Ferdinando Palmieri, Professor, Department of Biosciences, Biotechnologies and Biopharmaceutics, Laboratory of Biochemistry and Molecular Biology, University of Bari, Italy.

Full Name: Ferdinando Palmieri

Born: April 26, 1939 in Lumezzane, Brescia, Italy

<u>University education</u>: 1963, graduated in Medicine cum laude at the University of Naples

Lecturer of Biochemistry: 1/11/1963 - 31/10/1971, University of Bari Establishment as University lecturer: 1/11/1968

Establishment as University lecturer: 1/11/1968

Associated Professor: 1/11/1971 - 31/10/1973, University of Bari

Full Professor in Biochemistry: 1/11/1973, University of Bari

- <u>Visiting lecturer:</u> 15/01/1966-31/12/1966, Physiologische-Chemische Institüt der Philipps-Universität, Marburg, W. Germany; 1/10/1968-31/12/1968, Institüt fur Physiologische Chemie und Physikalische Biochemie der Universität Munchen, W. Germany
- <u>Visiting</u> Professor: June-August 1974, 1/12/1975-31/01/1976, Dept. of Molecular Biology, Vanderbilt University, Nashville, Tennessee, USA; June-August 1979, University of Pennsylvania, School of Medicine, Johnson Research Foundation, Philadelphia, Pennsylvania, USA

Honors and Awards

- Recipient of the "Gold Medal 2000" Award from the President of the Italian Republic for contributions to Science and Culture.
- Recipient of the "Renoir" Cultural Award from the Apulia Region, 2006.
- Nominated Honorary Professor of Lomonosov Moscow State University (Russia), 2010.
- Recipient of the "Caduceo d'Oro" from Order of the Italian Chemists, 2010.
- Member of the "Accademia Nazionale dei Lincei" (Rome), the Academia Europaea "The Academy of Europe" (London); the "Accademia delle scienze" (Turin), the "Accademia di scienze e lettere, Istituto Lombardo" (Milan), the "Società nazionale di scienze, lettere e arti" (Naples).
- <u>Nominated Emeritus Professor</u> of the University of Bari by the Minister of Education, University and Research (MIUR): 2011.
- <u>Member of the Fellowships Committee</u> of the Federation of the European Biochemical Societies (FEBS), 1984-1989.
- <u>Member of the National Evaluation Committee of the Ministery</u> of Education, University and Research (MIUR) for funding research projects: 1985-1997 and again in 2004-2005.
- <u>President of the National Evaluation Committee for the University of</u> <u>Bari</u>: 2003-2008.

- Recipient of the "Gold Medal 2000" Award from the University of Bari, 2011
- <u>Member of the National Evaluation Committee</u> for the University of Catania: 2009-2012
- Recipient of the "Mitchell Medal and Lecture 2024" Award for achievements in bioenergetics (see website of EBEC 2024: www.ebec2024.org.)

Scientific Contributions:

- Author/co-author of 390 publications.
- <u>Co-editor of the following books:</u>

a) Horizons in Biochemistry and Biophysics (E. Quagliariello, F. Palmieri and T.P. Singer, eds.), Addison-Wesley, MA, USA: volume 1, 1975

- " 2, 1976
- " 3, 1977
- " 4, 1978
- " 5. 1979

Horizons in Biochemistry and Biophysics (E. Quagliariello and F. Palmieri, eds.), John Wiley & Sons Publishers, London-New York):

- 6, 1982
- " 7, 1983
- " 8, 1985
- " 9, 1989

b) Electron Transfer Chains and Oxidative Phosphorylation (E. Quagliariello, S. Papa, F. Palmieri, E.C. Slater and N. Siliprandi, eds.), North-Holland/American Elsevier, 1975

c) Function and Molecular Aspects of Biomembrane Transport (E. Quagliariello, F. Palmieri, S. Papa and M. Klingenberg, Eds.), North-Holland/American Elsevier, 1979

d) Vectorial Reactions in Electron and Ion Transport in Mitochondria and Bacteria (F. Palmieri, E. Quagliariello, N. Siliprandi and E.C. Slater, eds.), North-Holland/American Elsevier, 1981

e) Structure and Function of Membrane Proteins (E. Quagliariello and F. Palmieri, eds.), Elsevier Science Publishers, Amsterdam, 1983

f) Achievements and Perspectives of Mitochondrial Research. Volume I: bioenergetics (E. Quagliariello, E.C. Slater, F. Palmieri, C. Saccone and A.M. Kroon, eds.), Elsevier Science Publishers, Amsterdam, 1985

g) Achievements and Perspectives of Mitochondrial Research. Volume II: biogenesis (E. Quagliariello, E.C. Slater, F. Palmieri, C. Saccone

and A.M. Kroon, eds.), Elsevier Science Publishers, Amsterdam, 1985

h) Molecular Basis of Biomembrane Transport (E. Quagliariello and F. Palmieri, eds.), Elsevier Science Publishers, Amsterdam, 1988

i) Structure, Function and Biogenesis of Energy Transfer Systems (E. Quagliariello and F. Palmieri, eds.), Elsevier Science Publishers, Amsterdam, 1990

