

## Curriculum

Name: Rosa Anna Vacca

Date of Birth: March 26, 1963

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### EDUCATION AND TRAINING

1987 - Degree in Biological Sciences (110/110) (Biochemistry and Molecular Biology oriented), Faculty of Sciences, University of Bari, Italy.

1992-1993 - Research training, Department of Biochemistry, University of Zurich, Zurich, Switzerland

1998 - PhD in Biochemistry and Molecular Biology, Department of Biochemistry and Molecular Biology, Faculty of Sciences, University of Bari, Italy

### PROFESSIONAL APPOINTMENTS

1998-to date – CNR Research Investigator, Institute of Biomembranes and Bioenergetics (IBBE), Bari, Italy

1994-1998 – Contract of CNR Research Investigator, Institute of Biomembranes and Bioenergetics (IBBE), Bari, Italy.

1993-1994 – Doctoral fellow of Department of Biochemistry and Molecular Biology, Faculty of Sciences, University of Bari, Italy.

1991-1993 – Research fellowship from CNR Centro di Studio sui Mitochondri e Metabolismo Energetico (CSMME) Bari, Italy

1988-1990 – Research fellowship from Comune di Trani to attend the scientific organization and made research into the CNR CSMME molecular biology laboratory of Trani (BA), Italy.

Visiting Scientist

1998 – Department of Biochemistry, University of Naples Federico II, Naples, Italy (Prof. Alberto Di Donato)

1992, 1994, 1995 – Biochemistry Institute of Zurich University Switzerland (Prof. Philipp Christen)

1990 – Department of Life Sciences University of East London, England (Prof. Shawn Doonan)

1989 – Biochemistry Institute of Zurich University Switzerland (Prof. Philipp Christen)

### GRANTS

#### Principal Investigator

2013-2015 Grand Awarded by Jérôme Lejeune Foundation, Paris; Project: (1093-VR2012B) “Oxidative stress and mitochondrial dysfunctions in Down Syndrome”

2010-2012 Project MIUR-PRIN (2010-2012) “Genetic and metabolic regulation of the cell redox state in Down syndrome: role of the ubiquitin-proteasome system, of mitochondrial

metabolism, of miRNAs, and protective effect of natural anti-oxidant compounds” (2008FHM37R\_002).

2008-2010 Grand Awarded by Jérôme Lejeune Foundation, Paris; Project: (615-VRI-2008A) “Molecular determinants and mitochondrial bioenergetics in Down syndrome”

### **Co-investigator**

2011-2014 CNR Project FaReBio di Qualità (FBdQ) “Farmaci Innovativi - Modelli cellulari e murini e studi funzionali”

2011-2015 Project FIRB-MERIT (1-RBNE08HWLZ-012) “Molecular basis of aging-related syndroms”

### **RESEARCH ACTIVITY**

Dr. Vacca’s research activity has been focused on different subjects whose main theme has been the “Mitochondrial biogenesis and function in higher organisms under different physiopathological conditions.

MOLECULAR MECHANISMS IN THE PHATOGENESIS OF SOME GENETIC INTELLECTUAL DISABILITIES

MOLECULAR BASIS OF CELL PROLIFERATION

BIOENERGETICS IN PROGRAMMED CELL DEATH

MITOCHONDRIAL BIOGENESIS: NUCLEAR-ENCODED MITOCHONDRIAL PROTEIN TRANSPORT.

PROTEIN ENGINEERING OF VITAMIN B<sub>6</sub>-DEPENDENT PROTEIN CATALYSTS: STRUCTURE/FUNCTION RELATIONSHIP OF MITOCHONDRIAL ASPARTATE AMINOTRANSFERASE.

Dr. Vacca’s reaserch activity is documented by:

- 32 articles on international peer-reviewed JCR journals;
- 7 articles on books and non-JCR journals;
- 14 articles on Italian journals
- 50 congress proceedings.

She is peer-reviewer of several highly reputed international scientific journals.

She was invited speakers in national and international scientific meeting and held lectures in several scientific institutions in Italy and abroad.

### **COLLABORATIONS**

- Prof. Laura Moro, Dipartimento di Scienze del Farmaco - Università del Piemonte Orientale “Amedeo Avogadro”, Novara.
- Prof. Generoso Andria, Dipartimento di Pediatria - Università “Federico II”, Napoli.

- Dr. Leonardo Rossi, Dipartimento di Morfologia Umana e Biologia Applicata, Sezione di Biologia e Genetica - Università di Pisa, Pisa.
- Dr. Giovanni Laviola, Dipartimento di Biologia Cellulare e Neuroscienze - Istituto Superiore di Sanità, Roma.
- Dr. Andrea Contestabile, Istituto Italiano di Tecnologia, Genova.
- Dott. Alessandro Cocchella, Laboratorio Biomolecolare del Dipartimento di Gerontologia e Scienze Motorie - Ospedali Galliera di Genova.
- Dr. Alexandra Henrion-Caude, Dipartimento di Genetica INSERM U781 - Hôpital Necker-Enfants Malades, Paris, Francia.

