Exocytosis of Insulin

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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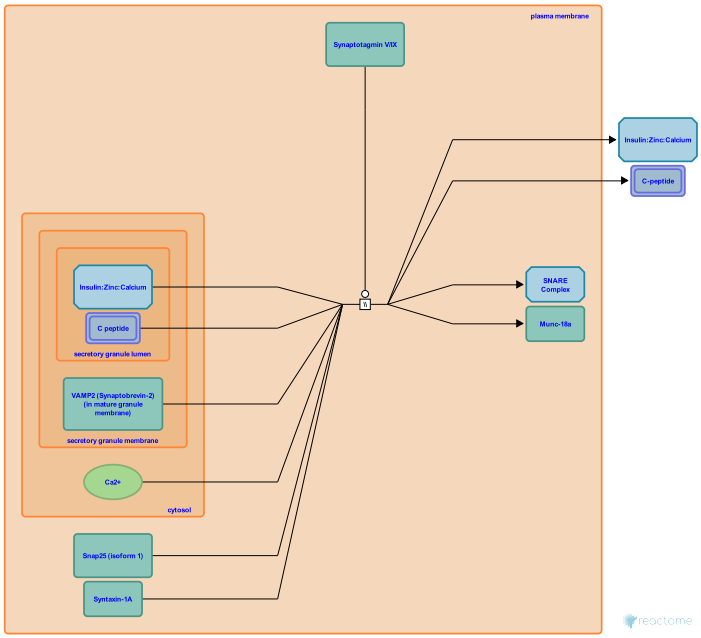
Type: omitted

Compartments: plasma membrane



Exocytosis of insulin-zinc granules occurs by the calcium-dependent fusion of the membrane of the secretory granule with the plasma membrane. In general, exocytosis proceeds by formation of a "SNARE pair", a complex between a SNARE-type protein on the granule and a SNARE-type protein on the plasma membrane. (The interaction is between coiled coil domains on each SNARE-type protein.)

In the particluar case of insulin granules in beta cells, the SNARE protein on the granule is Synaptobrevin2/VAMP2 and the SNARE protein on the plasma membrane is Syntaxin1A in a complex with SNAP-25. Munc18-1 binds Syntaxin1A and thereby prevents association with Synaptobrevin2 until dissociation of Munc18-1. Syntaxin 4 is also involved and binds filamentous actin but its exact role is unknown.

Insulin exocytosis occurs in two phases: 1) a rapid release of about 100 of the 1000 docked granules within the first 5 minutes of glucose stimulation and 2) a subsequent slow release over 30 minutes or more due to migration of internal granules to the plasma membrane. Data from knockout mice show that Syntaxin 1A is involved in rapid release but not slow release, whereas Syntaxin 4 is involved in both types of release.

Calcium dependence of membrane fusion is conferred by Synaptotagmin V/IX, which binds calcium ions and associates with the Syntaxin1A-Synaptobrevin2 pair. The exact mechanism of Synaptotagmin's action is unknown. The migration of internal granules to the plasma membrane during slow release is also calcium dependent.

Microscopically, exocytosis is seen to occur as a "kiss and run"" process in which the membrane of the secretory granule fuses transiently with the plasma membrane to form a small pore of about 4 nm between the interior of the granule and the exterior of the cell. Only a portion of the insulin in a granule is secreted after which the pore closes and the vesicle is recaptured back into the cell. Dynamin-1 and NSF may play a role in recapture but the mechanism is not fully known.

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Editions

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