I) Molecular Mechanisms of Transport (E. Quagliariello and F. Palmieri eds.), Elsevier Science Publishers, Amsterdam, 1992

m) Thirty Years of Progress in Mitochondrial Bioenergetics and Molecular Biology (F. Palmieri et al., eds.) Elsevier Science Publishers, Amsterdam, 1995

 n) Special Issue "Mitochondrial Transport Proteins" published in Biomolecules, ISBN 978-3-0365-3409-1, April 2022, 476 pages (23 papers); see link:

https://www.mdpi.com/journal/biomolecules/special issues/mitochondrial tran sport protein

o) Special Issue "Transport Mechanisms of Mitochondrial Membrane Proteins" published in International Journal of Molecular *Sciences* ISSN 1422-0067, April 2024 (6 papers); see link:

https://www.mdpi.com/journal/ijms/special_issues/mitochondrial_transporters

p) Special Issue "Advances in Mitochondrial Transport Research" published in Biomolecules ISSN 2218-273X, June 2024 (10 papers); see link:

https://www.mdpi.com/journal/biomolecules/special_issues/mitochondrial_ transport_research

Member of the Editorial Board or Advisory Board of the following Journals:

Biochemical Journal, Journal of Bioenergetics and Biomembranes, Biochemical Medicine and Metabolic Biology, Molecular Membrane Biology, Molecular Genetics and Metabolism, Bulletin of Molecular Biology and Medicine, Biochemical and Molecular Medicine, International J. of Molecular Sciences.

Referee also of other Journals:

Nature, Science, PNAS, EMBO Journal, JBC, Biochemistry, The European Journal of Biochemistry – FEBS Journal, Biochim. Biophys. Acta, Eur. Biophysics Journal, FEBS Letters, Nature communications, Arch. Biochem. Biophys., Plant Physiology, Molecular and Cellular Biology, American J. of Human Genetics, Molecular Microbiology, J. of Molecular Biology, The Plant Journal, Human Molecular Genetics, J. of Inherited Metabolic Disease, Molecular Pharmacology, etc.

Speaker at the following international congresses (among others) :

- International Congress of Biochemistry: Luzern 1970, Stockholm 1973, Prague 1988, Bari 1992
- FEBS Meetings: Budapest 1974, Dresden 1978, Rome 1989, Helsinki 1994, Warsaw 2004
- European Bioenergetics Conferences (EBEC): Lyon 1982, Prague 1986, Amsterdam 1990, Helsinki 1992, Louvain-la Neuve 1996, Pisa 2004, Moscow 2006, Dublin 2008, Innsbruck 2024
- Gordon Conferences in USA: 1981, 1987
- International Biophysics Congress: Bristol 1984, Amsterdam 1996
- Physicochemical basis of ion transport through biological membranes, in Riga 1970
- Biomembranes, in Madurai 1973
- Membrane bioenergetics, Spetsai 1977
- Structure and Function of energy-transducing membranes, Amsterdam 1977
- Mechanisms of proton and calcium pumps, Padua 1977
- 7th Colloquim on bioenergetics and mitochondria, Gdansk 1977
- FEBS Advanced Course No.59, Bioenergetics and transport at mitochondrial and cellular levels, Warsaw (Poland), 1980
- 12th Meeting of the GDR Biochemical Society, Magdeburg (E. Germany), 1980
- The Mitochondrion, Baltimore (USA), 1986
- Joint Meeting American Society for Biochemistry and Molecular Biology and the American Society for Cell Biology, San Francisco (USA),1989
- 112th Conference of the Gesellschaft fur Biologishe Chemie, Munich (Germany) 1994
- International Symposium on "Proton-Linked Pumps and Transporters" Bristol (UK) 1995
- Fourth European Symposium of the Protein Society, Paris (France) 2001
- International Symposium on "Citrin deficiency and the related diseases" Kagoshima (Japan) 2005
- International Conference on "Mitochondria, from Molecular Insight to Physiology and Pathology" Bari (Italy) 2005
- Proteins in Health and Disease: from structure to function, Lisboa 2007
- Symposium on Science for the Study of Inborn Errors of Metabolism, Hamburg (Germany), 2007
- European Science Foundation Conference in Biomedicine on "Rare Diseases: Channels and Transporters", Barcelona (Spain), March 2008
- 11th International Congress on Amino Acids, Peptides and Proteins, Vienna (Austria), 2009
- 43rd European Metabolic Group (EMG), Salzburg, 2011
- 12th International Conference on Inborn Errors of Metabolism, Barcelona (Spain), 2013
- The Evolving Concept of Mitochondria: From Symbiotic Origins to Therapeutic Opportunities, Cold Spring Harbor (USA), 2018