## MAIN PUBLICATIONS

1. Valenti D, de Bari L, De Filippis B, Henrion-Caude A, **Vacca RA (2014)** Mitochondrial dysfunction as a central actor in intellectual disability-related diseases: an overview of Down syndrome, autism, Fragile X and Rett syndrome. **Neuroscience & Biobehavioral Reviews** (*in press* DOI:10.1016/j.neubiorev.2014.01.012).
2. Valenti D, de Bari L, De Filippis B, Ricceri L, **Vacca RA (2014)** Preservation of mitochondrial functional integrity in mitochondria isolated from small-cryopreserved mouse brain areas. **Anal Biochem** 444:25-31.
3. Valenti D, De Rasmio D, Signorile A, Rossi L, de Bari L, Scala I, Granese B, Papa S, **Vacca RA (2013)** Epigallocatechin-3-gallate prevents oxidative phosphorylation deficit and promotes mitochondrial biogenesis in human cells from subjects with Down's syndrome. **Biochim Biophys Acta (BBA-DIS)** 1832:542-52;
4. Granese B, Scala I, Spatuzza C, Valentino A, Coletta M, **Vacca RA**, De Luca P, Andria G (2013) Validation of microarray data in human lymphoblasts shows a role of the ubiquitin-proteasome system and NF- $\kappa$ B in the pathogenesis of Down syndrome. **BMC Med Genomics** 6:24.
5. Valenti D, de Bari L, Manente GA, Rossi L, Mutti L, Moro L, **Vacca RA (2013)** Negative modulation of mitochondrial oxidative phosphorylation by epigallocatechin-3 gallate leads to growth arrest and apoptosis in human malignant pleural mesothelioma cells. **Biochim Biophys Acta (BBA-DIS)** 1832:2085-2096.
6. Manente AG, Valenti D, Pinton G, Jithesh PV, Daga A, Rossi L, Gray SG, O'Byrne KJ, Fennell DA, **Vacca RA**, Nilsson S, Mutti L, Moro L (2013) Estrogen receptor  $\beta$  activation impairs mitochondrial oxidative metabolism and affects malignant mesothelioma cell growth in vitro and in vivo. **Oncogenesis** 2:e72.
7. Valenti D, Manente GA, Moro L, Marra E, **Vacca RA (2011)** "Deficit of complex I activity in human skin fibroblasts with chromosome 21 trisomy and overproduction of reactive oxygen species by mitochondria: involvement of cAMP/PKA signaling pathway." **Biochem. J.** 435: 679-688.
8. Valenti D, Tullo A, Caratozzolo MF, Merafina RS, Scartezzini P, Marra E, **Vacca RA (2010)** "Impairment of F1F0-ATPase, adenine nucleotide translocator and adenylate kinase causes mitochondrial energy deficit in human skin fibroblasts with chromosome 21 trisomy." **Biochem. J.** 431: 299-310.
9. **Vacca RA**, Giannattasio S, Capitani G, Marra E, Christen P. (2008) Molecular evolution of B6 enzymes: binding of pyridoxal-5'-phosphate and Lys41Arg substitution turn ribonuclease A into a model B6 protoenzyme. **BMC Biochem.** 9: 17-27.
10. Valenti D, **Vacca RA**, Guaragnella N, Passarella S, Marra E, Giannattasio S. (2008) Transient proteasome activation is needed for acetic acid-induced programmed cell death to occur in *Saccharomyces cerevisiae*. **FEMS Yeast Res.** 8: 400-404.

