Drosophila S6 kinase like inhibits neuromuscular junction growth by downregulating the BMP receptor Thickveins

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Synaptic connections must be precisely controlled to ensure proper neural circuit formation. In *Drosophila melanogaster*, bone morphogenetic protein (BMP) promotes growth of the neuromuscular junction (NMJ) by binding and activating the BMP ligand receptors wishful thinking (Wit) and thickveins (Tkv) expressed in motor neurons. We report here that an evolutionally conserved, previously uncharacterized member of the S6 kinase (S6K) family S6K like (S6KL) acts as a negative regulator of BMP signaling. *S6KL* null mutants were viable and fertile but exhibited more satellite boutons, fewer and larger synaptic vesicles, larger spontaneous miniature excitatory junctional potential (mEJP) amplitudes, and reduced synaptic endocytosis at the NMJ terminals. Reducing the gene dose by half of *tkv* in *S6KL* mutant background reversed the NMJ overgrowth phenotype. The NMJ phenotypes of *S6KL* mutants were accompanied by an elevated level of Tkv protein and phosphorylated Mad, an effector of the BMP signaling pathway, in the nervous system. In addition, Tkv physically interacted with S6KL in cultured S2 cells. Furthermore, knockdown of S6KL enhanced Tkv expression, while S6KL overexpression downregulated Tkv in cultured S2 cells. This latter effect was blocked by the proteasome inhibitor MG132. Our results together demonstrate for the first time that S6KL regulates synaptic development and function by facilitating proteasomal degradation of the BMP receptor Tkv.