FKBP1A binds sirolimus

Jassal, B., Shoichet, BK.
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: 82

This document contains 1 reaction (see Table of Contents)
FKBP1A binds sirolimus

Stable identifier: R-HSA-9679044

Type: binding

Compartments: cytosol

Sirolimus is a macrolide compound obtained from Streptomyces hygroscopicus that acts by selectively blocking the transcriptional activation of cytokines thereby inhibiting cytokine production. It is bioactive only when bound to immunophilins. Sirolimus is a potent immunosuppressant and possesses both antifungal and antineoplastic properties. Sirolimus inhibits T lymphocyte activation and proliferation that occurs in response to antigenic and cytokine (Interleukin IL-2, IL-4, and IL-15) stimulation by a mechanism that is distinct from that of other immunosuppressants. Sirolimus also inhibits antibody production. In cells, sirolimus binds to the immunophilin, peptidyl-prolyl cis-trans isomerase (FKBP1A, FKBP-12), to generate an immunosuppressive complex. The sirolimus:FKBP1A complex has no effect on calcineurin activity (Bierer et al. 1991). This complex binds to and inhibits the activation of the mammalian Target Of Rapamycin (mTOR), a key regulatory kinase. This inhibition suppresses cytokine-driven T-cell proliferation, inhibiting the progression from the G1 to the S phase of the cell cycle (Sehgal 1998, 2003).

Literature references


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020-03-23</td>
<td>Authored, Edited</td>
<td>Jassal, B.</td>
</tr>
<tr>
<td>2020-05-14</td>
<td>Reviewed</td>
<td>Shoichet, BK.</td>
</tr>
</tbody>
</table>