NFAT modulates expression of CG42340 to alter plasticity at the pre-synapse

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Transcriptional mechanisms regulate long-term neuronal plasticity and underlie behaviors such as learning and addiction. Although most transcription factors studied to date, such as Fos and CREB, are positive regulators of plasticity, much less is known about proteins that constrain long-term changes in the structure and function of neurons. Using the model organism Drosophila melanogaster, our laboratory has determined that NFAT (Nuclear Factor of Activated T-cells) is expressed in the nervous system, inhibits pre-synaptic growth and transmitter release, and negatively regulates activity-dependent pre-synaptic plasticity. While NFAT-mediated regulation of synapse growth engages the microtubule based cytoskeleton, NFAT also alters calcium dependence of transmitter release. To derive mechanistic understanding of the role of NFAT in activity-dependent plasticity, we have focused on CG42340, a gene that encodes a dual-pore potassium leak channel and is regulated by neural activity. Western blot analysis from adult brain extracts suggests that NFAT could be a key controller of CG42340 protein levels in the brain; CG42340 protein levels are elevated following over-expression of NFAT and reduced in the NFATΔAB deletion mutant. Functional analysis of CG42340 also reveals an increase in synapse size for larvae lacking the entire coding region of CG42340. We propose a model in which neuronal activity induces expression of CG42340 in an NFAT dependent manner to constraint synaptic plasticity.