176. Genetic Analysis of the Putative SUP-9/SUP-10/UNC-93 Two-Pore Domain K^+ Channel Complex

Long Ma, Bob Horvitz
HHMI, Dept. Biology, MIT, Cambridge, MA 02139, USA

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, the animals contract and relax along their entire bodies 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 by picking animals with better locomotion and identified five partial suppressor strains. These five strains have better locomotion and a weaker rubberband phenotype, and are either homozygous sterile or carry mutations that cause sterility and that are closely linked to the suppressors. As an alternative approach to identify *unc-93(e1500*sd) suppressors essential for development and/or survival, we are currently screening using RNAi clones reported to cause sterility or lethality from the whole-genome RNAi library[1].

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