

## A forward genetic screen identifies modifiers of a voltage- and calcium-activated K<sup>+</sup> channel in left-right neuronal asymmetry

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The developing nervous system generates a large diversity of cell types with distinct patterns of gene expression and functions. One way to establish neuronal diversity is to specify neuronal subtypes across the left-right axis. The *C. elegans* left and right AWC olfactory neurons communicate to specify asymmetric subtypes, AWC<sup>OFF</sup> and AWC<sup>ON</sup>. The default AWC<sup>OFF</sup> is specified by a Ca<sup>2+</sup>-regulated kinase cascade that is activated by influx of Ca<sup>2+</sup> through the voltage-gated Ca<sup>2+</sup> channel UNC-2/UNC-36. Intercellular communication between the two AWC neurons and other neurons through the NSY-5/innexin gap junction network antagonizes *unc-2/unc-36* Ca<sup>2+</sup> signaling in the induced AWC<sup>ON</sup> cell. Our recent data suggest that voltage- and calcium-activated SLO BK potassium channels *slo-1* and *slo-2* acts redundantly downstream of *nsy-5* to inhibit *unc-2/unc-36* Ca<sup>2+</sup> signaling in the specification of AWC<sup>ON</sup>. To identify the genes required for *slo-1* function in inhibiting *unc-2/unc-36* Ca<sup>2+</sup> signaling for promoting AWC<sup>ON</sup>, we performed a non-biased forward genetic screen to isolate *mok* (modifier of K<sup>+</sup> channel) mutants that suppress the *slo-1(gf)* 2-AWC<sup>ON</sup>-neuron phenotype. From about 6,000 genomes screened, we identified 16 new mutants that define genes required for *slo-1* function in promoting AWC<sup>ON</sup>. The molecular lesions of all these *mok* mutants were identified using one-step whole genome sequencing and SNP mapping. Molecular characterization of these *mok* genes will begin to address how gap junction-mediated transient signaling coordinates long-term stochastic neuronal subtypes through downstream Ca<sup>2+</sup>-activated K<sup>+</sup> channels and MOK molecules. Strategies of forward genetic screens and one-step whole genome sequencing/SNP mapping will be presented in the seminar and workshop.