Cristae formation

Harper, JW., Kozjak-Pavlovic, V., May, B.

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.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

13/11/2022
**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 2 reactions (see Table of Contents)
Cristae are invaginations of the inner mitochondrial membrane that extend into the matrix and are lined with cytochrome complexes and F1Fo ATP synthase complexes. Cristae increase the surface area of the inner membranes allowing greater numbers of respiratory complexes. Cristae are also believed to serve as "proton pockets" to generate localized regions of higher membrane potential. The steps in the biogenesis of cristae are not yet completely elucidated (reviewed in Zick et al. 2009) but the formation of the Mitochondrial Contact Site and Cristae Organizing System (MICOS, formerly also known as MINOS, reviewed in Rampelt et al. 2016, Kozjak-Pavlovic 2016, van der Laan et al. 2016) and localized concentrations of cardiolipin are known to define the inward curvature of the inner membrane at the bases of cristae. MICOS also links these regions of the inner membrane with complexes (the SAM complex and, in fungi, the TOM complex) embedded in the outer membrane. CHCHD3 (MIC19) and IMMT (MIC60) subunits of MICOS also interact with OPA1 at the inner membrane (Darshi et al. 2011, Glytsou et al. 2016).

Formation of dimers or oligomers of the F1Fo ATP synthase complex causes extreme curvature of the inner membrane at the apices of cristae (reviewed in Seelert and Dencher 2011, Habersetzer et al. 2013). Defects in either MICOS or F1Fo ATP synthase oligomerization produce abnormal mitochondrial morphologies.

Literature references


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author/Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016-11-26</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2017-01-12</td>
<td>Reviewed</td>
<td>Harper, JW.</td>
</tr>
<tr>
<td>2017-02-05</td>
<td>Reviewed</td>
<td>Kozjak-Pavlovic, V.</td>
</tr>
</tbody>
</table>
Formation of MIB complex containing the MICOS complex causes curvature of mitochondrial inner membrane

**Location:** Cristae formation

**Stable identifier:** R-HSA-8949609

**Type:** omitted

**Compartments:** mitochondrial inner membrane

**Inferred from:** Formation of MIB complex containing the MICOS complex (Saccharomyces cerevisiae)

Assembly of the MICOS complex on the inner mitochondrial membrane appears to cause curvature of the inner membrane into the matrix to form invaginations known as cristae (Guarani et al. 2015, Huynen et al. 2016). The order of steps by which the MICOS complex assembles is unknown, however the MICOS complex is known to contain two subcomplexes: the MIC60 subcomplex and the MIC10 subcomplex which may associate via CHCHD3 (MIC19, MINOS3) (Huynen et al. 2016, nomenclature of subunits in Pfanner et al. 2014). HSPA9 also associates with MIC10 (MINOS1) in the complex (Alkhaja et al. 2012). The oxidation state of MIC19 regulates assembly of the MICOS complex (Sakowska et al. 2015). QIL1 (MIC12, MIC13), which has a distant orthologue in yeast (Huynen et al. 2016), is required for assembly of MIC10, MIC26, and MIC27 into the MICOS complex but not for formation of the MIC60 subcomplex (Guarani et al. 2015, Anand et al. 2016, Zerbes et al. 2016). Mutations in QIL1 cause loss of MICOS complex assembly and cristae junction architecture (Guarani et al. 2016, Zeharia et al. 2016)

The MICOS complex associates with the SAM complex of the outer membrane to form the Mitochondrial Intermembrane space Bridging complex (MIB complex) that links the inner and outer membranes (Kozjak-Pavlovic et al. 2007, Xie et al. 2007, Ott et al. 2012, Ding et al. 2015, Huynen et al. 2016). Oligomerization of the MINOS1 (MIC10) subunit (Alkhaja et al. 2012) within the MIC10 subcomplex is responsible for the curvature of the inner membrane (inferred from yeast). Dimerization of the F1Fo ATP synthase occurs at the interior-most regions of the cristae to form the curvature there (inferred from yeast).

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016-11-26</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2017-01-12</td>
<td>Reviewed</td>
<td>Harper, JW.</td>
</tr>
<tr>
<td>2017-02-05</td>
<td>Reviewed</td>
<td>Kozjak-Pavlovic, V.</td>
</tr>
</tbody>
</table>
**F1Fo ATP synthase dimerizes**

**Location:** Cristae formation

**Stable identifier:** R-HSA-8949580

**Type:** binding

**Compartments:** mitochondrial inner membrane

At the inner mitochondrial membrane, an F1Fo ATP synthase complex binds another F1Fo ATP synthase complex to form a dimer that causes curvature of the inner mitochondrial membrane at internal regions of cristae (Habersetzer et al. 2013, inferred from bovine homologs in Strauss et al. 2008, Davies et al. 2011, Davies et al. 2012, inferred from yeast homologs in Arnold et al. 1998, Couoh-Cardel et al. 2010). The dimers are observed in rows along the highly curved apices of cristae (inferred from bovine homologs in Davies et al. 2014).

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016-11-26</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2017-01-12</td>
<td>Reviewed</td>
<td>Harper, JW.</td>
</tr>
<tr>
<td>2017-02-05</td>
<td>Reviewed</td>
<td>Kozjak-Pavlovic, V.</td>
</tr>
</tbody>
</table>
Table of Contents

Introduction .................................................. 1

* Cristae formation .......................................... 2
  ** Formation of MIB complex containing the MICOS complex causes curvature of mitochondrial inner membrane ................. 4

▷ F1Fo ATP synthase dimerizes ................................ 6

Table of Contents ............................................. 7