DEVELOPMENT

Maternal instinct

A crucial early step in establishing the dorsoventral polarity in *Xenopus* embryos is the dorsal accumulation of β-catenin, a component of the canonical WNT pathway. It has previously been thought that this process does not involve WNTs, but is regulated by an unidentified intracellular signal with dorsalizing activity. A new study shows that maternal WNT11 is the initial signal that, together with other extracellular factors, activates the canonical pathway in fertilized eggs.

Previous studies that manipulated *Wnt11* expression in early embryos did not show any defects in axis formation. Tao and colleagues conjectured that the time window that is important for establishing polarity occurs shortly after fertilization and, therefore, might have been missed in these studies. They injected *Wnt11* mRNA into oocytes before fertilization took place and found that this caused dorsalization — a process that depended on β-catenin activity and that was associated with increased expression of WNT target genes. By contrast, depleting *Wnt11* expression in oocytes led to a reduction in dorsoanterior embryonic structures, which could be rescued by dorsal injection of β-catenin mRNA.

Activation of WNT pathways usually requires interaction of WNTs with specific extracellular cofactors. The authors show that a *Xenopus* EGF–CFC protein, fibroblast growth factor receptor ligand 1 (FRL1), and heparan sulphate proteoglycans (HSPGs) are two such cofactors for WNT11 in the axial initiation pathway. When either FRL1 or Exostosin (an enzyme that is required for the synthesis of HSPGs) was removed from oocytes, the resulting embryos had phenotypes that mimicked WNT11 depletion. This could be reversed by overexpressing β-catenin.

As the role of WNTs in pattern formation is evolutionarily conserved, it will be interesting to determine whether maternal WNTs are also important for axial initiation in other animal groups.

Jane Qiu

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NEURODEGENERATIVE DISORDERS

Tracking changes in Alzheimer's disease

The development of methods for the early diagnosis of Alzheimer's disease is an important challenge for neuroscientists, and could provide a potential therapeutic window before irreversible neurodegeneration occurs. Efforts to achieve this have mainly focused on the detection of amyloid-β plaques, the accumulation of which is a key feature of Alzheimer's disease that occurs before the onset of overt neurological symptoms. However, until now the visualization of amyloid-β plaques has not been achieved at a sufficiently high contrast and specificity in living brains. A recent study published in *Nature Neuroscience* takes us a step closer to meeting this challenge with an MRI approach for visualizing amyloid plaques in living mice.

Higuchi and co-workers had previously created a fluorine-containing compound, known as FSB, which specifically binds to amyloid-β plaques. They used a well-established transgenic mouse model of Alzheimer's disease in which amyloid precursor protein is overexpressed, leading to a rapid build-up of amyloid-β. Intravenous delivery of FSB into these mice and the use of fluorine-sensitive MRI methods revealed amyloid deposits in the hippocampus and entorhinal cortex. This distribution of FSB was later confirmed with immunohistological analyses.

Importantly, the authors showed that the quantities of FSB required for detection using this method are not associated with toxic side effects. This MRI-based approach could, therefore, provide a potentially useful diagnostic tool for Alzheimer's disease, with the advantages of good spatial resolution and the avoidance of radioactive tracers.

As the authors recognize, before this technology can be assessed in human clinical trials, there is a need for tracers with better pharmacokinetic properties and MRI compatibility, as well as further improvements in MRI specificity and sensitivity. However, this new work not only paves the way for such developments, but it also provides a valuable tool for tracking the progression of disease and assessing the efficacy of potential therapeutic interventions in mouse models of Alzheimer's disease.

Alison Rowan

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