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Ca^{2+}/CALMODULIN CAUSES RAB3A TO DISSOCIATE FROM SYNAPTOSOMAL MEMBRANES

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Rab3A is a synaptic vesicle-associated, GTP-binding protein that has been implicated in the regulation of neurotransmission. We show here that Ca2+/calmodulin can form a 1:1 complex with Rab3A and cause it to dissociate from synaptosomal membranes. Formation of the complex requires both the lipidated C-terminus of Rab3A and the presence of guanine nucleotide. Ca^{2+}/Calmodulin appears to bind to a site within the Rab3A K62-R85 sequence because a synthetic peptide corresponding to this sequence can bind to Ca^{2+}/calmodulin, prevents the formation of a Rab3A-Ca^{2+}/calmodulin complex, and disrupt a preformed complex. When the peptide disrupts Rab3A-Ca^{2+}/calmodulin in the presence of Rab3A-depleted synaptosomal membranes, Rab3A transfers to the membranes. Ca^{2+}/Calmodulin competes with Rab guanine nucleotide dissociation inhibitor protein for binding to Rab3A, apparently because the two proteins bind to similar sites within the Rab3A K62-R85 sequence. The synthetic K62-R85 peptide can prevent the Rab3A-dissociating effects of the Rab guanine nucleotide dissociation inhibitor protein and disrupt a preformed complex between this protein and Rab3A. Taken together, our results identify a Ca^{2+}-dependent mechanism for controlling the content and distribution of Rab3A in synaptosomal membranes.