



## **Prof. Salvatore Passarella**

Ordinario di Biochimica presso la Facoltà di Economia  
dell'Università degli Studi del Molise

Since 1990 Professor Salvatore Passarella is full professor of Biochemistry in the University of Molise where he is coordinatore of the PhD course in Applied Biochemistry and Chemistry.

He was Dean of the Faculty of Agriculture (1993-1996) and since 1995 he is Prorettore of the University of Molise. Prof. Passarella has published more than 125 papers.

The recent Passarella's research topics include:

1. Energy metabolism in animal, plant and yeast mitochondria
    - 1.1 Mitochondrial transport of metabolites and vitamins
    - 1.2 Novel pathways and enzymes
    - 1.3 The laser light sensitivity of isolated cells, mitochondria, enzymes and molecules
- A review on the role of mitochondrial transport in energy metabolism has been recently published.

In particular, Professor Passarella has shown the occurrence of the malate/oxaloacetate shuttle aimed at transferring reducing equivalents from cytosol to mitochondria. Such a shuttle has been shown to play a major role in the oxidation of NADH by mitochondria isolated from plants, with a minor role to the external NAD(P)H dehydrogenases; this provides a novel metabolic pathway in plant biochemistry. That malate/oxaloacetate shuttle largely contributes to the oxidation of externally added NADH with respect to other shuttles including the malate/aspartate shuttle was also shown by reconstructing these shuttles with mitochondria from heart left ventricular from rats subjected to hypertension/hypertrophy.

The capability of both yeast and mammalian mitochondria to synthesise FAD from taken up riboflavin and to export it has been shown as well as the existence of mitochondrial enzymes devoted to FAD and FMN catabolism. In this regard, the occurrence of the riboflavin/riboflavine derivative cycle was shown to account for localization and recovery of these compounds in mammalian mitochondria.

A major contribution was given to shed light on the mitochondrial metabolism of the lactate isomers: D-lactate metabolism was discovered in mammalian, yeast and plant mitochondria as due to a putative D-lactate dehydrogenase localized in the inner mitochondrial compartments where D-lactate is transported both in a proton compensated symport and via a variety of antiporters. L-lactate was shown to contribute to gluconeogenesis via its matrix metabolism and export of oxaloacetate in the extramitochondrial phase in exchange with further L-lactate.

The capability of He-Ne laser irradiation to improve the quality of turkey semen has been shown (6).

## 2. Cell death in animal, plant and yeast cells

2.1 The role of mitochondria in the necrosis and apoptosis in granule cerebellar cells

2.2 The bioenergetics of the programmed cell death in heat shocked tobacco cells

2.3 Yeast and apoptosis

A review on the glutamate neurotoxicity in cerebellar granule cells has been published.

The role of mitochondria in the necrosis and apoptosis in cerebellar granule cells: this field of research concerns the manner by which cerebellar granule cell die via apoptosis/necrosis with a special emphasis on the role played by mitochondria in these processes. In rat cerebellar granule cells it was shown that cytochrome c release takes place during both glutamate toxicity and apoptosis due to deprivation of depolarizing levels of potassium. In both cases, the released cytochrome c, present in the cytosolic fraction obtained from cerebellar granule cells undergoing apoptosis, can operate as a ROS scavenger and as a respiratory substrate. Thus proposal was made that in cerebellar granule cell death, the released cytochrome c can contribute per se to provide

ATP required to prevent energy deficit in necrosis and for the cell programmed death to occur. Consistently it was shown that cellular ATP content increases in cerebellar granule cell apoptosis, that the role of oxidative phosphorylation is facultative, i.e. ATP can also derive from anaerobic glycolysis, and that the type of cell death depends on the ATP availability.

In the early phase of apoptosis the production in the extramitochondrial phase of ATP as synthesised via oxidative phosphorylation and exported outside mitochondria via the adenine nucleotide carrier (ANT) is impaired due to reactive oxygen species, but not to caspase. Later due to caspase action on proteins different from the ADP/ATP translocator, ANT becomes a component of the permeability transition pore which itself is dispensable for apoptosis to occur.

Some features of the programmed cell death in plants has been shown including the ROS production, the involvement of mitochondria and the cytochrome c release.

