Ferdinando Palmieri: Peter Mitchell medal award 2024

- Ferdinando Palmieri é nato a Lumezzane (Brescia) nel 1939 e si è laureato in Medicina con 110 e lode presso l'Università di Napoli "Federico II".
- E' stato prof. Ordinario di Biochimica presso l'Università di Bari ed é ora prof. Emerito presso la stessa Università e prof. Onorario presso l'Università di Mosca (Lomonosov Moscow State University).

- Ha ricevuto la Medaglia d’oro ai Benemeriti della Scienza e della Cultura dal Presidente della Repubblica nel 2000, il premio di Cultura Renoir Regione Puglia nel 2006 e il premio “Caduceo d’Oro” dall’Ordine dei farmacisti di Bari nel 2010.
- E’ membro dell’Accademia Nazionale dei Lincei, dell’Accademia delle Scienze di Torino, dell’Istituto Lombardo Accademia di scienze e lettere (Milano), della Società nazionale di scienze, lettere e arti (Napoli) e della “The academy of Europe” (Londra).

- E’ Co-Editore di 19 libri scientifici pubblicati da Addison-Wesley (5), John Wiley (4) e Elsevier (10).
- E’ autore di 371 lavori su riviste internazionali, è reviewer o membro del Comitato Editoriale di molte riviste internazionali ed é stato relatore (speaker su invito) in più di 40 congressi internazionali.

- Il prof. Ferdinando Palmieri, Socio Nazionale dell'Accademia dei Lincei, già Professore Ordinario di Biochimica e attualmente Professore Emerito presso l'Università degli Studi di Bari Aldo Moro, è stato insignito della prestigiosa "Medaglia Mitchell", il massimo riconoscimento internazionale nel campo della Bioenergetica.
- Il prof. Palmieri è il primo scienziato italiano a cui viene attribuita la Medaglia da quando il premio è stato istituito nel 1994 all'indomani della scomparsa di Mitchell.

I trasportatori mitocondriali

- Il principale interesse scientifico del Prof. Palmieri è l'identificazione, caratterizzazione funzionale e farmacologica dei trasportatori mitocondriali. La ricerca del Prof. Palmieri in questo campo è stata estremamente prolifica ed il suo gruppo di ricerca all'università di Bari è stato negli anni un punto di riferimento mondiale per questo fondamentale campo di ricerca.

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SPECIAL ISSUE

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Mitochondrial transport and metabolism of the vitamin B-derived cofactors thiamine pyrophosphate, coenzyme A, FAD and NAD$^+$, and related diseases: A review

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Abstract

Multiple mitochondrial matrix enzymes playing key roles in metabolism require cofactors for their action. Due to the high impermeability of the mitochondrial inner membrane, these cofactors need to be synthesized within the mitochondria or be imported, themselves or one of their precursors, into the organelles. Transporters belonging to the protein family of mitochondrial carriers have been identified to transport the coenzymes: thiamine pyrophosphate, coenzyme A, FAD and NAD$^+$, which are all structurally similar to nucleotides and derived from different B-vitamins. These mitochondrial cofactors bind more or less tightly to their enzymes and, after having been involved in a specific reaction step, are regenerated, spontaneously or by other enzymes, to return to their active form, ready for the next catalysis round. Disease-causing mutations in the mitochondrial cofactor carrier genes compromise not only the transport reaction but also the activity of all mitochondrial enzymes using that particular cofactor and the metabolic pathways in which the cofactor-dependent enzymes are involved. The mitochondrial transport, metabolism

Abbreviations: ALS, acetolactate synthase; BCAA, branched-chain amino acid; BCKDH(c), branched-chain α-ketoacid dehydrogenase (complex); CHO, chinese hamster ovary; CoA, coenzyme A; COASY, coenzyme A synthase; EPRA, expression, purification, reconstitution and transport assay; FAD, flavin adenine dinucleotide; FADS, flavin adenine dinucleotide synthase; FMN, flavin mononucleotide; MADD, multiple acyl-CoA dehydrogenase deficiencies; MC, mitochondrial carrier; NAAD, nicotinic acid adenine dinucleotide; NAD$^+$, nicotinamide adenine dinucleotide; NAMN, nicotinate mononucleotide; NUDIX, nucleoside diphosphate-linked moiety X; OADH(c), 2-oxoadipate dehydrogenase (complex); OGDH(c), oxoglutarate dehydrogenase (complex); PANK, pantothenate kinase; PAP, adenosine 3′,5′-diphosphate; PDC, pyruvate decarboxylase; PDH(c), pyruvate dehydrogenase (complex); RDA, recommended daily allowance; SAM, S-adenosylmethionine; SM, synthetic minimal; TCA, tricarboxylic acid; ThMP, thiamine monophosphate; ThPP, thiamine pyrophosphate; ThTP, thiamine triphosphate; THTPA, thiamine triphosphatase; TKT, transketolase; TPC, thiamine pyrophosphate carrier; TPK1, thiamine pyrophosphatase 1.

