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Uniform nomenclature for the mitochondrial contact site and cristae organizing system

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The mitochondrial inner membrane contains a large protein complex that functions in inner membrane organization and formation of mitochondrial contact sites. The complex was variably named the mitochondrial contact site complex, mitochondrial inner membrane organizing system, mitochondrial organizing structure, or Mitofilin/Fcj1 complex. To facilitate future studies, we propose to unify the nomenclature and term the complex "mitochondrial contact site and cristae organizing system" and its subunits Mic10 to Mic60.

Mitochondria possess two membranes of different architecture and function (Palade, 1952; Hackenbrock, 1968). Both membranes work together for essential shared functions, such as protein import (Schatz, 1996; Neupert and Herrmann, 2007; Chacinska et al., 2009). The outer membrane harbors machinery that controls the shape of the organelle and is crucial for the communication of mitochondria with the rest of the cell. The inner membrane harbors the complexes of the respiratory chain, the F1Fo-ATP synthase, numerous metabolite carriers, and enzymes of mitochondrial metabolism. It consists of two domains: the inner boundary membrane, which is adjacent to the outer membrane, and invaginations of different shape, termed cristae (Werner and Neupert, 1972; Frey and Mannella, 2000; Hoppins et al., 2007; Pellegrini and Scorrano, 2007; Zick et al., 2009; Davies et al., 2011). Tubular openings, termed cristae junctions (Perkins et al., 1997), connect inner boundary membrane and cristae membranes (Fig. 1, A and B). Respiratory chain complexes and the F1Fo-ATP synthase are preferentially located in the cristae membranes, whereas preprotein translocases are enriched in the inner boundary membrane (Vogel et al., 2006; Wurm and Jakobs, 2006; Davies et al., 2011). Contact sites

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between outer membrane and inner boundary membrane promote import of preproteins, metabolite channeling, lipid transport, and membrane dynamics (Frey and Mannella, 2000; Sesaki and Jensen, 2004; Hoppins et al., 2007, 2011; Neupert and Herrmann, 2007; Chacinska et al., 2009; Connerth et al., 2012; van der Laan et al., 2012).

To understand the complex architecture of mitochondria, it will be crucial to identify the molecular machineries that control the interaction between mitochondrial outer and inner membranes and the characteristic organization of the inner membrane. A convergence of independent studies led to the identification of a large heterooligomeric protein complex of the mitochondrial inner membrane conserved from yeast to humans that plays crucial roles in the maintenance of cristae junctions, inner membrane architecture, and formation of contact sites to the outer membrane (Fig. 1 A). Several names were used by different research groups to describe the complex, including mitochondrial contact site (MICOS) complex, mitochondrial inner membrane organizing system (MINOS), mitochondrial organizing structure (MitOS), Mitofilin complex, or Fcj1 (formation of crista junction protein 1) complex (Table 1; Harner et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Alkhaja et al., 2012). Mitofilin, also termed Fcj1, was the first component identified (Icho et al., 1994; Odgren et al., 1996; Gieffers et al., 1997; John et al., 2005) and was observed enriched at cristae junctions (Rabl et al., 2009). Mutants of Mitofilin/Fcj1 as well as of other MICOS/MINOS/MitOS subunits show a strikingly altered inner membrane architecture. They lose crista junctions and contain large internal membrane stacks, the respiratory activity is reduced, and mitochondrial DNA nucleoids are altered (Fig. 1 B; John et al., 2005; Hess et al., 2009; Rabl et al., 2009; Mun et al., 2010; Harner et al., 2011; Head et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Alkhaja et al., 2012; Itoh et al., 2013). It has been reported that the complex interacts with a variety of outer membrane proteins, such as channel proteins and components of the protein translocases and mitochondrial fusion machines, and defects impair the biogenesis of mitochondrial proteins (Xie et al., 2007; Darshi et al., 2011; Harner et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Alkhaja et al., 2012; An et al., 2012). Figure by M. Bohnert (Institute of Biochemistry and Molecular Biology, University of Freiburg, Freiburg, Germany).
Table 1. New nomenclature of MICOS