## 3. Oxidative/environmental stress in plant cell

3.1 The role of potassium channel, uncoupling protein and alternative oxidase in mitochondrial bioenergetics

3.2 The role of mitochondria in the plant defence against environmental stresses causing excess reactive oxygen species (ROS) production

The existence of the potassium channel in plant mitochondria has been discovered, moreover a novel property of the plant uncoupling protein as been shown in aged-dehydrated mitochondria from Jerusalem artichoke, namely the sensitivity to ROS.

Citation Year Score

Glutamate neurotoxicity, oxidative stress and mitochondria. FEBS Lett 497 : 1-5 2001

Cytochrome c is released from mitochondria in a reactive oxygen species (ROS) dependent manner. *J Biol Chem* 275 : 37159-66 2000

Caspase-dependent alteration of the ADP/ATP translocator triggers the mitochondrial permeability transition. *J Neurochem* 97 : 1166-81 2006

Cytochrome c is released in a reactive oxygen species-dependent manner and is degraded via the ubiquitin-proteasome pathway. *Plant Physiol* 141 : 208-19 2006

Mitochondrial energy metabolism in the left ventricular tissue of spontaneously hypertensive rats. *Clin Exp Hypertens* 20 : 345-58 1998

The role of mitochondrial transport in energy metabolism. *Mitochondrion* 2 : 319-43 2003

Abnormal transport of inorganic phosphate in left ventricular mitochondria from spontaneously hypertensive rats. *Cardiologia* 44 : 719-25 1999

In the early phase of programmed cell death in Tobacco Bright Yellow 2 cells the mitochondrial membrane potential is depolarized. *Biochim Biophys Acta* 1608 : 104-13 2004

An increase in the ATP levels occurs in cerebellar granule cells en route to apoptosis. *Biochim Biophys Acta* 1708 : 50-62 2005

Increase of proton electrochemical potential and ATP synthesis in rat liver mitochondria irradiated with ultraviolet light. *FEBS Lett* 175 : 95-9 1984

Increase in the H<sup>+</sup>/e<sup>-</sup> ratio of the cytochrome c oxidase reaction in mitochondria irradiated with ultraviolet light. *Biochem Mol Biol Int* 34 : 817-26 1994

Riboflavin uptake and FAD synthesis in *Saccharomyces cerevisiae* mitochondria: involvement of the mitochondrial membrane. *J Biol Chem* 279 : 95-102 2004

Effects of fatty acids, nucleotides and reactive oxygen species on durum wheat mitochondria. *FEBS Lett* 470 : 88-92 2000

Production of reactive oxygen species, alteration of cytosolic ascorbate peroxidase, and inhibition of ATP synthase in wheat mitochondria. *Plant Physiol* 134 : 1100-12 2004

Apoptosis and cytochrome c release in cerebellar granule cells. *In Vivo* 18 : 335-44 2004

The existence of the K<sup>+</sup> channel in plant mitochondria. *J Biol Chem* 274 : 26683-90 1999

Transport and metabolism of D-lactate in Jerusalem artichoke mitochondria. *Biochim Biophys Acta* 1708 : 13-22 2005

Glutamate neurotoxicity in rat cerebellar granule cells involves cytochrome c release from mitochondria. *J Neurochem* 73 : 237-46 1999

Mitochondria as cell targets of AZT (zidovudine). *Gen Pharmacol* 31 : 531-8 1998

A protein factor of rat liver mitochondrial matrix involved in flavinylation of dimethylglyoxime. *Eur J Biochem* 267 : 4346-54 2000

Two separate pathways for d-lactate oxidation by *Saccharomyces cerevisiae* mitochondria. *Biochim Biophys Acta* 1608 : 104-13 2004

A novel property of adenine nucleotides: sensitivity to helium-neon laser in mitochondrial membranes. *Biochem Mol Biol Int* 41 : 449-60 1997

Stimulation of ATP synthesis via oxidative phosphorylation in wheat mitochondria irradiated with ultraviolet light. *Biochem Mol Biol Int* 39 : 149-57 1996

L-lactate metabolism in potato tuber mitochondria. *FEBS J* 274 : 1459-69 2007

Mitochondria and L-lactate metabolism. *FEBS Lett* 464 : 107-11 2008

Flavin adenine dinucleotide and flavin mononucleotide metabolism in rat liver--the occurrence of a novel pathway. *Eur J Biochem* 249 : 777-85 1997

[Existence of 2 binding sites for substrates of the carrier of dicarboxylic acids in rat I Boll Soc Ital Biol Sper 49 : 263-9 1973

Proteasome function is required for activation of programmed cell death in heat shocked to FEBS Lett 0 : 2007.

