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 pathway and 5 reactions (see Table of Contents)
The survival of Mtb, depends on its ability to invade the host, replicate, and transmit infection. At its initial peripheral infection Mtb infects macrophages, and part of the immune evasion is accomplished by using cell-surface-associated phthiocerol dimycoceroserate (PDIM) (Siegrist M S & Bertozzi C R, 2013). In nature, fatty acids must be activated before they can be assimilated into various metabolic pathways. The universal mechanism of n-fatty acid activation involves conversion of fatty acids by a family of omnipresent fatty acyl-CoA ligases (FACLs). The biosynthesis of PDIM, an alternate mechanism of fatty acid activation, catalyzed by fatty acyl-AMP ligases (FAALs) was established in Mtb (Arora P, 2008).

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-13</td>
<td>Authored, Edited</td>
<td>Pardo, AM., Koile, I.</td>
</tr>
<tr>
<td>2019-02-13</td>
<td>Reviewed</td>
<td>Stephan, R.</td>
</tr>
</tbody>
</table>
Mtb FadD proteins (FadD26 and FadD28) are a class of long-chain fatty acyl-AMP ligases (FAALs) that catalyze the transfer of an adenylyl group from ATP to long-chain fatty acids (LCFA) to form LCFA adenylyl esters (LCFA adenylate ester). This transfer has the effect of activating fatty acids for further chain extension (Trivedi et al. 2004).

**Followed by:** FadD26, FadD28 transfer LCFA adenylate ester to Pks5

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-13</td>
<td>Authored, Edited</td>
<td>Pardo, AM., Koile, I.</td>
</tr>
<tr>
<td>2019-02-13</td>
<td>Reviewed</td>
<td>Stephan, R.</td>
</tr>
</tbody>
</table>
FadD26, FadD28 transfer LCFA adenylate ester to Pks5

**Location:** Dimycocersyl phthiocerol biosynthesis

**Stable identifier:** R-MTU-9635428

**Type:** transition

**Compartments:** cytosol

Mtbb FadD proteins (FadD26 and FadD28) are a class of long-chain fatty acyl-AMP ligases (FAALs) that bind activated fatty acids (LCFA adenylate esters) to polyketide synthase Pks5 (Pks5). This binding has the effect of activating fatty acids for further chain extension (Trivedi et al. 2004).

**Preceded by:** FadD26, FadD28 transfer adenylyl group to a LCFA

**Followed by:** Pks5 transforms LFCA adenylate ester to mycocerosyl

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author/Editor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-13</td>
<td>Authored, Edited</td>
<td>Pardo, AM., Koile, I.</td>
</tr>
<tr>
<td>2019-02-13</td>
<td>Reviewed</td>
<td>Stephan, R.</td>
</tr>
</tbody>
</table>
**Pks5 transforms LFCA adenylate ester to mycocerosyl**

**Location:** Dimycocersyl phthiocerol biosynthesis

**Stable identifier:** R-MTU-9635452

**Type:** transition

**Compartments:** cytosol

Mtb Pks5 (a mas homolog) synthesizes multimethylated mycocerosic acids. This protein acts on long-chain fatty acids adenylate esters (LCFA adenylate esters) in the LCFA adenylate ester:Pks5 complex by incorporating methylmalonyl residues, to form tri- or tetra-methylated branched fatty acids (mycocerosyl) (Roussau et al. 2003; Trivedi et al. 2005).

**Preceded by:** FadD26, FadD28 transfer LCFA adenylate ester to Pks5

**Followed by:** PapA5 transforms mycocerosyl to PDIM

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Author(s)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-13</td>
<td>Authored, Edited</td>
<td>Pardo, AM., Koile, I.</td>
</tr>
<tr>
<td>2019-02-13</td>
<td>Reviewed</td>
<td>Stephan, R.</td>
</tr>
</tbody>
</table>
**PapA5 transforms mycocerosyl to PDIM**

**Location:** Dimycocersyl phthiocerol biosynthesis

**Stable identifier:** R-MTU-9635440

**Type:** transition

**Compartments:** cytosol

Mtb PapA5 catalyzes the transesterification of mycocerosyl. This protein catalyzes the synthesis of dimycocerosyl phthiocerol from mycocerosyl and phthiocerol (Trivedi et al. 2005).

**Preceded by:** Pks5 transforms LFCA adenylate ester to mycocerosyl

**Followed by:** MmpL7 transports PDIM from the cytosol to the cell wall

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-13</td>
<td>Authored, Edited</td>
<td>Pardo, AM., Koile, I.</td>
</tr>
<tr>
<td>2019-02-13</td>
<td>Reviewed</td>
<td>Stephan, R.</td>
</tr>
</tbody>
</table>
MmpL7 transports PDIM from the cytosol to the cell wall

Location: Dimycersyl phthiocerol biosynthesis

Stable identifier: R-MTU-9637589

Type: transition

Compartments: plasma membrane, cell wall, cytosol

Among the main constituents of the Mtb outer cell wall are phthiocerol dimycocerosates (PDIM). After biosynthesis PDIM get exported through the inner cell membrane by the phthiocerol dimycocerosate exporter MmpL7 efflux pump (MmpL7) (Cox et al. 1999; Szekely and Cole 2016).

Preceded by: PapA5 transforms mycocerosyl to PDIM

Literature references


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019-02-13</td>
<td>Authored</td>
<td>Pardo, AM., Koile, I.</td>
</tr>
<tr>
<td>2019-02-19</td>
<td>Edited</td>
<td>Pardo, AM.</td>
</tr>
<tr>
<td>2019-02-19</td>
<td>Reviewed</td>
<td>Stephan, R.</td>
</tr>
</tbody>
</table>

https://reactome.org
# Table of Contents

- Introduction
- Dimycocersyl phthiocerol biosynthesis
  - FadD26, FadD28 transfer adenylyl group to a LCFA
  - FadD26, FadD28 transfer LCFA adenylate ester to Pks5
  - Pks5 transforms LFCA adenylate ester to mycocerosyl
  - PapA5 transforms mycocerosyl to PDIM
  - MmpL7 transports PDIM from the cytosol to the cell wall

Table of Contents