Uniform nomenclature for the protein transport machinery of the mitochondrial membranes

Most mitochondrial proteins are synthesized as precursors in the cytosol and are imported into the organelle by a specific protein transport machinery. In the past few years, the combined efforts of several groups have led to the identification of many proteins of this transport machinery and to the cloning of the corresponding genes. As different groups have used different nomenclatures for the same or homologous components of the membrane-linked transport machinery, the situation has become rather confusing. Table I lists the different names used so far; in addition to the original references given in the table, numerous additional sequences for transport components have been deposited in databases.

All groups who have identified a component of the membrane-linked protein transport machinery of mitochondria have now agreed to establish a new uniform nomenclature with the following rules.

(1) Each protein of the transport machinery is named by three letters (a capital letter, followed by two small letters) and a number (Table I). The outer membrane proteins are named 'Tom' (translocase of outer mitochondrial membrane), the inner membrane proteins are named 'Tim' (translocase of inner mitochondrial membrane) ('T' includes intracellular and intramitochondrial targeting). The size of the protein (in kDa) is used as number, e.g. Tom20 and Tim23.

(2) The same number is used for the corresponding proteins of all organisms (e.g. Tom20 for yeast, human, rat and potato). The numbers of the currently known components are shown in Table I.

(3) The number of a novel component will be taken from that organism for which the size was determined first (date of submission of a published article). As long as the sequence is unknown, the number is put in parentheses and will be corrected after sequencing of the gene, using that organism for which the gene was sequenced first. When a component is proteolytically processed, the size of the mature protein is used; when the exact size of the mature protein is unknown, the size of the pre-sequence has to be assessed (e.g. by *in vitro* processing) and subtracted from the predicted primary sequence (the group who sequenced the gene first should agree with the decision about the number).

(4) For the corresponding genes, the same new nomenclature is used according to standard rules, e.g. in *Saccharomyces cerevisiae TOM20* and *TIM23*. The names of genes and proteins in databases will be changed according to the new names in Table I, as will be the names of mutants as long as they contain the gene name.

(5) In cases where it is important to define the organism, e.g. yeast, human, rat or potato, the prefixes y, h, r or p could be added, e.g. hTom20.

Figure 1 shows a model of the transport machinery of the mitochondrial membranes with the new names. The unification of the nomenclature should eliminate the confusion for researchers inside and outside the field of protein targeting and simplify future work on the mitochondrial protein transport machinery.

