Diseases of Immune System

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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: 81

This document contains 2 pathways (see Table of Contents)
The immune system is a complex network of the biological processes that provide defense mechanisms during infection or in response to an intrinsic danger signal. Compromised immune response may present itself as either overactivity or underactivity of the immune system leading to a broad spectrum of clinical phenotypes that can be categorized into four main groups - autoimmunity, immunodeficiency (ID) with a greater susceptibility to infectious diseases, hypersensitivity to compounds that are usually not harmful and malignancy. Several host conditions may cause the dysfunctional immunity. Among them are inherited and somatic mutations found in the components of immune signaling pathways. In addition to genetic defects, infection with pathogen such as human immunodeficiency virus (HIV), or interaction of immune cells with immunosuppressive drugs result in non-genetic immunodeficiencies. Age-associated alterations in immunity may also contribute to pathogenesis of immunodeficiency.

The Reactome module represents selected defects of the immune system and provides a short description of their clinical phenotypes. The module also describes functional features of defective molecules by both providing a published source for experimental functional analysis data and linking to the corresponding normal process within the Reactome database.

**Literature references**


## Editions

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Toll-like receptors (TLRs) are sensors of the innate immune system that detect danger signals derived from pathogens (pathogen-associated molecular patterns - PAMP) or damaged cells (damage-associated molecular patterns - DAMP) (Pasare C and Medzhitov R 2005; Barton GM and Kagan JC 2009; Kawai T and Akira S 2010). Signaling by these sensors promotes the activation and nuclear translocation of transcription factors (IRFs, NFkB and AP1). The transcription factors induce secretion of inflammatory cytokines such as IL-6, TNF and pro-IL1beta that direct the adaptive immune response. Inherited or acquired abnormalities in TLR-mediated processes may lead to increased susceptibility to infection, excessive inflammation, autoimmunity and malignancy (Picard C et al. 2010; Netea MG et al. 2012; Varettoni M et al. 2013). Here we describe four primary immunodeficiency (PID) disorders associated with defective TLR-mediated responses. First, MyD88 or IRAK4 deficiency is characterized with a greater susceptibility to pyogenic bacteria in affected patients (Picard C et al. 2003; von Bernuth H et al. 2008). Second, defects in the TLR3 signaling pathway are associated with a greater susceptibility to herpes simplex virus encephalitis (Zhang SY et al. 2013). Third, immunodeficiencies due to defects in NFkB signaling components are linked to impaired TLR-mediated responses (Courtois G et al. 2003; Fusco F et al. 2004). Finally, events are annotated showing constitutive activation of a somatically mutated MyD88 gene which results in malignancy (Varettoni M et al. 2013).

Literature references


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