

 GENE REGULATION

One cell, one smell

Despite many influential theories, we have yet to account fully for the remarkable ability of mammalian olfactory neurons to select and then express only one among hundreds of olfactory receptor (OR) genes. By using a transgenic approach in the mouse, Minh Nguyen and colleagues show that the controls for single-allele expression lie in the OR gene itself.

The choice to express only one of the 2,600 OR alleles in each mouse neuron involves two steps — the selection of an allele, and a feedback mechanism that inhibits expression of all other alleles. To understand the basis for these two processes, the authors devised a transgenic scheme in which the gene for the Tet transactivator (TTA) is under the control of an endogenous OR promoter — expression of TTA leads

to the transcription, *in trans*, of an exogenous OR coding region and of a visible marker.

When TTA was turned on, either early in neuron maturation (before OR gene expression) or late (after OR allele selection), a proportion of cells expressed the transgene; importantly, in both cases, expression of the transgene and of an endogenous OR gene was mutually exclusive. Given that the transgenic OR gene is represented only by its coding region, the authors suggest that this two-way suppression is mediated by the OR gene sequence itself, which is therefore sufficient both to direct suppression and to be the target of feedback from endogenous ORs.

Early-expressed transgenes are more likely to be chosen by cells than those under a late-acting promoter. To explain this discrepancy the

authors call on a ‘first takes all’ mechanism by which an early-expressed transgene escapes suppression by endogenous loci, which become active only later. Indeed, when early and late promoters are coexpressed the transgenic OR is selected in almost all cells — the transgene is chosen and then maintained without interference by endogenous OR proteins.

As well as highlighting several layers of control in OR gene suppression, this study has also provided the experimental setup to investigate other pressing questions, not least concerning the nature of the feedback mechanism.

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ORIGINAL RESEARCH PAPER

Nguyen, M. Q. *et al.* Prominent roles for odorant receptor coding sequences in allelic exclusion. *Cell* **131**, 1009–1017 (2007)

