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698. CHARACTERIZING THE NEURONAL FUNCTION OF THE SUP-9/SUP-10/UNC-93 TWO-PORE K+ CHANNEL COMPLEX

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Rare altered-function mutations in the genes *unc-93*, *sup-9*, and *sup-10* result in the abnormal regulation of muscle contraction. These mutants move sluggishly, are unable to lay eggs, and exhibit the rubberband phenotype: when worms are prodded on the head, they contract and relax along their entire bodies without moving backwards. Genetic studies suggest that these three genes act at the same step and likely encode subunits of a protein complex. We have shown that *sup-9* encodes a two-pore K^+ channel subunit with similarity to the mammalian Two-pore Acid Sensitive K^+ channels TASK-1 and TASK-3. *unc-93* and *sup-10* encode novel putative transmembrane proteins.

We have found that in addition to being expressed in muscle, *sup-9::gfp* and *unc-93::gfp* are both expressed in 10 to 15 neurons in the head, including the four SIA neurons. The SIA neurons form very few synapses with other neurons, and their function remains unknown. To identify neuronal defects caused by *sup-9(gf)* mutations but masked by its muscle-induced paralysis, we are expressing *sup-9(gf)* under global neuronal promoters. Since in muscle the *sup-9(gf)* defect requires *unc-93* function, we hypothesize that a broadly expressed SUP-9(gf) K^+ channel will affect only those neurons in which endogenous *unc-93* is expressed.

We are also continuing our efforts to identify biophysically K^+ currents produced by the putative SUP-9/UNC-93/SUP-10 channel complex. We have generated stable HEK293 cell lines transfected with cDNAs encoding these proteins. Using whole-cell voltage clamp techniques we are characterizing the currents present in these cells. Mammalian two-pore K^+ channels are regulated by multiple factors, including pH, membrane stretch, arachidonic acid, local and volatile anesthetics, and temperature. We hope to identify the factors that regulate the activity of the SUP-9 channel complex and the roles that UNC-93 and SUP-10 play in this regulation.