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Minireview

The diverse members of the mitochondrial carrier family in plants

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Abstract Sequencing of plant genomes allowed the identification of various members of the mitochondrial carrier family (MCF). In plants, these structurally related proteins are involved in the transport of solutes like nucleotides, phosphate, di- and tricarboxylates across the mitochondrial membrane and therefore exhibit physiological functions similar to known isoforms from animal or yeast mitochondria. Interestingly, various studies led to the recognition of MCF proteins which mediate the transport of different substrates like folates, *S*-adenosylmethionine, ADP-glucose or ATP, ADP and AMP in plastids.

Keywords: Mitochondrial carrier family; Arabidopsis; Plant; Transport; Mitochondrion; Plastid

1. Introduction

Mitochondria, as the site of electron transport and ATP synthesis play a dominant role in the energy metabolism of almost every eukaryotic cell. The mitochondrion is surrounded by two membranes. The mitochondrial outer membrane shows a very high phospholipid to protein ratio, contains pores and channels allowing the influx of solutes and smaller molecules up to 5000 Da [1], while the inner membrane is tightly packed not only with protein complexes of the electron transport chain and ATP synthases, but also with a wide number of carrier proteins at a surprisingly high density [2].

Apart from ATP and ADP, various intermediates of the Krebs cycle and several other solutes are transferred across the mitochondrial inner membrane via structurally related hydrophobic proteins, representing the mitochondrial carrier family (MCF) [2–5]. Characteristic features of MCF proteins are (i) a molecular mass of about 30 kDa, (ii) three repeated domains each of about 100 amino acids in length consisting of two transmembrane spanning α-helices and (iii) the presence of one to three highly conserved sequence motifs, named the mitochondrial energy signature [6,7]. In 2003, Millar and Heazlewood reported 45 genes encoding MCF proteins in Arabidopsis [5], and an extended *in silico* screening allowed the identification of 13 additional members [3].

Several subgroups of MCF proteins were classified on basis of biochemical characteristics, phylogenetic relationships, amino acid similarities and ortholog/paralog analyses between corresponding carriers of yeast, animals and plants [3–5]. Assigning functions to unknown carriers often relies on their affiliation to a subgroup containing functionally related members. However, annotation of the function without experimental evidence is never decisive and maybe misleading.

Interestingly, not all members of the MCF are located in mitochondria since recent findings document that MCF carriers are also present in peroxisomes, glyoxysomes or plastids [8–13]. Therefore, computer based prediction of the localisation of MCF proteins is only one step towards a subcellular localisation and is sometimes ambiguous [3,5].

Furthermore, various mitochondrial located MCF proteins from mammals or plants possess cleavable N-terminal extensions, while others lack comparable targeting sequences but also enter this cellular domain. Several studies indicate that these extensions are not essential for correct targeting into mitochondria but probably enhance import specificity and efficiency [14–16].

Accordingly, the determination of the physiological role of a so far uncharacterised carrier not only requires the analysis of its biochemical properties and expression pattern but also the establishment of its exact cellular localisation. Furthermore, to investigate the physiological impact of carriers detailed analyses of transgenic plants with reduced amounts of the corresponding proteins are necessary.

This review summarises important characteristics of different mitochondrial and plastidic MCF proteins in plants.

1.1. ADP/ATP carriers and phosphate carriers

ADP/ATP carriers (AAC) mediate the export of ATP generated in the mitochondrion in counter exchange with cytosolic ADP. Their substrate affinities are regulated by the membrane potential and transport is inhibited by bongkrekic acid, atractyloside and carboxyatractyloside [2,17–19]. Due to the general importance of mitochondrial ATP production it is not surprising that in potato, a slight reduction of *aac* transcripts by antisense-technique resulted in a strong decrease of the tuber yield (Haferkamp, Tjaden unpublished data).

Analyses on basis of *aac*-promoter–reporter genes revealed ubiquitous expression of *aac1* (At3g08580) and *aac2* (At5g13490) with highest rates for *aac1* and moderate rates for *aac2* (Haferkamp, unpublished data). Expression of *aac3* (At4g28390) was solely detectable within actively growing tissues. These data are consistent with the relative occurrence of the individual AAC proteins in the mitochondrial membrane

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proteome from Arabidopsis [5]. Therefore, it can be postulated that the highly abundant carrier AAC1 fulfils the main function in energy transfer of Arabidopsis mitochondria.

During oxidative phosphorylation in mitochondria ATP is regenerated from ADP and Pi. The latter is provided by mitochondrial phosphate carriers (PiC) which catalyse a Pi/OH^- antiport [20] or a Pi/H^+ symport [16]. The two phosphate carriers PiC1 (At5g14040) and PiC2 (At3g4880) from Arabidopsis were shown to complement a yeast mutant lacking the endogenous carrier [21]. Interestingly, a third putative PiC from Arabidopsis (At2g17270) did not restore phosphate transport into mitochondria of the deletion mutant.

The high abundance of PiC1 and AAC1 in the mitochondrial proteome supports the idea of a metabolic interaction of these two proteins during ATP regeneration in Arabidopsis [5] (Fig. 1).