Rat liver mitochondria can synthesize nicotinamide adenine dinucleotide from nicotinamide Biochem Mol Biol Int 38 : 297-306 1996

[Quantitative evaluation of the specific binding sites for glutamate in the mitochondrial Boll Soc Ital Biol Sper 48 : 337-40 1972

[Specificity of the carrier of dicarboxylic acids in rat liver mitochondria. I] Boll Soc Ital Biol Sper 48 : 341-5 1972

[Specificity of the carrier of dicarboxylic acids in rat liver mitochondria. II] Boll Soc Ital Biol Sper 48 : 345-7 1972

Transport of proteins into mitochondria. Int Rev Cytol 91 : 141-86 1984

[Interaction of 3-[3H]-2-n-nonyl-4-hydroxy-quinoline-N-oxide with submitochondrial particle Boll Soc Ital Biol Sper 55 : 2406-11 1979

[Initial experimental evidence of fumarate transport in rat heart mitochondria] Boll Soc Ital Biol Sper 54 : 40-5 1978

[Interaction of 3-[3H]-2-n-nonyl-4-hydroxyquinoline-N-oxide with submitochondrial particle Boll Soc Ital Biol Sper 55 : 2412-8 1979

[Interaction of 3-(3H)-2-n-nonyl-4-hydroxyquinoline-N-oxide with submitochondrial particle Boll Soc Ital Biol Sper 55 : 2419-24 1979

Transport and metabolism of L-lactate occur in mitochondria from cerebellar granule cells Biochim Biophys Acta 0 : 2007

Plant uncoupling protein in mitochondria from aged-dehydrated slices of Jerusalem Biochimie 88 : 179-88 2006

Partial reconstruction of in vitro gluconeogenesis arising from mitochondrial L-lactate up Biochem J 380 : 231-42 2004

Phosphoenolpyruvate metabolism in Jerusalem artichoke mitochondria. Biochim Biophys Acta 0 : 2007

Metabolite transport in isolated yeast mitochondria: fumarate/malate and succinate/malate FEBS Lett 462 : 313-6 1999

L-Lactate transport into rat heart mitochondria and reconstruction of the L-lactate/pyruvate Biochem J 364 : 101-4 2002

Rapid uncoupling of oxidative phosphorylation accompanies glutamate toxicity in rat cerebellum Neuroreport 7 : 2519-23 1996

Mitochondrial transport in proline catabolism in plants: the existence of two separate transporters Planta 0 : 1-11 2005

Inhibition of nucleoside diphosphate kinase in rat liver mitochondria by added 3'-azido-3' FEBS Lett 444 : 291-5 1999

Saccharomyces cerevisiae mitochondria can synthesize FMN and FAD from externally added riboflavin FEBS Lett 428 : 245-9 1998

Rat liver mitochondria can hydrolyse thiamine pyrophosphate to thiamine monophosphate which FEBS Lett 435 : 6-10 1998

Uptake of aspartate aminotransferase into mitochondria in vitro causes efflux of malate dehydrogenase Biochim Biophys Acta 1022 : 273-82 1990

Carrier-mediated transport controls hydroxyproline catabolism in heart mitochondria from s  
FEBS Lett 396 : 279-84 1996

The citric cycle intermediates transport in rat liver mitochondria. Biochimie 58 : 989-1001  
1976 Jerusalem artichoke mitochondria can export reducing equivalents in the form of  
malate as Biochem Biophys Res Commun 335 : 1224-30 2005

A peptide containing residues 26-44 of tau protein impairs mitochondrial oxidative  
phosphorylation acting at the level of the adenine nucleotide translocator. Biochim Biophys  
Acta 0 : 2008

The role of metal ions in the transport of substrates in mitochondria. FEBS Lett 38 : 91-5  
1973