• The SLC25 mitochondrial carrier family: identification, properties and physiopathology, Innsbruck (Austria), 2024

Major research achievements

- <u>in the 60ies</u> establishment of the anisotropy of cytochrome c oxidase and succinate dehydrogenase; relationships between metabolite anion and cation transport
- <u>in the 70ies</u> establishment and stoichiometry of the delta-pH dependent phosphate, malate, citrate and azide transport, and establishment of the membrane potential dependence of thiocyanate transport and the aspartate/glutamate (cysteinesulfate) exchange across the mitochondrial membrane
- <u>in the 70ies</u> characterization of several mitochondrial metabolite carriers in isolated mitochondria
- <u>in the 70ies</u> development of direct transport measurements across natural and artificially made membranes (liposomes)
- <u>in the 80ies</u> purification of 10 mitochondrial metabolite carriers and reconstitution in an active state
- <u>in the late 80ies and in the 90ies</u> (before the genomic era) determination of the primary structure of the oxoglutarate/malate carrier and the carnitine/acylcarnitine carrier
- <u>in the 90ies</u> for the first time, a membrane protein, i.e. the oxoglutarate/malate carrier, was successfully expressed in *E. coli* in a reconstitutively active state
- in the 90ies establishment of the topology of several mitochondrial metabolite carriers in the inner mitochondrial membrane and in liposomes (i. e., both the N- and the C- terminal ends are exposed towards the mitochondrial intermembrane space and the proteins have an even number of alpha-helices)
- <u>in the 90ies</u> discovery that the 2 phosphate carrier isoforms are encoded by a single gene by an alternative splicing; tissue expression and biochemical characterization of the 2 phosphate carrier isoforms
- in the late 90ies and the first 2 decades of the 21st century the molecular identification of 26 mitochondrial metabolite (di- and tricarboxylates, amino acids, nucleotides, coenzymes, etc.) carriers in humans, 19 in Arabidopsis thaliana and 18 in Saccharomyces cerevisiae was achieved (see attachments 1, 2 and 3)
- in the late 90ies and the first 2 decades of the 21st century the identification of 10 monogenic diseases due to genetic alterations of specific mitochondrial metabolite carriers was accomplished (see attachment 4); and understanding of their physiopathology, biochemical comprehension of their symptoms and, in some cases, successful therapeutic treatments were achieved.

Scientific/Professional Activities:

- <u>Member of the Executive Committee of the Italian Biochemical Society</u> 1977-1982; 1990-1994
- <u>Treasurer</u> of the Italian Biochemical Society (SIB),1977-1979
- Secretary of the Italian Biochemical Society (SIB), 1980-82; 1993-94.
- <u>President</u> of the Italian Group of Bioenergetics,1999-2000; and three times Vice-President, 1977-1978; 1986-1990; 1997-1998
- Member of the Fellowships Committee of FEBS: 1984-1989
- <u>National Representative of the International Union of Biological</u> <u>Sciences</u> (IUBS) of the International Council of Scientific Unions (ICSU), 2010-2012
- <u>Member of the Scientific Committee</u> of the National Research Council (CNR): "CNR Institute for the Study of Mitochondria and Bioenergetics", Dept. of Biochemistry, University of Bari, Italy: 1972-2002; "CNR Institute for the Study of Physiology and the Biochemistry of Hemocyanines and other Metalloproteins", Dept. of Physiology, University of Padua, Italy: 1977-1997; and CNR National Strategic Scientific Projects.
- <u>Member of the Scientific Committee</u> of the National Research Council (CNR) project of the Study of Cancer: 1978-1982
- <u>Member of the Scientific Committee</u> of the G. Lorenzini Foundation (Milan), 1988-2006.
- Member of the "Consiglio Universitario Nazionale" (CUN): 1997 2006
- <u>President</u> of the "Centro Interdipartimentale di Servizi per gli Studi Biologici (CISBi)" of the University of Bari: 1995-2010
- <u>Scientific Coordinator</u> of the "Centro di Eccellenza in Genomica comparata (CEGBA), University of Bari 2001-2010
- <u>Supervisor</u> of more than 40 Ph.D.s
- Member of the Scientific Committee of many national and international congresses

