Insulin receptor recycling

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12/03/2019
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


Reactome database release: 67

This document contains 1 pathway and 6 reactions (see Table of Contents)
Insulin receptor recycling

Stable identifier: R-HSA-77387

Triggered by acidification of the endosome, insulin dissociates from the receptor and is degraded. The receptor is dephosphorylated and re-integrated into the plasma membrane, ready to be activated again by the binding of insulin molecules.

Editions

2003-07-31  Authored  Bevan, AP.
ATP6AP1 binds V-ATPase

**Location:** Insulin receptor recycling

**Stable identifier:** R-HSA-5252133

**Type:** binding

**Compartments:** early endosome membrane, cytosol

Vacuolar-type H+ ATPases (V-ATPases) are proton pumps that acidify intracellular cargos and deliver protons across the plasma membrane of many specialised cells. V-type proton ATPase subunit S1 (A-TP6AP1) is thought to function as an accessory subunit of the V0 subcomplex of V-ATPase, facilitating acidification (Supek et al. 1994). Experiments with the mouse orthologue reveals a role for Atp6ap1 in osteoclast formation and function (Qin et al. 2011).

**Literature references**


**Editions**

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**Endosome acidification**

**Location:** Insulin receptor recycling

**Stable identifier:** R-HSA-74723

**Type:** transition

**Compartments:** endosome

The effect of the proton pump is to allow entry of [H+] ions into the lumen of the endosome. The net effect of this is to lower the pH of the lumen from pH 7.4 (the pH at the plasma membrane) to pH 6.0 (documented with studies using FITC-labeled insulin - a pH dependent fluorescence marker).

**Followed by:** Dissociation of insulin from insulin receptor

**Literature references**


**Editions**

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**Dissociation of insulin from insulin receptor**

**Location:** Insulin receptor recycling

**Stable identifier:** R-HSA-74726

**Type:** dissociation

**Compartments:** endosome

As the endosomal lumen acidifies, the insulin dissociates from the insulin receptor, making it available for degradation by the insulin degrading activity (IDA) present in the endosomal membrane.

**Preceded by:** Endosome acidification

**Followed by:** Insulin degradation, Insulin receptor de-phosphorylation

**Literature references**


**Editions**

2003-07-31  Authored  Bevan, AP.
**Insulin degradation**

**Location:** Insulin receptor recycling

**Stable identifier:** R-HSA-74730

**Type:** omitted

**Compartments:** endosome

At the beginning of this reaction, 1 molecule of 'insulin' is present.

This reaction takes place in the 'endosome' and is mediated by the 'insulysin activity of IDA (insulin degrading activity)' of 'IDA (insulin degrading activity)'.

**Preceded by:** Dissociation of insulin from insulin receptor

**Literature references**


**Insulin receptor de-phosphorylation**

**Location:** Insulin receptor recycling

**Stable identifier:** R-HSA-74733

**Type:** transition

**Compartments:** cytosol, endosome membrane

With insulin dissociated from its receptor the signal to sustain the receptor kinase's activity is also removed. Thus endosomally-associated protein tyrosine phosphatases (PTPs) are able to dephosphorylate the receptor which now can not rephosphorylate themselves since insulin is removed and the receptor is in the inactive protein conformation. (The identity of these PTPs is not clearly established yet.)

The dephosphorylation of the receptor is also a signal for the receptor to recycle back to the plasma membrane.

**Preceded by:** Dissociation of insulin from insulin receptor

**Followed by:** Re-integration of insulin receptor into plasma membrane

**Literature references**


**Editions**

2003-07-31 Authored Bevan, AP.
Re-integration of insulin receptor into plasma membrane

Location: Insulin receptor recycling

Stable identifier: R-HSA-74734

Type: omitted

Compartments: plasma membrane, endosome membrane

The endosome fuses with the plasma membrane allowing the insulin receptor to re-integrate there. Any degraded insulin remnants which remained in the endosome are also expelled (The majority having been excreted into the cytoplasm and secreted out of the cell via other mechanisms).

The cycle is complete with the dephosphorylated receptor now back in the plasma membrane available to bind the next insulin molecule presented to it. There is some insulin receptor degradation over time when damaged insulin receptors are not recycled but fuse instead with the lysosomes where they are degraded. However the majority of insulin receptors are recycled back to the plasma membrane with greater than 95% efficiency.

Preceded by: Insulin receptor de-phosphorylation

Literature references


Editions

2003-07-31 Authored Bevan, AP.
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