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SENSORY SYSTEMS

Staying silent

Simon Belcher / Alamy

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Olfactory sensory neurons (OSNs) each express one particular olfactory receptor (OR), the identity of which determines their functional properties. To achieve this specificity, the expression of other OR genes is repressed. Ngai and colleagues now reveal a key role for the G protein βγ subunit in mediating this repression in zebrafish.

Current models suggest that the expression of a 'chosen' OR gene prevents the concurrent expression of a second OR by the same OSN. In keeping with this hypothesis, the authors showed that overexpression of an exogenous OR in OSNs in zebrafish embryos reduced the number of OSNs expressing one of three endogenous ORs. ORs are G protein-coupled receptors (GPCRs), and the authors found that overexpression of a constitutively active form of the β2 adrenergic receptor, a closely related GPCR, suppressed OR expression to an even greater extent, suggesting that GPCR activity is important in driving OR silencing.

GPCR activation releases Gα and Gβγ subunits, which activate downstream signalling cascades. As previous work had ruled out a role for Gα subunits in OR silencing, the authors focused their attention on Gβγ subunits. Blocking Gβγ activity using gallein, a small-molecule inhibitor, or by expressing a dominant negative inhibitor of Gβγ increased endogenous OR expression and even resulted in the expression of multiple OR genes in some OSNs. By contrast, overexpression of Gβγ subunits decreased endogenous OR expression.

Studies in mice suggest that histone methylation mediates OR gene silencing. Here, the authors confirmed that the chromatin associated with zebrafish OR genes is highly methylated and showed that compounds that drive or inhibit histone methylation altered the expression of endogenous OR genes. The authors also showed that Gβγ promotes the expression of a number of genes involved in histone methylation, suggesting that it could drive this process during OR silencing. Treatment of zebrafish embryos with both gallein and a histone methylation inhibitor increased endogenous OR expression as expected, but the magnitude of the combined effect was no greater than that of either treatment alone, indicating that Gβγ signalling and histone methylation act within the same signalling pathway.

This study shows that OR activity, through Gβγ signalling, can drive the epigenetic silencing of alternative OR genes to ensure that OSNs maintain their 'one receptor, one neuron' status.

Katherine Whalley

ORIGINAL RESEARCH PAPER Ferreira, T. *et al.* Silencing of odorant receptor genes by G protein βγ signaling ensures the expression of one odorant receptor per olfactory sensory neuron. *Neuron* **81**, 847–859 (2014)

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