The *C. elegans* homologs of MASH1 and Mediator drive neurogenesis from a mesoderm lineage

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Understanding how a neuron specifies its cell fate is important for both developmental neurobiology and regenerative medicine. In C. elegans, six pharyngeal neurons, including I4, are generated from progenitor cells that primarily give rise to mesodermal tissues, raising the possibility that these neurons overcome a mesodermal cell fate to be specified as a neuron.

Using a GFP reporter that specifically labels I4, we have identified mutants in which the I4 neuron adopts a muscle-like cell fate. Identification of the genes defined by these mutants and genetic analysis revealed that at least two sets of proteins function in parallel to specify I4. One set contains the bHLH transcription factor HLH-3, which is the C. elegans homolog of Mash1/Ascl1, a protein shown to promote neuronal reprogramming in mammals. The other set includes subunits of the evolutionarily conserved Mediator complex. We found that hlh-3 and Mediator genes function redundantly to specify I4. We are investigating how these genes cooperate to specify the neuronal cell fate of I4 from mesodermal lineages, which might inform strategies for neuronal reprogramming in mammals.

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