Activity-induced synaptic refinement

Thompson-Peer, K., Bai, J., Hu, Z., and Kaplan, J. (2012). HBL-1 patterns synaptic remodeling in C. elegans. Neuron *73*, 453-465.

Circuit refinement (i.e. the dynamic addition and loss of synapses) is typically restricted to specific critical periods during development. Here we describe a transcriptional mechanism that dictates the timing and cell specificity of activity-dependent synaptic remodeling in *C. elegans*. The embryonic GABAergic DD motor neurons remodel their synapses, while the later born VD neurons do not. This specificity is mediated by differential expression of a transcription factor (HBL-1), which is expressed in DD neurons but is repressed in VDs by UNC-55/COUP-TF. DD remodeling is delayed in *hbl-1* mutants whereas precocious remodeling is observed in mutants lacking the microRNA *mir-84*, which inhibits *hbl-1* expression. Mutations increasing and decreasing circuit activity cause corresponding changes in *hbl-1* expression, and corresponding shifts in the timing of DD plasticity. Thus, convergent regulation of *hbl-1* expression defines a genetic mechanism that patterns activity-dependent synaptic remodeling across cell types and across developmental time. Current projects aim to determine how activity regulates this process, and to identify genes required for remodeling.

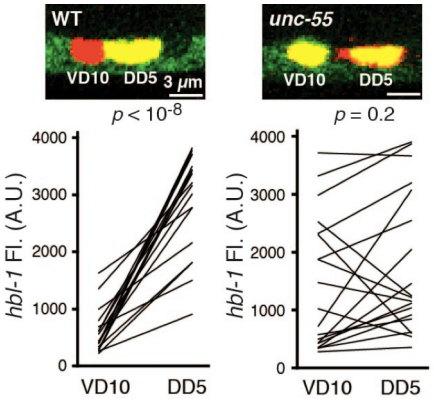

Fig. 1. UNC-55 represses HBL-1 expression in VD neurons. Expression of an *hbl-1* transcriptional reporter (green) is shown in VD10 and DD5 neurons, identified by GAD expression (red). Expression of *hbl-1* in DD5 is significantly higher than in VD10 and this effect is abolished in *unc-55* mutants.

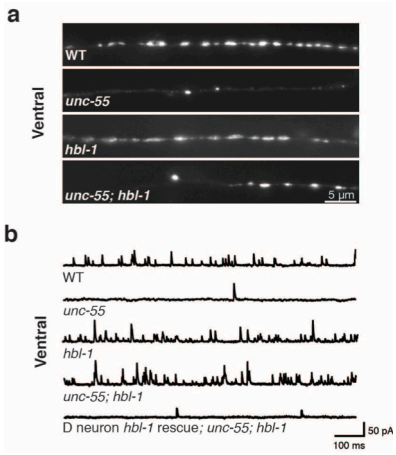

Fig. 2. HBL-1 is required for VD synapse remodeling in *unc-55* mutants. Ventral VD synapses labeled with GFP-tagged endophilin (a) and ventral IPSCs recordings (b) are shown for the indicated genotypes. Ventral VD synapses and IPSCs are eliminated in *unc-55* mutants and these effects are suppressed in double mutants lacking HBL-1.