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Nikolaus Pfanner
University of Freiburg

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Uniform nomenclature for the mitochondrial contact site and cristae organizing system

Nikolaus Pfanner,1,2 Martin van der Laan,1,2 Paolo Amati,3 Roderick A. Capaldi,4 Amy A. Caudy,5,6 Agnieszka Chacinska,7 Manjula Darshi,8 Markus Deckers,11 Suzanne Hoppins,12 Tateo Icho,13 Stefan Jakobs,14,15 Jianguo Ji,16 Vera Kozjak-Pavlovic,17 Chris Meisinger,1,2 Paul R. Odgren,18 Sang Ki Park,19 Peter Rehling,11,15 Andreas S. Reichert,20,21 M. Saeed Sheikh,22 Susan S. Taylor,8,9,10 Nobuo Tsuchida,23 Alexander M. van der Bliek,24 Ida J. van der Klei,25 Jonathan S. Weissman,26,27 Benedikt Westermann,28 Jiping Zha,29 Walter Neupert,30 and Jodi Nunnari31

1Institut für Biochemie und Molekularbiologie, Zentrum für Biochemie und Molekulare Zellforschung, and 2BIOSS Centre for Biological Signalling Studies, Universität Freiburg, 79104 Freiburg, Germany
3Department of Molecular and Cellular Biology, University of California, Davis, Davis, CA 95616
4Metabolic Profiling, Inc., Eugene, OR 97401
5Donnelly Centre for Cellular and Biomolecular Research and 6Department of Molecular Genetics, University of Toronto, Toronto, Ontario M5S 3E1, Canada
6The International Institute of Molecular and Cell Biology, 02-109 Warsaw, Poland
7Howard Hughes Medical Institute, Department of Pharmacology, and 8Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA 92093
8Department of Biochemistry II, University of Göttingen, 37073 Göttingen, Germany
9Department of Biochemistry, University of Washington, Seattle, WA 98195
10Somehi Orchid Laboratory, Chofu, Tokyo 182-0023, Japan
11Department of Neurology, University Medical Center, 37075 Göttingen, Germany
12Max Planck Institute for Biophysical Chemistry, 37077 Göttingen, Germany
13The Rockefeller University Press
14Department of Molecular Cellular Oncology and Microbiology, Tokyo Medical and Dental University, Bunkyo-ku, Tokyo 113-8549, Japan
15Deutsches Krebsforschungszentrum Heidelberg, 69120 Heidelberg, Germany
16The National Laboratory of Protein Engineering and Plant Genetic Engineering, College of Life Sciences, Peking University, Beijing, P.R. China 100871
17Department of Pharmacology, Biocenter, University of Würzburg, 97074 Würzburg, Germany
18Department of Cell and Developmental Biology, University of Massachusetts Medical School, Worcester, MA 01655
19Department of Life Sciences, Pohang University of Science and Technology, Pohang 790-784, South Korea
20Department of Molecular Biology, Buchmann Institute for Molecular Life Sciences and 21Centre for Molecular Medicine, Goethe University, 60438 Frankfurt am Main, Germany
21Department of Pharmacology, State University of New York Upstate Medical University, Syracuse, NY 13210
22Department of Molecular Cellular Oncology and Microbiology, Tokyo Medical and Dental University, Bunkyo-ku, Tokyo 113-8549, Japan
23Department of Biological Chemistry, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA 90095
24Molecular Cell Biology, University of Groningen, 9700 CC Groningen, Netherlands
25Howard Hughes Medical Institute
26Mitochondrial Biology, Buchmann Institute for Molecular Life Sciences and 27Centre for Molecular Medicine, Goethe University, 60438 Frankfurt am Main, Germany
27Zellbiologie, Universität Bayreuth, 95440 Bayreuth, Germany
28Zellbiologie, Universität Bayreuth, 95440 Bayreuth, Germany
29Crown Bioscience, Inc., Taicang City, Jiangsu Province, P.R. China 215400
30Abteilung für Zelluläre Biochemie, Max-Planck-Institut für Biochemie, 82152 Martinsried, Germany
31Department of Molecular and Cellular Biology, University of California, Davis, Davis, CA 95616

The mitochondrial inner membrane contains a large protein complex that functions in inner membrane organization and 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 F1F0-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 crista junctions (Perkins et al., 1997), connect inner boundary membrane and cristae membranes (Fig. 1, A and B). Respiratory chain complexes and the F1F0-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...
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 cristae 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; Bohnert et al., 2012; Körner et al., 2012; Ott et al., 2012; Zerbes et al., 2012; Jans et al., 2013; Weber et al., 2013). The MICOS/MINOS/MitOS/Mitofilin/Fcj1 complex thus plays crucial roles in mitochondrial architecture, dynamics, and biogenesis. However, communication of results in this rapidly developing field has been complicated by several different nomenclatures used for the complex as well as for its subunits (Table 1).

To rectify this situation, all authors of this article have agreed on a new uniform nomenclature with the following guidelines. (a) The complex will be called “mitochondrial contact site and cristae organizing system” (MICOS). The protein subunits of MICOS are named Mic10 to Mic60 as listed in Table 1. (b) The names, including the numbers shown in Table 1, will be used in all organisms, e.g., Mitofilin/Fcj1 will be named Mic60 in any organism. In case the name MicX has been given to another gene/protein in an organism or a database requires a longer name, the
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 not be changed. The use of capital and small letters as well as of name MiccX will be used in this organism, but the number will

### 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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<tr>
<td><strong>Complex</strong></td>
<td></td>
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<tr>
<td>MICOS</td>
<td>MINOS, MitOS, 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><strong>Subunits</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mic10</td>
<td>Mcs10, Mio10, Mos1, 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; Ogden 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>
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APOOL, apolipoprotein O–like; HMP, heart muscle protein; IMMT, inner mitochondrial membrane protein; MIB, mitochondrial intermembrane space bridging.

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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### References


