Genetic Screen for and Molecular Characterization of Novel Suppressors of the SUP-9/SUP-10/UNC-93 Two-Pore Domain K^+ Channel Complex

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sup-9, *sup-10* and *unc-93* encode components of a presumptive *C. elegans* two-pore domain K^+ channel complex. Rare gain-of-function mutations of each of these three genes cause abnormal body muscle contraction and are thought to activate the SUP-9 K^+ channel. The mutant animals are defective in egg laying, sluggish and exhibit the "rubberband" phenotype: when prodded on the head, an animal contracts and relaxes along its entire body without moving backwards. The SUP-9 protein is similar to the mammalian Two-pore Acid Sensitive K^+ channels TASK-1 and TASK-3. *sup-10* encodes a novel single transmembrane protein without apparent mammalian orthologs. *unc-93* encodes a multiple transmembrane protein that defines a novel family of proteins conserved from *C. elegans* to mammals. Previous screens for recessive suppressors of the mutant phenotype of *unc-93*(*e1500*sd) animals identified only loss-of-function mutations of *unc-93*, *sup-9* or *sup-10*.

To seek essential genes that interact with *sup-9*, *sup-10* and/or *unc-93*, we screened ~10,000 EMS-mutagenized F1 *unc-93*(*e1500*sd) animals clonally for animals with better locomotion. We identified three partial suppressors that either cause recessive sterility or carry mutations that cause sterility and are closely linked to the suppressors. We have mapped two of the suppressors to small regions of LG IV and LG V. We will report our progress in cloning and characterizing these two suppressors.

As an alternative approach to identify *unc-93*(*e1500*sd) suppressors essential for development and/or survival, we have screened ~1170 RNAi clones reported to cause sterility or lethality from a whole-genome RNAi library[1]. One of the RNAi clones that suppresses the locomotory defects of *unc-93(e1500*sd*)* targets gene *C47E12.4*, which encodes a *C. elegans* ortholog of inorganic pyrophosphatase. A deletion mutant of *C47E12.4* isolated in our laboratory arrests at an early larval stage and is suppressed for the locomotory defects *of unc-93*(*e1500*sd*)*. We will report further characterization of this suppressor.

[1]Kamath et al. (2003) Nature 421: 231-237.

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Poster

Session topic 1: Cell Biology/Morphogenesis/Muscle
Session topic 2: Behavior/sensory transduction
Keyword: Muscle function