Ferdinando Palmieri and Magnus Monné contributed equally to this work.

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Review

The mitochondrial transporter family SLC25: Identification, properties and physiopathology ☆

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ABSTRACT

SLC25 is a large family of nuclear-encoded transporters embedded in the inner mitochondrial membrane and in a few cases other organelle membranes. The members of this superfamily are widespread in eukaryotes and involved in numerous metabolic pathways and cell functions. They can be easily recognized by their striking sequence features, i.e., a tripartite structure, six transmembrane α-helices and a 3-fold repeated signature motifs. SLC25 members vary greatly in the nature and size of their transported substrates, modes of transport (i.e., uniport, symport or antiport) and driving forces, although the molecular mechanism of substrate translocation may be basically the same. Based on substrate specificity, 24 subfamilies, well conserved throughout evolution, have been functionally characterized mainly by transport assays upon heterologous gene expression, purification and reconstitution into liposomes. Several other SLC25 family members remain to be characterized. In recent years mutations in the SLC25 genes have been shown to be responsible for 11 diseases, highlighting the important role of SLC25 in metabolism.

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Molecular Identification and Functional Characterization of *Arabidopsis thaliana* Mitochondrial and Chloroplastic NAD^+ Carrier Proteins*[S]

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The *Arabidopsis thaliana* L. genome contains 58 membrane proteins belonging to the mitochondrial carrier family. Two mitochondrial carrier family members, here named *At*NDT1 and *At*NDT2, exhibit high structural similarities to the mitochondrial nicotinamide adenine dinucleotide (NAD^+) carrier *Sc*NDT1 from bakers' yeast. Expression of *At*NDT1 or *At*NDT2 restores mitochondrial NAD^+ transport activity in a yeast mutant lacking *Sc*NDT. Localization studies with green fluorescent protein fusion proteins provided evidence that *At*NDT1 resides in chloroplasts, whereas only *At*NDT2 locates to mitochondria. Heterologous expression in *Escherichia coli* followed by purification, reconstitution in proteoliposomes, and uptake experiments revealed that both carriers exhibit a submillimolar affinity for NAD^+ and transport this compound in a counter-exchange mode. Among various substrates ADP and AMP are the most efficient counter-exchange substrates for NAD^+. *Atndt1-* and *Atndt2-promoter-GUS* plants demonstrate that both genes are strongly expressed in developing tissues and in particular in highly metabolically active cells. The presence of both carriers is discussed with respect to the subcellular localization of *de novo* NAD^+ biosynthesis in plants and with respect to both the NAD^+-dependent metabolic pathways and the redox balance of chloroplasts and mitochondria.

Nucleotides are metabolites of enormous importance for all living cells. They are the essential building blocks for DNA and RNA synthesis, energize most anabolic and many catabolic important roles in the operation and control of a wide range of dehydrogenase activities. Accordingly, nucleotides are essential in nearly all cell organelles, and transport of these solutes into mitochondria, plastids, the endoplasmic reticulum, the Golgi apparatus, and peroxisomes has been observed (4–7).

Two types of nucleotide transport proteins have been identified to date at the molecular level: nucleotide transporter (NTT)[2] type carriers and members of the mitochondrial carrier family. The former transporters occur in plastids from all plants (8) and in a limited number of intracellular pathogenic bacteria (9). Most NTT-type carrier proteins catalyze an $ATP/ADP+P_i$ counter-exchange mode of transport (10–13), but several bacterial NTT proteins mediate either H^+/nucleotide transport or NAD^+/ADP counter-exchange (12, 14, 15). With the exception of the bacterial NAD^+/ADP carrier (14), all NTT proteins exhibit 12 predicted trans-membrane domains, whereas none of the NTT proteins share structural or domain similarities to members of the mitochondrial carrier family (11).

Carriers belonging to the mitochondrial carrier family (MCF) represent the second group of nucleotide transporters (16, 17). The most prominent member is the mitochondrial ADP/ATP carrier AAC (4), but MCF-type nucleotide transporters have also been identified in peroxisomes (7, 18), in plastids (19, 20), and in the endoplasmic reticulum of higher plants (21). The transport modes catalyzed by MCF-type adenylate nucleotide transporters range from typical ADP/ATP counter-exchange in mitochondria (4) to ATP/AMP exchange in peroxisomes (7, 18) and in *Arabidopsis* mitochondria (22) range