The role of metal ions in the uptake of aspartate aminotransferase and malate  
dehydrogenase FEBS Lett 189 : 235-40 1985

The transport of oxaloacetate in rat heart mitochondria. FEBS Lett 90 : 61-4 1978

Inhibition of phosphate transport in rat heart mitochondria by 3'-azido-3'-deoxythymidine  
Biochem Pharmacol 64 : 201-6 2002

Isolated durum wheat and potato cell mitochondria oxidize externally added NADH mostly  
via Plant Physiol 133 : 2029-39 2003

Demonstration of an intramitochondrial invertase activity and the corresponding sugar  
transporters of the inner mitochondrial membrane in Jerusalem artichoke (*Helianthus  
tuberosus* L.) tubers. Planta 0 : 2008

AZT inhibition of the ADP/ATP antiport in isolated rat heart mitochondria. Int J Mol Med 6 :  
93-6 2000

Cytochrome c is released from coupled mitochondria of yeast en route to acetic acid-  
induced programmed cell death and can work as an electron donor and a ROS scavenger.  
FEBS Lett 0 : 2008

Kinetic studies of the uptake of aspartate aminotransferase and malate dehydrogenase  
into Biochem J 228 : 493-503 1985

Removal of an N-terminal peptide from mitochondrial aspartate aminotransferase  
abolishes i Biochem J 228 : 609-14 1985

Selective permeability of rat liver mitochondria to purified malate dehydrogenase isoenzym  
Biochem J 192 : 649-58 1980

AZT side effect on mitochondria does not depend on either inhibition of electron flow or m  
Int J Mol Med 1 : 601-3 1998

Uptake of aspartate aminotransferase into mitochondria in vitro depends on the  
transmembrana Biochem J 202 : 353-62 1982

ATP synthesis and export in heart left ventricle mitochondria from spontaneously  
hypertens Int J Mol Med 1 : 709-16 1998

Fumarate permeation in normal and acidotic rat kidney mitochondria: fumarate/malate and fu  
Biochem Biophys Res Commun 243 : 711-8 1998

The riboflavin/FAD cycle in rat liver mitochondria. Eur J Biochem 267 : 4888-900 2000  
Mitochondria from the left heart ventricles of both normotensive and spontaneously  
hyperte Int J Mol Med 18 : 177-86 2006

Spectroscopic study of hydroxyproline transport in rat kidney mitochondria. Biochem  
Biophys Res Commun 202 : 58-64 1994



Fumarate permeation in rat heart mitochondria. *Biochem Biophys Res Commun* 90 : 498-505 1979  
Metabolite transport in rat kidney mitochondria: ornithine/phosphate translocator. *Biochem Biophys Res Commun* 158 : 870-9 1989

Pyruvate/malate antiporter in rat liver mitochondria. *Biochem Biophys Res Commun* 182 : 931-8 1992

Certain N-terminal peptides inhibit uptake of mature aspartate aminotransferase by isolate *Biochem Biophys Res Commun* 170 : 609-15 1990

Uncoupling of mitochondrial oxidative phosphorylation by hexetidine. *Biochem Biophys Res Commun* 147 : 801-8 1987

Increase in the ADP/ATP exchange in rat liver mitochondria irradiated in vitro by helium-n *Biochem Biophys Res Commun* 156 : 978-86 1988

Fumarate permeation in rat liver mitochondria: fumarate/malate and fumarate/phosphate tran *Biochem Biophys Res Commun* 132 : 8-18 1985

D-Lactate transport and metabolism in rat liver mitochondria. *Biochem J* 365 : 391-403 2002  
Carrier mediated GABA translocation into rat brain mitochondria. *Biochem Biophys Res Commun* 121 : 770-8 1984

Is there a pyruvate kinase in pig liver mitochondria? *Ital J Biochem* 56 : 270-4 2007

Mitochondria isolated from local market potato tubers contain L-lactate dehydrogenase in an inactive state. *Ital J Biochem* 56 : 289-94 2007

Oxaloacetate uptake into rat brain mitochondria and reconstruction of the malate/oxaloacet *Biochem Biophys Res Commun* 119 : 1039-46 1984

