RLR (RIG-like receptor) mediated induction of IFN alpha/beta

Garapati, P V., Shamovsky, V.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.
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 (P41 HG003751), 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: 79

This document contains 5 pathways and 2 reactions (see Table of Contents)
In human, RIG-I-like receptor (RLR) family is crucial for triggering response to cytosolic viral RNA. RLR family is composed of retinoic acid-inducible gene 1 protein (RIG-I), melanoma differentiation-associated protein 5 (MDA5), and laboratory of genetics and physiology 2 (LGP2) [Yoneyama et al 2005].

RIG1, MDA5 and LGP2 are cytosolic multidomain proteins. They all contain a central DexD/H-box RNA helicase/adenosine triphosphatase (ATPase) domain that can bind viral RNA, and a C-terminal regulatory domain (RD) that prevents signaling in the absence of viral RNA. RIG-I and MDA5, but not LGP2, also encode two N-terminal caspase activation and recruitment domains (CARDs) that transmit the signal by binding to CARD domain of mitochondrial IFN-beta promoter stimulator protein (IPS-1; also known as MAVS, VISA or Cardif). This CARD-CARD interaction leads to production of IFN alpha/beta and pro-inflammatory cytokines. LGP2 that lacks CARD motifs but binds viral RNA is believed to regulate RLR signaling, however the mechanism of the regulation remains unclear; LGP2 was reported to act as negative regulator [Yoneyama et al 2005; Komuro and Horvath 2006; Saito et al 2007], while other studies suggested that LGP2 may cooperate with RIG-1 and MDA5 in sensing certain viral RNA [Venkataraman et al 2007; Satoh et al 2010].

Primary chick embryo cells produced IFN-alpha in response to Newcastle disease virus (NDV) and produced both IFN-alpha and IFN-beta in response to vaccinia virus or influenza A [Shwartz H et al 2004]. Those viruses have been reported to induce TLR3, RIG-1 and MDA5 signaling in mammals [Delaloye J et al 2009, Kato H et al 2006, Childs et al 2007]. Although RLR signaling is conserved among vertebrates [Sarkar D et al 2008; Zou J et al 2009 and Feng H et al 2011], analysis of chicken genome revealed only orthologs for mammalian MDA5 and LGP2, while RIG-1 gene was not identified [Sarkar D et al 2008; Zou J et al 2009; and Barber MR et al 2010].

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011-01-05</td>
<td>Authored</td>
<td>Shamovsky, V.</td>
</tr>
<tr>
<td>2011-05-11</td>
<td>Edited</td>
<td>Shamovsky, V.</td>
</tr>
<tr>
<td>2011-05-16</td>
<td>Reviewed</td>
<td>Garapati, P V.</td>
</tr>
</tbody>
</table>
dsRNA binds to MDA5

Location: RLR (RIG-like receptor) mediated induction of IFN alpha/beta

Stable identifier: R-GGA-1227694