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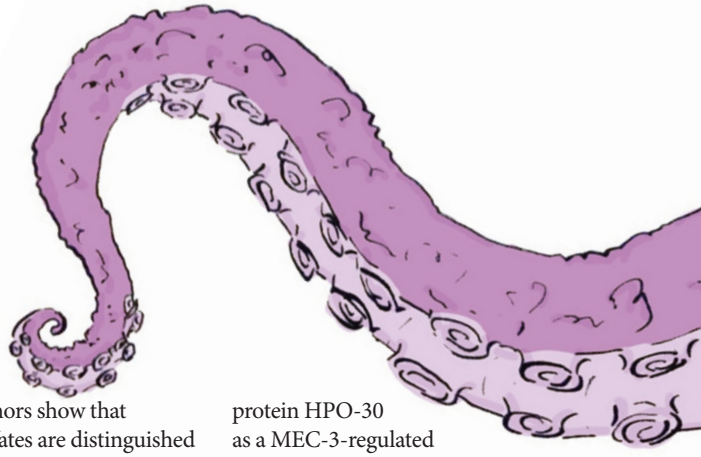

DEVELOPMENT

Branched for function

> sensory neuron fates are distinguished by a transcriptional switch that differentially regulates MEC-3 and downstream targets that control dendritic branching

Unique combinations of transcription factors are known to distinguish neuronal fates, but the downstream mechanisms that specify neuronal morphology are poorly understood. A new study in *Caenorhabditis elegans* shows that the combined action of three transcription factors — the LIM homeodomain transcription factor MEC-3, the aryl hydrocarbon receptor AHR-1 and the zinc-finger protein ZAG-1 — determines different mechanosensory neuron fates and their unique morphologies.

Sensory neurons adopt distinct architectures that enable them to respond to particular types of stimuli. In worms, AVM neurons (which detect light touch) exhibit an unbranched morphology, whereas PVD nociceptive neurons (which detect harsh mechanical force and low temperatures) are highly branched. Previous studies have shown that MEC-3 is involved in the specification of both of these neuron types, but how it achieves these distinctly different outcomes was unclear.

Here, the authors show that sensory neuron fates are distinguished by a transcriptional switch that differentially regulates MEC-3 and downstream targets that control dendritic branching. The first insight into this mechanism came from the finding that AVM neurons adopt the highly branched morphology of PVD cells in *ahr-1* mutants. Furthermore, AVM neurons are less likely to respond to light touch, and harsh touch elicits a similar calcium response in AVM neurons to that in PVD cells. These results suggested that AHR-1 normally acts in AVM neurons to block the PVD fate.

To shed light on the mechanism through which AHR-1 and MEC-3 determine the fate of PVD and AVM cells, the authors examined worms expressing mutant forms of both *mec-3* and *ahr-1*. They found that MEC-3 function is required to generate the branched morphology of both PVD cells and AVM cells in *ahr-1* mutants. This finding must have been initially surprising because MEC-3 levels are actually reduced in *ahr-1*-mutant AVM cells, and in wild-type animals, AVM cells express high levels of MEC-3. Thus, it seems that high levels of MEC-3 are required to activate the expression of genes involved in light-touch responsiveness, whereas low levels are sufficient to drive the expression of genes involved in branching.

Could AHR-1 prevent PVD-like branching in AVM cells by inhibiting a subset of MEC-3 targets? A PVD cell-specific profiling assay identified the claudin-like membrane protein HPO-30 as a MEC-3-regulated transcript that promotes dendritic branching and stabilization. The fact that HPO-30 is ectopically expressed in *ahr-1*-mutant AVM cells and that the PVD-like branched morphology of these cells was largely eliminated in worms expressing mutant forms of both *ahr-1* and *hpo-30* indicates that AHR-1 blocks the expression of HPO-30 in AVM cells to restrict branching. Together, these results suggest that AHR-1 ensures the touch neuron fate by activating *mec-3* expression in AVM cells while simultaneously repressing *mec-3*-dependent targets that result in a PVD-like morphology.

Interestingly, PVM neurons, another type of light-touch cells, were only mildly affected in *ahr-1* mutants. However, in *zag-1* mutants, PVM neurons displayed a PVD-like morphology and responsiveness. Thus, ZAG-1 prevents PVM cells from adopting a PVD-like fate through a mechanism that may parallel that of AHR-1 in AVM cells.

In summary this paper reveals a mechanism through which transcription factors regulate sensory neuron fate and branching in nematodes. The fact that the fly AHR-1 homologue, Spineless, has also been implicated in dendritic branching suggests that similar mechanisms may operate in more complex organisms.

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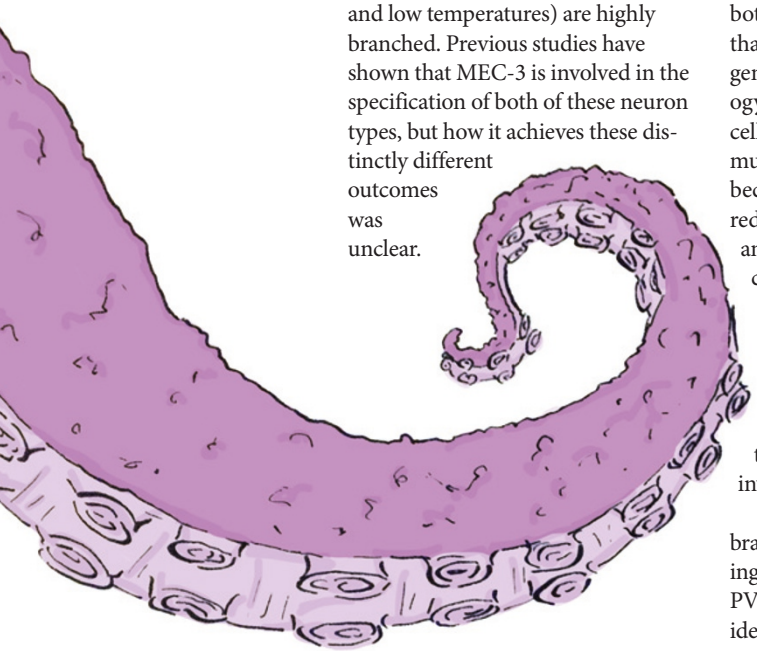
ORIGINAL RESEARCH PAPER Smith, C. J. *et al.* Sensory neuron fates are distinguished by a transcriptional switch that regulates dendrite branch stabilization. *Neuron* **79**, 266–280 (2013)



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