Adrenaline, noradrenaline inhibits insulin secretion

D'Eustachio, P., May, B.
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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 70

This document contains 1 pathway and 6 reactions (see Table of Contents)
Adrenaline, noradrenaline inhibits insulin secretion

Stable identifier: R-HSA-400042

Compartments: plasma membrane

The catecholamines adrenaline (epinephrine) and noradrenaline (norepinephrine) inhibit insulin secretion from pancreatic beta cells. Four effects are seen in the cells:

1. Inhibition of exocytosis of secretory granules, the major effect.
2. Opening of ATP-sensitive potassium channels (KATP channels) and repolarization of the cell.
3. Closing of L-type voltage-dependent calcium channels and inhibition of calcium influx.
4. Inhibition of adenylyl cyclase activity.

The first event in adrenaline/noradrenaline signaling in beta cells is the binding of adrenaline or noradrenaline to alpha-2 adrenergic receptors, which are G-protein coupled receptors. Binding activates the alpha subunits in heterotrimeric Gi and Go complexes to exchange GDP for GTP, forming the active G alpha:GTP complex. Experiments using specific antibodies against the alpha subunits in mice show that Gi alpha-1, Gi alpha-2, and Go alpha-2 are responsible for adrenergic effects. The exact beta and gamma subunits of the heterotrimeric G-proteins are unknown.

After activation by GTP, the heterotrimeric complex dissociates into the G alpha:GTP complex and the beta:gamma complex. The G alpha:GTP complex causes the inhibition of exocytosis by an unknown mechanism that involves protein acylation. This is responsible for most of the observed inhibition of insulin secretion. Additionally, the G alpha:GTP complex activates (opens) KATP channels, allowing the cell to repolarize. The beta:gamma complex inhibits (closes) voltage-dependent calcium channels, reducing the intracellular calcium concentration, and inhibits adenylyl cyclase, reducing the intracellular cAMP concentration.

Literature references


**Editions**

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Alpha-2A, alpha-2C Adrenergic Receptors bind adrenaline or noradrenaline

Location: Adrenaline, noradrenaline inhibits insulin secretion

Stable identifier: R-HSA-400071

Type: binding

Compartments: plasma membrane, extracellular region

The pancreatic beta cell contains Alpha2A and Alpha2C Adrenergic Receptors. These are G-protein coupled receptors that can bind either adrenaline or noradrenaline.

Followed by: Alpha-2A, alpha-2C Adrenergic Receptors activate Gi, Go heterotrimeric G proteins

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https://www.reactome.org
In the pancreatic beta cell, alpha2 adrenergic receptors are coupled to Gi and Go heterotrimeric G-proteins. Binding of adrenaline or noradrenaline by the alpha2 adrenergic receptor acts through protein-protein interaction to stimulate the Gi alpha subunit or Go alpha subunit in heterotrimeric G-protein complexes to exchange GDP for GTP. The particular G alpha subunits have been identified in mice as Gi alpha1, Gi alpha 2, and Go alpha2.

**Preceded by:** Alpha-2A,alpha-2C Adrenergic Receptors bind adrenaline or noradrenaline

**Followed by:** Gi,Go Heterotrimeric G-protein complex dissociates

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Gi,Go Heterotrimeric G-protein complex dissociates

**Location:** Adrenaline, noradrenaline inhibits insulin secretion

**Stable identifier:** R-HSA-400037

**Type:** dissociation

**Compartments:** plasma membrane

Exchange of GDP for GTP by the alpha subunit of the heterotrimeric G-protein complex causes the complex to dissociate into the G alpha:GTP complex and the beta-gamma complex. Both complexes have effector functions.

**Preceded by:** Alpha-2A, alpha-2C Adrenergic Receptors activate Gi.Go heterotrimeric G proteins

**Followed by:** Low conductance potassium channels in pancreatic beta cells open in response to epinephrine, L-type Calcium Channels close in pancreatic beta cells, G-beta:G-gamma inhibits Adenylate cyclase

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L-type Calcium Channels close in pancreatic beta cells

**Location:** Adrenaline, noradrenaline inhibits insulin secretion

**Stable identifier:** R-HSA-400046

**Type:** omitted

**Compartments:** plasma membrane

**Inferred from:** Closing of L-type Calcium Channels (rat) (Rattus norvegicus)

Closing (inhibition) of the L-type calcium channels in the plasma membrane prevents the flow of calcium ions across the membrane.

**Preceded by:** Gi, Go Heterotrimeric G-protein complex dissociates

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Low conductance potassium channels in pancreatic beta cells open in response to epinephrine

**Location:** Adrenaline, noradrenaline inhibits insulin secretion

**Stable identifier:** R-HSA-400063

**Type:** omitted

**Compartments:** plasma membrane

**Inferred from:** Opening of Low Conductance Potassium Channels (Mus musculus)

ATP-sensitive Potassium channels open and allow an inward rectifying current of potassium ions to flow, reestablishing the resting potential of the cell.

**Preceded by:** Gi, Go Heterotrimeric G-protein complex dissociates

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G-beta:G-gamma inhibits Adenylate cyclase

**Location:** Adrenaline, noradrenaline inhibits insulin secretion

**Stable identifier:** R-HSA-400097

**Type:** binding

**Compartments:** plasma membrane

Adenylyl cyclases V and VI are the particular adenylyl cyclases present in beta cells of the human pancreas. The G-protein beta-gamma complex interacts with adenylyl cyclases via protein-protein interactions with the C1 and C2 cytoplasmic loops of adenylyl cyclase. The interaction may produce either stimulation or inhibition of the adenylyl cyclase depending on the particular adenylyl cyclase. In the case of adenylyl cyclases V and VI the interaction inhibits cyclase activity.

**Preceded by:** Gi, Go Heterotrimeric G-protein complex dissociates

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