging techniques with other methods that might allow us to get additional information from the activation signal. A good example is the use of magnetoencephalography (MEG) — the detection of the small magnetic fields that are generated by neuronal activity — in combination with imaging methods, usually positron emission tomography (PET). The underlying idea is that the high temporal resolution that MEG affords is a perfect complement for the relatively good spatial resolution of PET. But a recent paper reports on the development of magnetic-source magnetic resonance imaging (msMRI) as a powerful alternative to reach the same goal in a simpler way.



The theoretical foundation of msMRI is relatively simple. The basic MRI signal depends on the use of a strong magnetic field to induce phase-coherent nuclear spins, the relaxation of which is subsequently detected. But if these spins are exposed to the intrinsic magnetic field that is generated by neuronal activity, their coherence will decrease, leading to a reduction in the magnitude of the MRI signal. Xiang *et al.* set out to establish whether detecting such a decrease was possible, using a simple visuomotor task that elicits well-characterized activations of the visual, motor and premotor cortices. msMRI allowed them to detect activations with the same spatial resolution (3 mm) and of the same strength (1% of the baseline signal) as functional MRI, but with a much higher temporal resolution (100 ms), comparable to what is obtained with electrophysiological methods.

In addition to increasing the temporal resolution of current imaging methods without compromising on spatial resolution, msMRI offers other advantages. In contrast to PET and functional MRI, msMRI does not depend on the haemodynamic brain response and its complex relationship with neuronal activity. And in contrast to MEG, msMRI does not depend on the detection of neuronal magnetic fields at the scalp, but allows us to look directly at their source in the brain parenchyma. Owing to this combination of attributes, msMRI should be received as a welcome and powerful addition to the imaging arsenal.

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**References and links**

**ORIGINAL RESEARCH PAPER** Xiong, J. *et al.* Directly mapping magnetic field effects of neuronal activity by magnetic resonance imaging. *Hum. Brain Mapp.* **20**, 41–49 (2003)