<table>
<thead>
<tr>
<th>Standard name</th>
<th>Former names</th>
<th>Yeast ORF</th>
<th>References</th>
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</thead>
<tbody>
<tr>
<td>Complex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MICOS</td>
<td>MINOS, MtOS, MIB, Mitofilin complex, and Fcj1 complex</td>
<td></td>
<td>Xie et al., 2007; Rabl et al., 2009; Darshi et al., 2011; Harner et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Alkhaja et al., 2012; An et al., 2012; Bohnert et al., 2012; Ott et al., 2012; Jans et al., 2013; Weber et al., 2013</td>
</tr>
<tr>
<td>Subunits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mic10</td>
<td>Mics10, Mio10, Mio1, and MINOS1</td>
<td>YCL057C-A</td>
<td>Harner et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Alkhaja et al., 2012; Itoh et al., 2013; Jans et al., 2013; Varabyova et al., 2013</td>
</tr>
<tr>
<td>Mic12</td>
<td>Aim5, fmp51, and Mcs12</td>
<td>YBR262C</td>
<td>Hess et al., 2009; Harner et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Varabyova et al., 2013</td>
</tr>
<tr>
<td>Mic19</td>
<td>Aim13, Mcs19, CHCH3, CHCHD3, and MINOS3</td>
<td>YFR011C</td>
<td>Xie et al., 2007; Hess et al., 2009; Darshi et al., 2011; Head et al., 2011; Alkhaja et al., 2012; Ott et al., 2012; Jans et al., 2013; Varabyova et al., 2013</td>
</tr>
<tr>
<td>Mic25 (metazoan Mic19 homologue)</td>
<td>CHCHD6 and CHCM1</td>
<td></td>
<td>Xie et al., 2007; An et al., 2012</td>
</tr>
<tr>
<td>Mic26</td>
<td>Mcs29, Mio27, and Mos2</td>
<td>YGR235C</td>
<td>Harner et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011</td>
</tr>
<tr>
<td>Mic27</td>
<td>Aim37, Mcs27, APOOL, and MOMA-1</td>
<td>YNL100W</td>
<td>Hess et al., 2009; Harner et al., 2011; Head et al., 2011; Hoppins et al., 2011; von der Malsburg et al., 2011; Weber et al., 2013</td>
</tr>
<tr>
<td>Mic60</td>
<td>Fcj1, Aim28, Fmp13, Mitofilin, HMP, IMMT, and MINOS2</td>
<td>YKR016W</td>
<td>Icho et al., 1994; Odgren et al., 1996; Gieffers et al., 1997; John et al., 2005; Wang et al., 2008; Rabl et al., 2009; Rossi et al., 2009; Mun et al., 2010; Park et al., 2010; Körner et al., 2012; Zerbes et al., 2012; Itoh et al., 2013; Varabyova et al., 2013</td>
</tr>
</tbody>
</table>

APOOL, apolipoprotein O–like; HMP, heart muscle protein; IMMT, inner mitochondrial membrane protein; MIB, mitochondrial intermembrane space bridging.

name MiccX will be used in this organism, but the number will not be changed. The use of capital and small letters as well as of italics will follow species-specific conventions, e.g., in budding yeast (Saccharomyces cerevisiae), MiccX will be used in this organism, but the number will be used. The number Y will be used. The name MiccX and the number Y will follow species-specific conventions, e.g., in budding yeast (Saccharomyces cerevisiae), MiccX will be used in this organism, but the number Y will be used. The name MiccX and the number Y will only be given to genuine orthologues in other organisms, i.e., these orthologues are also currently used for three non-MICOS yeast proteins (Gabriel et al., 2007; Vögtle et al., 2012) will be changed to Mic14, Mic17, and Mic23 (mitochondrial intermembrane space CXnC motif proteins) in the Saccharomyces Genome Database, and the new nomenclature will be used for orthologues identified in other organisms.

The MICOS complex is of central importance for the maintenance of mitochondrial inner membrane architecture and the formation of contact sites between outer and inner membranes and thus is involved in the regulation of mitochondrial dynamics, biogenesis, and inheritance. We expect that the uniform nomenclature will facilitate future studies on mitochondrial membrane architecture and dynamics.

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