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The microtubule destabilizing protein stathmin-2 interacts with Ca_v2.2 N-type channels

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N-type calcium channels are expressed at presynaptic nerve terminals where they govern calcium entry that triggers neurotransmitter release. They are also implicated in guidance of neuronal growth cones and growth cone protrusion. Using yeast two hybrid assays with the C-terminus of the Ca_v2.2 calcium channel as bait, we identified 257 clones that survived quadruple drop out media. The most frequently isolated sequences in our screen were derived from SCG10 (superior cervical ganglia 10), also known as stathmin-2 (STMN2). Stathmin-2 is a neuronal-specific microtubule destabilizing protein that has been implicated in trafficking of receptor-activated ion channels in neurons. STMN2-derived sequences did not discriminate between e37a and e37b containing sequences but interacted specifically with C-termini baits of Ca_v2.2, and not those containing the intracellular II-III linker of Ca_v2.2. We confirmed that STMN2 interacts with full length Ca_v2.2 and the closely related Ca_v2.1 P/Q-type channel by co-immunoprecipitation. We used immuno-staining to localize endogenous Ca_v2.2 and STMN2 proteins in cultured hippocampal neurons. While Ca_v2.2 signals were consistent with mostly surface localization and STMN2 with mostly intracellular labeling, the two proteins appeared to co-localize at the leading edge of neurite growth cones. We are using siRNA to STMN2 to test the possibility that its interaction with Ca_v2.2 is required for Ca_v2.2 trafficking to growth cones. Supported by NS29967 (D.L.)