1.2. Uncoupling proteins

Uncoupling proteins (UCP) catalyse a nucleotide-sensitive, fatty-acid-mediated proton transport across the inner

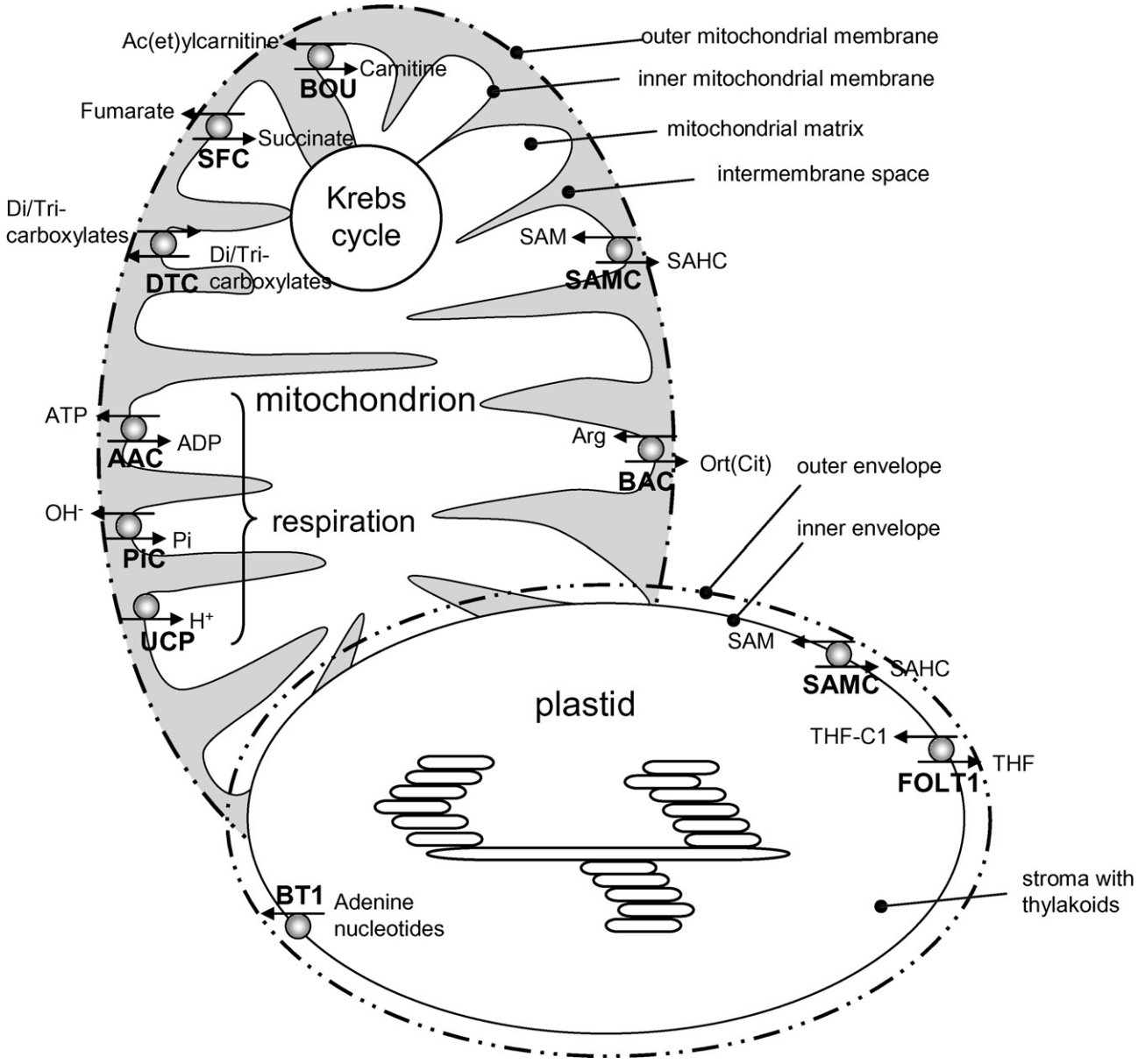

Fig. 1. Simplified model of the localisation and function of characterised MCF members from *Arabidopsis thaliana*. Intermediates of the Krebs cycle are the substrates of the SFC (succinate/fumarate carrier) and of the DTC (dicarboxylate/tricarboxylate carrier). Therefore, these carriers connect the Krebs cycle with various metabolic processes outside the mitochondrion. The AAC (ADP/ATP carrier) and the PiC (phosphate carrier) provide the substrates for ATP synthesis. The proton export mediated by the UCP (uncoupling protein) reduces the electrochemical gradient across the inner mitochondrial membrane. Arginine (Arg) is converted by mitochondrial localised enzymes to ornithine (Ort) or citrulline (Cit). BAC (basic amino acid carriers) mediate the required Arg/Ort or Arg/Cit exchange. With respect to the provision or removal of one-carbon units the substrates of the carriers SAMC (*S*-adenosylmethionine carrier) and FOLT1 (folate transporter) play an important role in different metabolic processes. The carrier BT1 exports adenine nucleotides which are exclusively synthesised in the plastids. BOU1 is assumed to mediate acylcarnitine/carnitine exchange which links fatty acid mobilisation with the Krebs cycle.