NEURAL CIRCUIT ASSEMBLY

A molecular matchmaker

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Sensory processing relies on the formation of specific synapses between sensory neurons and projection neurons that carry coded information to the cortex. The development of these connections involves multiple mechanisms that are not fully understood. Three new papers demonstrate a role for the axon guidance molecule semaphorin 1A (SEMA1A) in axon and dendrite targeting in the olfactory system.

The researchers made use of a common model of sensory development — the *Drosophila melanogaster* olfactory system — together with some elegant genetic manipulations. This allowed them to pick apart how olfactory receptor neuron (ORN) axons from the antennae and from the maxillary palps that express the same olfactory receptors converge in a single distinct glomerulus in the antennal lobe, where they synapse with projection neuron (PN) dendrites.

Two papers published in *Neuron* employed genetic mosaic systems, generated by inducing mutations in small groups of neurons within an otherwise wild-type fly, to investigate these events. Luo and colleagues used flies with a mutation in *smoothened*, which causes occasional loss of the antennae and/or maxillary palps, to show that antennal ORN axons, which arrive early at the antennal lobe, constrain the targeting of late-arriving maxillary palp axons. This indicates that signalling between neighbouring axons is likely to be important for targeting. Both this study and a second paper by Hummel and colleagues examined the role of *Sema1a* in this process.

Hummel's group showed that *Sema1a* mutations result in targeting defects: axons of the same type of ORN projected to multiple glomeruli rather than converging on a single glomerulus. Furthermore, overexpression of *Sema1a* in ORNs disrupted glomerular formation. The requirement for *Sema1a* was specific to particular classes of ORN, and the targeting defects observed varied between classes. Similarly, Luo and colleagues showed that *Sema1a* is required for targeting of all maxillary palp, and some antennal, ORN axons. Some $Sema1a^{-/-}$ ORNs developed normally, whereas wild-type ORNs on a mutant background showed targeting defects, indicating that *Sema1a* acts non-cell-autonomously. Both studies suggest that SEMA1A exerts its targeting effects through the repulsive receptor plexin A.

In a third paper, published in *Cell*, Luo's group showed that *Sema1a* is also required for the targeting of axons and dendrites of olfactory PNs to the cortex and antennal lobe, respectively. However, in this case, *Sema1a* acts cell-autonomously. The cytoplasmic domain of SEMA1A was crucial for this activity, providing a link to downstream signalling mechanisms. The authors observed a gradient of *Sema1a* expression in PN dendrites, and showed that the levels of SEMA1A direct PN dendritic targeting. The use of molecular gradients in this discrete map is similar to continuous maps formed, for example, in the visual system.

These studies highlight the importance of a single molecule, SEMA1A, in multiple stages of olfactory system development. Future research might concentrate on integrating these findings with other mechanisms known to be important for ORN and PN targeting as well as extending these findings to mammalian systems.

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ORIGINAL RESEARCH PAPERS
Sweeney, L. B. *et al.* Temporal target restriction of olfactory receptor neurons by Semaphorin-1a/PlexinA-mediated axon–axon interactions. *Neuron* **53**, 185–200 (2007) | Lattemann, M. *et al.* Semaphorin-1a controls receptor neuron-specific axonal convergence in the primary olfactory center of *Drosophila*. *Neuron* **53**, 169–184 (2007) | Komiyama, T., Sweeney, L. B., Schuldiner, O., Garcia, C. & Luo, L. Graded expression of semaphorin-1a cell-autonomously directs dendritic targeting of olfactory projection neurons. *Cell* **128**, 399–410 (2007)