Fc epsilon receptor (FCERI) signaling

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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


Reactome database release: 79

This document contains 5 pathways and 8 reactions (see Table of Contents)
Fc epsilon receptor (FCERI) signaling

Stable identifier: R-HSA-2454202

Compartments: plasma membrane

Mast cells (MC) are distributed in tissues throughout the human body and have long been recognized as key cells of type I hypersensitivity reactions. They also play important roles in inflammatory and immediate allergic reactions. Activation through FCERI-bound antigen-specific IgE causes release of potent inflammatory mediators, such as histamine, proteases, chemotactic factors, cytokines and metabolites of arachidonic acid that act on the vasculature, smooth muscle, connective tissue, mucous glands and inflammatory cells (Borish & Joseph 1992, Amin 2012, Metcalfe et al. 1993). FCERI is a multimeric cell-surface receptor that binds the Fc fragment of IgE with high affinity. On mast cells and basophils FCERI exists as a tetrameric complex consisting of one alpha-chain, one beta-chain, and two disulfide-bonded gamma-chains, and on dendritic cells, Langerhans cells, macrophages, and eosinophils it exists as a trimeric complex with one alpha-chain and two disulfide-bonded gamma-chains (Wu 2011, Kraft & Kinet 2007). FCERI signaling in mast cells includes a network of signaling molecules and adaptor proteins. These molecules coordinate ultimately leading to effects on degranulation, eicosanoid production, and cytokine and chemokine production and cell migration and adhesion, growth and survival.

The first step in FCERI signaling is the phosphorylation of the tyrosine residues in the ITAM of both the beta and the gamma subunits of the FCERI by LYN, which is bound to the FCERI beta-chain. The phosphorylated ITAM then recruits the protein tyrosine kinase SYK (spleen tyrosine kinase) which then phosphorylates the adaptor protein LAT. Phosphorylated LAT (linker for activation of T cells) acts as a scaffolding protein and recruits other cytosolic adaptor molecules GRB2 (growth-factor-receptor-bound protein 2), GADS (GRB2-related adaptor protein), SHC (SRC homology 2 (SH2)-domain-containing transforming protein C) and SLP76 (SH2-domain-containing leukocyte protein of 76 kDa), as well as the exchange factors and adaptor molecules VAV and SOS (son of sevenless homologue), and the signalling enzyme phospholipase C gamma1 (PLC-gamma1). Tyrosine phosphorylation of enzymes and adaptors, including VAV, SHC GRB2 and SOS stimulate small GTPases such as RAC, RAS and RAF. These pathways lead to activation of the ERK, JNK and p38 MAP kinases, histamine release and cytokine production. FCERI activation also triggers the phosphorylation of PLC-gamma which upon membrane localisation hydrolyse PIP2 to form IP3 and 1,2-diacylglycerol (DAG) - second messengers that release Ca2+ from internal stores and activate PKC, respectively. Degranulation or histamine release follows the activation of PLC-gamma and protein kinase C (PKC) and the increased mobilization of calcium (Ca2+). Receptor aggregation also results in the phosphorylation of adaptor protein NTAL/LAT2 which then recruits GAB2. PI3K associates
with phosphorylated GAB2 and catalyses the formation of PIP3 in the membrane, which attracts many PH domain proteins like BTK, PLC-gamma, AKT and PDK. PI3K mediated activation of AKT then regulate the mast cell proliferation, development and survival (Gu et al. 2001).

**Literature references**


**Editions**

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IgE binds FCERI

Location: Fc epsilon receptor (FCERI) signaling

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