11. **Vacca R. A.**, Valenti D., Bobba A., de Pinto M.C., Merafina S., De Gara L., Passarella S., E. Marra (2007) "Proteasome function is required for activation of programmed cell death in heat shocked Tobacco Bright Yellow 2 cells" **FEBS lett.** 581: 917-922.
12. Valenti D., **Vacca R.A.**, de Pinto M.C., De Gara L., Marra E., Passarella S. (2007) "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. (BBA-BIO)** 1767: 66-78
13. Giannattasio S., Bobba A., Jurgelevičius V., **Vacca R.A.**, Lattanzio P., Merafina R.S., Utkus A., Kučinskas V., E. Marra (2006) "Molecular basis of cystic fibrosis in Lithuania. Incomplete CFTR mutation detection by PCR-based screening protocols" **Genetic Testing**, 10: 169-173.
14. **Vacca R.A.**, Valenti D., Bobba A., Merafina R.S., Passarella S., Marra E. (2006) "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.** 141: 208-219.
15. **Vacca R.A.**, de Pinto M.C., Valenti D., Passarella S., Marra E., De Gara L. (2004) "Production of reactive oxygen species, alteration of cytosolic ascorbate peroxidase, and impairment of mitochondrial metabolism are early events in heat shock-induced programmed cell death in tobacco Bright-Yellow 2 cells". **Plant Physiol.** 134: 1100-1112.
16. **Vacca R.A.**, Moro L., Maiorano E., Selvaggi L., Marra E., Perlino E. (2004) "Alternatively Spliced Variants of  $\beta 1$  Integrin Are Involved in the Modulation of Human Endometrial Transformation in Different Physiological/Pathological Conditions" **Recent Res Devel Proteins**, 2: 25-47 Review.
17. **Vacca R.A.**, Moro L., Carraccio G., Guerrieri F., Marra E., Greco M. (2003). "Thyroid hormone administration to hypothyroid rats restores the mitochondrial membrane permeability properties" **Endocrinology** 144: 3783-3788.
18. Lovecchio M., Maiorano E., **Vacca R.A.**, Loverro G., Fanelli M., Resta L., Stefanelli S., Selvaggi L., Marra E., E. Perlino (2003). " $\beta 1C$  integrin expression in human endometrial proliferative diseases" **Am. J. Pathol.** 163: 2543-2553.
19. **Vacca R.A.**, Marra E., Loverro G., Maiorano E., Napoli A., Lovecchio M., Selvaggi L., Perlino E. (2003). "Differential expression of  $\beta 1C$  integrin messenger ribonucleic acid and protein levels in human endometrium and decidua during the menstrual cycle and pregnancy" **J Clin. Endocrinol. Metab.** 88: 620-729.
20. Greco M., **Vacca R.A.**, Moro L., Perlino E., Petragallo V.A., Marra E., Passarella S. (2001). "Helium-Neon laser irradiation of hepatocytes can trigger increase of the mitochondrial membrane potential and can stimulate c-fos expression in  $Ca^{2+}$  dependent manner" **Lasers Surg. Med.** 29, 433-441.
21. Perlino E., Lovecchio M., **Vacca R.A.**, Fornaro M., L. Moro., Ditunno P., Battaglia M., Selvaggi F.P., Mastropasqua M., Bufo P., L. Languino (2000). "Regulation of mRNA and protein levels of  $\beta 1$  integrin variants in human prostate carcinoma" **Am. J. Pathol.** 157: 1727-1733.
22. Azzariti A, **Vacca R.A.**, Giannattasio S., Merafina R., Marra E., Doonan S. (1998) "Kinetic properties and thermal stability of mutant forms of aspartate aminotransferase" **Biochim. Biophys. Acta** 1386: 29-38.
23. **Vacca R.A.**, Moro L., Petragallo V., M. Greco (1997) "The irradiation of hepatocytes with He-Ne laser causes an increase of cytosolic free calcium concentration and an increase of membrane potential, correlated with it, both increases taking place in an oscillatory manner" **Biochem. Mol. Biol. Int.** 43: 1005-1014.
24. **Vacca R.A.**, Giannattasio S., Graber R., Sandmeier E., Marra E., P. Christen (1997) "Active-site Arg $\rightarrow$ Lys substitution alter reaction and substrate specificity of aspartate aminotransferase" **J. Biol. Chem.** 272: 21932-21937.

25. Marra E., **Vacca R.A.**, Moro L., M. Greco (1997) " Photomodulation of biosynthetic activities in cell systems by low-power visible light" **Trends in Photochem. Photobiol.** 4, 257-267  
Review
26. **Vacca R.A.**, Marra E., Passarella S., Petragallo V.A., M. Greco (1996)" Inceze in both cytosolic and mitochondria protein synthesis in isolated rat hepatocytes by Helium-Neon irradiation" **J. Photochem. Photobiol. B: Biol.** 34:197-202.
27. **Vacca R.A.**, Christen P., Malashkevich V.N., Jansonious J.N., Sandmeier E. (1995) "Substitution of apolar residues in the active site of aspartate aminotransferase by histidine. Effects on reaction and substrate specificity." **Eur. J. Biochem.** 227: 481-487.
28. Greco M., **Vacca R.A.**, Petragallo V.A., E. Marra (1995). "The effect of red, yellow and green light on in vitro transcription and translation" **Medicine, Biologie, Environment.** 23: 41-44.
29. Marra E., Perlino E., **Vacca R.A.**, Greco M. (1994). "Helium-Neon Laser Activation of Mitochondrial Biogenesis" **Trends in Photochemistry and Photobiology** 3, 441-548. Review
30. **Vacca R.A.**, Marra E., Quagliariello E., Greco M. (1994). "Increase of both transcription and translation activities following separate irradiation of the in vitro system components with He-He laser" **Biochem. Biophys. Res. Commun.** 203:991-997
31. **Vacca R.A.**, Marra E., Quagliariello E., Greco M. (1993). "Activation of mitochondrial DNA replication by He-Ne laser irradiation" **Biochem. Biophys. Res. Commun.** 195: 704-709.
32. Giannattasio S., Marra E., **Vacca R.A.**, Iannace G., Quagliariello E. (1992). "Import of mutant forms of mitochondrial aspartate aminotransferase into isolated mitochondria". **Arch. Biochem. Biophys.** 298: 532-537.