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題目：The Function of MACF1 in Regulated Exocytosis

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摘要：

Regulated exocytosis is a complicated process that is mediated by the fusion of vesicle membrane and plasma membrane. The SNARE proteins including the plasmalemmal protein SNAP-25, syntaxin, and vesicular membrane protein synaptobrevin will form a stable ternary complex for membrane fusion and finally lead to exocytosis. Although some exocytotic components have been identified, it is not enough to explain the complicated mechanism, suggesting that more regulatory factors are involved. MACF1 is a titanic cytoskeletal linker protein that bridge between actin filament and microtubules. MACF1 is abundant in neuronal tissues and could have other functions due to its multi-domain structure. Therefore we used yeast-two hybrid system to look for interaction proteins of MACF1 plakin domain. One of the clones is SNAP-25. SNAP-25 is a SNARE protein that is expressed in presynaptic terminals and involved in the fusion of secretory vesicles to cell membrane, leading to neurotransmitter release. Biochemical evidences showed that MACF1 interacts with the SNARE protein components including SNAP-25, syntaxin and synaptobrevin. Knockdown of MACF1 via siRNA in PC12 cells, a model cell line for studying neurotransmitter release, resulted in the decrease in dopamine secretion. We further examined the underlying mechanism and found out that membranous MACF1 is indispensable for mediating the binding between vesicle SNARE synaptobrevin and target SNARE SNAP-25, orchestrating the fusion of two membrane layers, and finally resulting in neurotransmitter release.