DENDRITE MORPHOGENESIS

DSCAM's branching business

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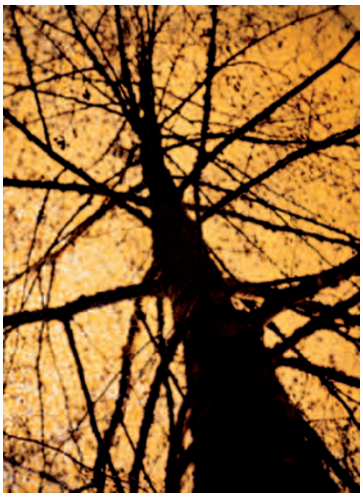

The need for a neuron to collect and integrate input signals underlies the distinct morphology of its dendritic tree. Although the striking morphological diversity of dendrites has been known since Cajal's days, the molecular basis for the organization of dendritic fields is unresolved. Three publications now provide evidence that Down syndrome cell-adhesion molecule (DSCAM) is essential for dendrite self-avoidance during morphogenesis of the *Drosophila* PNS.

Three rules ensure the efficient and unambiguous processing of sensory and synaptic inputs: isoneuronal dendrites do not cross (self-avoidance), neurons respect the territory of other sensory neurons of the same type (tiling) and neurons from different classes with different sensory functions can have overlapping sensory fields (co-existence). Dendrite arborisation (da) neurons in the PNS of *Drosophila* are divided into four classes (I–IV) with increasingly complex arborization, and they provide an easily accessible experimental system for studying morphogenetic patterns. During morphogenesis a mechanism is required to distinguish between self and non-self dendrites. DSCAM, which has been mainly studied in axonal development, is a transmembrane cell adhesion molecule with more than 38,000 different splice variants in *Drosophila*. Each fly neuron is thought to express a unique subset of DSCAM isoforms, making DSCAM an ideal candidate to be involved in self-avoidance.

All three publications examined flies with a loss-of-function mutation in *Dscam*. They found that isoneuronal dendrites were crossed and fasciculated in the mutant flies. However, the impairment in self-avoidance was not accompanied by defects in tiling.

Because of the diversity of DSCAM isoforms, only dendrites from the same neuron express identical DSCAM subsets. When a single isoform of DSCAM was expressed in class I da neurons in loss-of function mutants, the crossing and fasciculation phenotype was rescued. The authors concluded that a single DSCAM isoform is sufficient to establish self-recognition and dendrite self-avoidance.

What is the molecular basis of this avoidance? When a single, full-length DSCAM was overexpressed in wild-type, normally co-existing class I and III da neurons, segregation of dendritic fields was observed. The authors therefore concluded that the co-existence of dendritic fields of different types of neurons requires DSCAM diversity. When Matthews *et al.* expressed a single, C-terminal deleted DSCAM isoform in class I and III da neurons, the sensory fields of the two neuron classes overlapped as usual but the dendrites were impaired in self-avoidance. The authors concluded that self-avoidance is the result of the functional separation of recognition, which is encoded by the ectodomain, and repulsion, which is encoded by the cytoplasmic domain of DSCAM.

These studies identify DSCAM as the key mediator of self avoidance, with ectodomain-dependent recognition being translated into cytoplasmic domain-dependent repulsion. This might explain why molecularly diverse isotypes of DSCAM are needed to ensure that dendrites from the same neuron will avoid each other.

Future studies are required to identify the intracellular signalling pathways that are involved in this mechanism. As there is no DSCAM diversity in vertebrates, it remains to be seen how dendritic morphology is established in these species.

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ORIGINAL RESEARCH PAPERS
Matthews, B. J. *et al.* Dendritic self-avoidance is controlled by Dscam. *Cell* **129**, 593–604 (2007) | Soba, P. *et al.* *Drosophila* sensory neurons require Dscam for dendritic self-avoidance and proper dendritic field organization. *Neuron* **54**, 403–416 (2007) | Hughes, M. E. *et al.* Homophilic Dscam interactions control complex dendrite morphogenesis. *Neuron* **54**, 417–427 (2007)