SENSORY SYSTEMS

Connexin's auditory connection

Gap junctions — which contain intercellular channels composed of connexin proteins — allow molecules and ions to flow directly between most types of cell, and constitute electrical synapses between neurons. Mutations in connexin genes underlie approximately half of all cases of genetic deafness in childhood, but their modes of action are not well understood. A report in the *Journal of Neuroscience* provides new insights into the role of a recently identified connexin — CX29 — in auditory perception.

Four types of connexin, including CX29, are expressed in the cochlea. Tang and co-workers found that CX29 is abundantly and exclusively expressed in Schwann cells that myelinate the soma and processes of spiral ganglion neurons, which communicate sound signals transduced by hair cells to the cochlear nuclei in the brain stem. By contrast, the other connexins are primarily expressed in cochlear supporting cells and/or fibrocytes.

To determine the functions of CX29, Tang and colleagues studied mice that were deficient in *Cx29*. These mice were impaired in several aspects of auditory perception. Specifically, their hearing sensitivity across a range of frequencies was defective. In addition, they had sustained hearing loss for high-frequency sounds in response to stimulation with white noise, which resulted in only temporary impairments in wild-type mice.

The cochlear hair cells of these mice were morphologically normal, so what is the cellular mechanism that underlies these deficits? The presence of high levels of CX29 in Schwann cells suggested that myelination might be affected. Indeed, the myelin around the soma of spiral ganglion neurons was severely disorganized, although axonal myelin was normal.

CX29 is expressed in most Schwann cells and oligodendrocytes, yet only myelin in the spiral ganglion is affected in *Cx29*-knockout mice. Most myelinating glia express several connexin genes, each of which might compensate for the loss of another. However, these data suggest that spiral ganglion Schwann cells might express only CX29. Therefore, it seems that CX29 makes a unique contribution to myelination in the spiral ganglia and auditory perception.

This elegant study reveals the mechanisms by which CX29 plays its part in normal hearing. Moreover, the pattern of deficits in mice deficient in CX29 was consistent with that seen in patients with auditory neuropathies. Therefore, as the authors point out, these mice could provide a valuable model with which to explore the cellular and molecular basis of auditory neuropathy.

Alison Rowan

ORIGINAL RESEARCH PAPER Tang, W. *et al.* Connexin29 is highly expressed in cochlear Schwann cells, and it is required for the normal development and function of the auditory nerve of mice. *J. Neurosci.* **26**, 1991–1999 (2006)
FURTHER READING Söhl, G., Maxeiner, S. & Willecke, K. Expression and functions of neuronal gap junctions. *Nature Rev. Neurosci.* **6**, 191–200 (2005)

BEHAVIOURAL NEUROSCIENCE

Sniff and tell

Better known for their role in the adaptive immune response, genes of the major histocompatibility complex (MHC) also influence mating preference and social behaviour in vertebrates. Reporting in the *Journal of Neuroscience*, Spehr and co-workers show that non-volatile MHC peptides are recognized by olfactory sensory neurons in the main olfactory epithelium and transmit information used for social decision making in mice.

At least two anatomically and functionally distinct sensory organs allow mice to detect chemical signals: the vomeronasal organ, traditionally thought to transduce socially relevant chemical signals after direct contact with a source, and the main olfactory epithelium, a structure thought to detect only volatile molecules. The authors showed that during direct physical contact situations, such as sniffing and licking, non-volatile molecules could gain access to the main olfactory epithelium. Measurements of local field potentials showed a widely distributed sensitivity to remarkably low levels of non-volatile MHC peptides throughout this sensory tissue, whereas mutated control peptides did not elicit such highly sensitive responses.

> "…MHC peptides are recognized by … the main olfactory epithelium and transmit information used for social decision making in mice"

To identify the molecular mechanisms involved in transduction of peptide information, the authors disrupted elements of the evolutionarily conserved cyclic AMP (cAMP) second messenger system found in olfactory sensory neurons. Application of adenylyl cyclase antagonists or deletion of olfactory cyclic nucleotide-gated cation channels prevented the response of the main olfactory epithelium to MHC peptides, showing a requirement for cAMP signalling in the generation of peptide-evoked field potentials.

MHC peptides acting at the main olfactory epithelium were also shown to affect social preference of male mice *in vivo*. Male mice showed a preference for female urine from a different strain. Presented with identical female same-strain urine that had been supplemented with MHC peptides from either same-strain or different-strain mice, male mice showed a preference for urine containing MHC peptides from a different strain. This preference for disparate MHC peptides was also observed in mice lacking a functional vomeronasal organ, but was not seen in mice lacking olfactory cyclic nucleotide-gated cation channels or mice tested in a volatile-only paradigm.

Taken together, these findings suggest that MHC peptides act as social recognition cues in mice that are detected by olfactory sensory neurons of the main olfactory epithelium and communicated by an evolutionarily conserved cAMP-dependent signalling pathway. These findings challenge the widely held view that the main olfactory epithelium detects only volatile molecules, and add to a growing body of evidence suggesting a much greater complexity of olfactory sensory systems.

Daniel McGowan

ORIGINAL RESEARCH PAPER Spehr, M. *et al.* Essential role of the main olfactory system in social recognition of major histocompatibility complex peptide ligands. *J. Neurosci.* **26**, 1961–1970 (2006)
FURTHER READING Dulac, C. & Torello, A. T. Molecular detection of pheromone signals in mammals: from genes to behaviour. *Nature Rev. Neurosci.* **4**, 551–562 (2003)