Uptake of thiamin by isolated rat liver mitochondria. *Biochem Biophys Res Commun* 141 : 466-73 1986

Oxaloacetate permeation in rat kidney mitochondria: pyruvate/oxaloacetate and malate/oxalo *Biochem Biophys Res Commun* 129 : 1-10 1985

Mechanisms of toxicity of 3'-azido-3'-deoxythymidine. Its interaction with adenylate kinas *Biochem Pharmacol* 48 : 1405-12 1994

Protease resistance of aspartate aminotransferase imported in mitochondria. *FEBS Lett* 122 : 33-6 1980

3'-Azido-3'-deoxythymidine uptake into isolated rat liver mitochondria and impairment of AD *Biochem Pharmacol* 53 : 913-20 1997

Hematoporphyrin derivative (Photofrin II) photosensitization of isolated mitochondria: imp *Biochem Biophys Res Commun* 141 : 584-90 1986

Selective uptake of malate dehydrogenase isoenzymes into mitochondria in vitro [proceeding *Biochem Soc Trans* 7 : 514-6 1979

The mechanism of proline/glutamate antiport in rat kidney mitochondria. Energy dependence *Eur J Biochem* 241 : 171-7 1996

Glutamine transport in normal and acidotic rat kidney mitochondria. *Arch Biochem Biophys* 315 : 369-81 1994

Effect of amytal on the permeability of the mitochondrial membrane in rat liver mitochondr *Biochem Pharmacol* 29 : 2325-31 1980

Effect of ethacrynic acid on the permeability of the mitochondrial membrane in rat liver m *Biochem Pharmacol* 28 : 2267-72 1979

The transport of oxaloacetate in isolated mitochondria. *Arch Biochem Biophys* 180 : 160-8 1977  
Proline transport in rat kidney mitochondria. *Arch Biochem Biophys* 309 : 139-48

1994 Ornithine/phosphate antiport in rat kidney mitochondria. Some characteristics of the process Eur J Biochem 193 : 221-7 1990

The effect of sulfhydryl group reagents on the permeation of mitochondrial aspartate amino Arch Biochem Biophys 195 : 269-79 1979

Thiamine pyrophosphate uptake into isolated rat liver mitochondria. Arch Biochem Biophys 280 : 352-7 1990

Flavin adenine dinucleotide synthesis in isolated rat liver mitochondria caused by import Arch Biochem Biophys 305 : 442-7 1993

Photosensitization of isolated mitochondria by hematoporphyrin derivative (Photofrin): effect Photochem Photobiol 53 : 391-3 1991

Transport of mature proteins into isolated mitochondria: a model system to investigate mitochondrial Biochem Soc Trans 12 : 381-4 1984

Cytochrome c, released from cerebellar granule cells undergoing apoptosis or excitotoxicity J Neurochem 86 : 591-604 2003

Anion transport in rat brain mitochondria: fumarate uptake via the dicarboxylate carrier. Neurochem Res 12 : 255-64 1987

He-Ne laser irradiation of isolated mitochondria. J Photochem Photobiol B 3 : 642-3 1989

Specific helium-neon laser sensitivity of the purified cytochrome c oxidase. Int J Radiat Biol 76 : 863-70 2000

Effects of rhodamine 123 in the dark and after irradiation on mitochondrial energy metabolism Photochem Photobiol 56 : 471-8 1992

The membrane fatty acid-binding protein is not identical to mitochondrial glutamic oxaloacetyl Mol Cell Biochem 98 : 191-9 2000

Effects of selective irradiation on mammalian mitochondria. Photochem Photobiol 45 : 433-8 1987  
Reactive oxygen species inhibit the succinate oxidation-supported generation of membrane potential FEBS Lett 516 : 15-9 2002

Alternative oxidase in durum wheat mitochondria. Activation by pyruvate, hydroxypyruvate and Plant Cell Physiol 42 : 1373-82 2001

Carrier thiols are targets of Photofrin II photosensitization of isolated rat liver mitochondria J Photochem Photobiol B 7 : 21-32 1990

Increase in cytosolic and mitochondrial protein synthesis in rat hepatocytes irradiated in vivo J Photochem Photobiol B 34 : 197-202 1996

Haematoporphyrin derivative (Photofrin II) photosensitization of isolated mitochondria: in vivo J Photochem Photobiol B 4 : 35-46 1989

Helium-Neon laser irradiation of hepatocytes can trigger increase of the mitochondrial membrane Lasers Surg Med 29 : 433-41 2001

### *Supplemental Publications*

(the ones we missed)

Vacca RA, Valenti D, Bobba A, Merafina RS, Passarella S, Marra E.