Academic appointments:

- <u>Director</u> of the Institut of Biochemistry, Faculty of Pharmacy, University of Bari, 1974-1982
- <u>Director</u> of the Department of Pharmaco-Biology, University of Bari, 1983-87; 1992-97.
- <u>Member of the Board of Administration</u> of the University of Bari: 1986-1990
- <u>Member of the Managing Board of the Faculty of Pharmacy</u>, University of Calabria, 1992-1996.
- <u>President of the Management Board</u> of the Faculty of Pharmacy, University of Basilicata, 2007-2010.

- <u>Director of the Graduate School</u> of Functional and Applied Genomics and Proteomics (awarding doctoral degrees in Molecular Biochemistry and Biology, Cellular and Molecular Physiology and Biotechnology, Genetics and Molecular Evolution, and Biochemical and Pharmacological Science), 2004-2010.
- <u>Director of the Graduate School</u> of Cellular Biochemistry and Cellular Pharmacology (awarding doctoral degrees), 1998-2004.
- <u>Director of the School of Specialization</u> in Applied Pharmacology, University of Bari, 1983-1991.
- Collaboration with foreign scientists: J.E. Walker (MRC Cambridge, UK); M. Klingenberg (Munich, Germany); G. Brandolin (Grenoble, France); Nader Abraham (Medical College, New York, USA); A.R. Fernie (Golm, Germany); M. Hodges (Paris, France); E.R.S. Kunji (MRC Cambridge, UK); P. Maechler (Geneva, Switzerland); J.C. Polacco (Columbia, MO, USA); K.B. Storey (Ottawa, Canada); J.R. De Lucas (Madrid, Spain); A.M. Smeitink (Nijmegen, The Netherlands); A. Wedell (Stockholm, Sweden); M. J. Falk (Philadelphia, USA), T. Saheki (Kagoshima, Japan); G. Satrustegui (Spain).

Mitochondrial carriers identified in humans

	Carrier name	Gene name	Acronym	Reference in publication list of F. Palmieri
1	ornithine (isoform 2)	SLC25A2	ORC2	230
2	phosphate (isoform 1)	SLC25A3	PiC-A	187
3	phosphate (isoform 2)	SLC25A3	PiC-B	187
4	Uncoupling protein 2	SLC25A8	UCP2	334
5	dicarboxylate	SLC25A10	DIC	188
6	2-oxoglutarate	SLC25A11	OGC	142
7	aspartate/glutamate (isoform 1)	SLC25A12	AGC1	213
8	aspartate/glutamate (isoform 2)	SLC25A13	AGC2	213
9	sulfur oxyanions, phosphate, dicarboxylate (Uncoupling protein 5)	SLC25A14	UCP5	373
10	ornithine (isoform 1)	SLC25A15	ORC1	230
11	adenine nucleotide (peroxisomal)	SLC25A17	CFNC	313
12	glutamate (isoform 2)	SLC25A18	GC2	218
13	thiamine pyrophosphate	SLC25A19	TPC	206, 266
14	carnitine/acylcarnitine	SLC25A20	CAC	186
15	oxodicarboxylate	SLC25A21	ODC	207
16	glutamate (isoform 1)	SLC25A22	GC1	218
17	ATP-Mg/phosphate (isoform 1)	SLC25A24	APC1	240
18	ATP-Mg/phosphate (isoform 2)	SLC25A23	APC2	240
19	ATP-Mg/phosphate (isoform 3)	SLC25A25	APC3	240
20	S-adenosyl-methionine	SLC25A26	SAMC	237
21	basic amino acids	SLC25A29		339
22	sulfur oxyanions, phosphate,	SLC25A30	UCP6	373
	dicarboxylate (Uncoupling protein 6)			
23	ADP/ATP (isoform 4)	SLC25A31	AAC4	249
24	pyrimidine nucleotide (isoform 1)	SLC25A33	PNC1	342
25	pyrimidine nucleotide (isoform 2)	SLC25A36	PNC2	342
26	Coenzyme A	SLC25A42	CoAPC	287