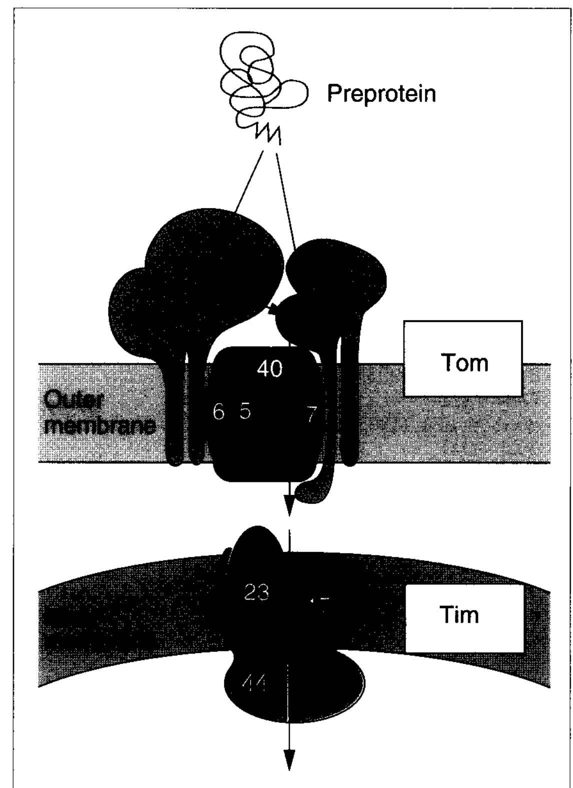

Figure 1
The protein transport machinery of the mitochondrial membranes. Preproteins are recognized by receptors (Tom70– Tom37 and/or Tom22–Tom20) on the mitochondrial surface and are translocated across the outer membrane by further translocase components, including Tom40, Tom7, Tom6, Tom5 (and possibly Tom22). The Tom proteins can assemble into a loose complex. Transport of preproteins across the inner membrane is mediated by the membrane proteins Tim44, Tim23, Tim17 and additional ones that have not yet been identified at a molecular level. In addition, protein import involves the action of soluble proteins, such as molecular chaperones in the cytosol and the matrix, and several processing peptidases; these proteins are not shown in the model.

Table I. Nomenclature of the protein transport machinery of the mitochondrial membranes

New name	Former names	Ref(s)
Translocase of outer mitochondrial membrane		
Tom70	Mas70, Mom72	1–4
Tom40	Isp42, Mom38	5–7
Tom37	Mas37	8
Tom22	Mas17, Mas22, Mom22	7, 9–13
Tom20	Mas20, Mom19, Pom23, Rir16	14–19
Tom7	Mom7	9, 20, 21
Tom6	Isp6, Mom8b	21, 22
Tom5	Mom8, Mom8a	9, 20, 21
Translocase of inner mitochondrial membrane		
Tim44	Isp45, Mim44, Mpi1	23–26
Tim23	Mas6, Mim23, Mpi3	27, 28
Tim17	Mim17, Mpi2, Sms1	28–30

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Tetratrico peptide repeats are present in the kinesin light chain

The tetratrico peptide repeat (TPR) motif is a modular 34 amino acid sequence that mediates intermolecular or intramolecular protein–protein interactions in a large array of structurally and functionally diverse proteins[1] (see Fig. 1a on opposite page). It is predicted to form two short amphipathic α helices, a 'knob' domain and a 'hole' domain, which are essential for TPR function[2–4]. We report here that the *Drosophila* kinesin light chain (KLC) is a TPR protein and propose that the TPR motifs of KLC might mediate the interaction of kinesin with intracellular cargoes.

To complement our ongoing analysis of *Drosophila* KLC function, we performed a BLASTP search[5] of the NCBI peptide sequence database, using amino acids 179–468 of *Drosophila* KLC[6] as the query sequence. This region of KLC contains six imperfect repeats that are highly conserved in KLCs from both vertebrates and invertebrates[6–11] (Fig. 1a). The results of this search and of a second BLASTP query, using the region of CELK04G7.3 most similar to KLC, raised the possibility that KLC contains TPR motifs. Figure 1a shows that at least five out of eight residues of the TPR consensus[2,3] are conserved in each KLC repeat, and that the identity of individual KLC repeats with the SNAP TPR consensus ranges from 44% to 59%, which is comparable to the degree of identity observed for other TPR proteins[12]. In addition, the predicted secondary structure of the KLC repeats is similar to the TPR motif (Fig. 1b). These results strongly suggest that the KLC repeat is homologous to the TPR motif.

Several functions have been proposed for KLC, such as mediating the tethering of intracellular cargoes to the kinesin motor domain, regulating the motor activity of the kinesin heavy chain, or regulating the interaction of the carboxyl terminus of the kinesin heavy chain with cargoes (see Ref. 13 for review). The presence of TPR motifs in KLC suggests that the KLC repeats have an active role in the protein–protein interactions necessary for kinesin-based intracellular transport, either in the binding of intracellular cargoes or the regulation of kinesin motor activity. Tzamarias and Struhl have shown that the region of TUP1 that interacts with TPR motifs 1–3 of CYC8 (SSN6) forms a predicted coiled-coil[14]. An attractive (and testable) hypothesis is that the KLC repeats mediate cargo binding by interacting with the proposed coiled-coil of kinectin, a cargo-bound receptor of kinesin, in a manner similar to the interaction between CYC8 and TUP1 (Refs 15–17).

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