Cytochrome c is released in a reactive oxygen species-dependent manner and is degraded via caspase-like proteases in tobacco Bright-Yellow 2 cells en route to heat shock-induced cell death.

Plant Physiol. 2006 141(1):208-19.

Di Martino C, Pizzuto R, Pallotta ML, De Santis A, Passarella S.

Mitochondrial transport in proline catabolism in plants: the existence of two separate translocators in mitochondria isolated from durum wheat seedlings.

Planta. 2006 223(6):1123-33.

Paventi G, Pastore D, Bobba A, Pizzuto R, Di Pede S, Passarella S.

Plant uncoupling protein in mitochondria from aged-dehydrated slices of Jerusalem artichoke tubers becomes sensitive to superoxide and to hydrogen peroxide without increase in protein level.

Biochimie. 2006 (2):179-88.

Giannattasio S, Atlante A, Antonacci L, Guaragnella N, Lattanzio P, Passarella S, Marra E.

Cytochrome c is released from coupled mitochondria of yeast en route to acetic acid-induced programmed cell death and can work as an electron donor and a ROS scavenger.

FEBS Lett. 2008, 582(10):1519-25.

Valenti D, Vacca RA, Guaragnella N, Passarella S, Marra E, Giannattasio S.

A transient proteasome activation is needed for acetic acid-induced programmed cell death to occur in *Saccharomyces cerevisiae*.

FEMS Yeast Res. 2008

3: Guaragnella N, Antonacci L, Giannattasio S, Marra E, Passarella S.

Catalase T and Cu,Zn-superoxide dismutase in the acetic acid-induced programmed cell death in *Saccharomyces cerevisiae*.

FEBS Lett. 2008 582(2):210-

Atlante A, de Bari L, Bobba A, Marra E, Passarella S.

Transport and metabolism of L-lactate occur in mitochondria from cerebellar granule cells and are modified in cells undergoing low potassium dependent apoptosis.

Biochim Biophys Acta. 2007 (11):1285-99.

Guaragnella N, Antonacci L, Passarella S, Marra E, Giannattasio S.

Hydrogen peroxide and superoxide anion production during acetic acid-induced yeast programmed cell death.

Folia Microbiol (Praha). 2007;52(3):237-40.



Paventi G, Pizzuto R, Chieppa G, Passarella S.

L-lactate metabolism in potato tuber mitochondria.

FEBS J. 2007 Mar;274(6):1459-69.

de Bari L, Valenti D, Pizzuto R, Atlante A, Passarella S.

Phosphoenolpyruvate metabolism in Jerusalem artichoke mitochondria.

Biochim Biophys Acta. 2007 Apr;1767(4):281-94. Epub 2007 Feb 23.

PMID: 17418088 [PubMed - indexed for MEDLINE]

Vacca RA, Valenti D, Bobba A, de Pinto MC, Merafina RS, De Gara L, Passarella

S, Marra E.

Proteasome function is required for activation of programmed cell death in heat shocked tobacco Bright-Yellow 2 cells.

FEBS Lett. 2007 Mar 6;581(5):917-22.

Valenti D, Vacca RA, de Pinto MC, De Gara L, Marra E, Passarella S.

In the early phase of programmed cell death in Tobacco Bright Yellow 2 cells the mitochondrial adenine nucleotide translocator, adenylate kinase and nucleoside diphosphate kinase are impaired in a reactive oxygen species-dependent manner.

Biochim Biophys Acta. 2007 1767(1):66-78.

Guaragnella N, Pereira C, Sousa MJ, Antonacci L, Passarella S, Côrte-Real M,

Marra E, Giannattasio S.

YCA1 participates in the acetic acid induced yeast programmed cell death also in a manner unrelated to its caspase-like activity.

FEBS Lett. 2006 Dec 22;580(30):6880-4.