Mitochondrial carriers identified in Arabidopsis thaliana

	Carrier name	Gene name	Acronym	Reference in
			-	publication
				list of F.
				Palmieri
1	NAD⁺ (isoform 2)	AT1G25380	NDT2	297
2	S-adenosyl-methionine (isoform 2)	AT1G34065	SAMC2	264
3	basic amino acids (isoform 2)	AT1G79900	BAC2	260
4	dicarboxylate (isoform 1)	AT2G22500	DIC1	276
5	dicarboxylate (isoform 2)	AT4G24570	DIC2	276
6	dicarboxylate (isoform 3)	AT5G09470	DIC3	276
7	basic amino acids (isoform 1)	AT2G33820	BAC1	228
8	nucleotide cofactors (peroxisomal)	AT2G39970	PXN	318
9	NAD⁺ (isoform 1)	AT2G47490	NDT1	297
10	aspartate, glutamate, dicarboxylate	AT3G54110	PUMP1	365
	(Uncoupling protein 1)			
11	aspartate, glutamate, dicarboxylate	AT5G58970	PUMP2	365
	(Uncoupling protein 2)			
12	ATP/AMP	AT4G01100	ADNT1	284
13	S-adenosyl-methionine (isoform 1)	AT4G39460	SAMC1	264
14	succinate/fumarate	AT5G01340	SFC1	378
15	ATP-Mg/phosphate (isoform 1)	AT5G61810	APC1	349
16	ATP-Mg/phosphate (isoform 2)	AT5G51050	APC2	349
17	ATP-Mg/phosphate (isoform 3)	AT5G07320	APC3	349
18	dicarboxylate tricarboxylate	AT5G19760	DTC	221
19	glutamate	AT5G46800	BOU	337

Mitochondrial carriers identified in Saccharomyces cerevisiae

	Carrier name	Gene name	Acronym	Reference in publication list of F. Palmieri
1	dicarboxylate	YLR348C	DIC	174
2	ornithine	YOR130C	ARG11(ORT1)	178
3	succinate/fumarate	YJR095W	SFC1(ACR1)	181
4	carnitine	YOR100C	CRC1	201
5	oxaloacetate, sulfate	YKL120W	OAC1	199, 282
6	oxodicarboxylate (isoform 1)	YPL134C	ODC1	206
7	oxodicarboxylate (isoform 2)	YOR222W	ODC2	206
8	ATP/AMP (peroxisomal)	YPR128C	ANT1	213
9	thiamine pyrophosphate	YGR096W	TPC1	223
10	S-adenosylmethionine	YNL003C	PET8 (SAM5)	235
11	aspartate/glutamate	YPR021C	AGC1	234
12	GDP/GTP	YDL198C	GGC1 (YHM1, SHM1)	240
13	pyrimidine nucleotides	YBR192W	RIM2	258
14	NAD⁺	YIL006W	NDT1 (YIA6)	259
15	NAD⁺	YEL006W	NDT2 (YEA6)	259
16	citrate/oxoglutarate	YMR241W	YHM2	300
17	APS/PAPS	YPR011C	MRX21	334
18	glutamate	YBR104W	YMC2	367

Diseases identified to be associated to mitochondrial carriers

Affected mitochondrial carrier	Phenotype	OMIM	Reference in publication list of F. Palmieri
SLC25A8, uncoupling protein 2 (UCP2)	Congenital hyperinsulinism		356
SLC25A10, dicarboxylate carrier (DIC)	Intractable epileptic encephalopathy with complex I deficiency	618972	364
SLC25A12, aspartate/glutamate carrier 1 (AGC1)	Early infantile epileptic encephalopathy 39 (AGC1 deficiency)	612949	294, 336
SLC25A13, aspartate/glutamate carrier 2 (AGC2)	Adult-onset citrullinemia type II (CTLN2) Neonatal-onset citrullinemia type II (NICCD)	603471 605814	214
SLC25A15	Hyperornithinemia- hyperammonemia- homocitrullinemia (HHH) syndrome	238970	231, 285
SLC25A19, thiamine pyrophosphate carrier (TPC)	Amish microcephaly	607196	222, 267
SLC25A20, carnitine/acylcarnitine carrier (CAC)	Carnitine-acylcarnitine translocase deficiency (CAC deficiency)	212138	180
SLC25A22, glutamate carrier 1 (GC1)	Early infantile epileptic encephalopathy 3 (EIEE3)	609304	249, 292
SLC25A26, S-adenosylmethionine carrier (SAMC)	Combined oxidative phosphorylation deficiency 28	616794	351
SLC25A36	Familial hyperinsulinemic hypoglycemia 8	620211	383