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EDUCATION AND TRAINING

1987 - Degree in Biological Sciences Biochemistry and Molecular Biology oriented, Faculty of Sciences, University of Bari, Italy.
1998 - PhD in Biochemistry and Molecular Biology, Department of Biochemistry and Molecular Biology, Faculty of Sciences, University of Bari, Italy
1992-1993 - Research training, Department of Biochemistry, University of Zurich, Zurich, Switzerland

PERSONAL STATEMENT

During her research activity Dr Rosa Anna Vacca has extensively participated to nuclear-cytoplasmic-mitochondrial cross-talk studies aimed to analyze signalling pathways and mitochondrial bioenergetics in models of neurodevelopmental/neurodegenerative diseases and cancer. Major scientific objectives of her research has been focused on understanding how cellular signalling networks regulate mitochondrial functions and discover novel natural compounds for targeted-drug development.

Since 2008 she is PI of research projects and coordinate studies aimed at identifying the molecular mechanism for mitochondrial dysfunctions in some intellectual disability-related genetic diseases such as Down syndrome, Rett syndrome and Fragile X syndrome. Her study has allowed to identifying new potential targets for mitochondrial dysfunctions and therapeutic strategies for these neurodevelopmental diseases.

POSITIONS AND HONORS

Employment history

1994-1998 - Temporary position as research investigator, Italian National Council of Research (CNR), Centre for the Study of Mitochondria and Bioenergetics Metabolism, Trani, Italy

1998-to date - Permanent position as research investigator, Italian National Council of Research (CNR) Institute of Biomembranes and Bioenergetics (IBBE), Bari, Italy

Honors

2017-2023 – Certification of Associate Professor of Biochemistry

June 2017-to date – Member of the Scientific Council of Fondation Jerome Lejeune, Paris, France

Selected Grants: PI for Research Projects (last 5 years)

Grand Awarded by Jérôme Lejeune Foundation, Paris for the project (615-VRI-2008A) "Molecular determinants and mitochondrial bioenergetics in Down syndrome" (2008-2010).

Responsible of Research Unit for the project of the Italian Minister of University and Research - MIUR-PRIN (2008FHM37R_002) "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" (2010-2012).

Grand Awarded by Jérôme Lejeune Foundation, Paris for the project (1093-VR2012B) "Oxidative stress and mitochondrial dysfunctions in Down Syndrome" (2013-2015).
Co-investigator

Selected Grants: Co-investigator for Research Projects (last 5 years)

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"

Awards

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 Mitocondri e Metabolismo Energetico (CSMME) Bari, Italy

1988-1990 – Research fellowship from Comune di Trani to attend the scientific organization to 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)

RESEARCH ACTIVITY

Dr. Vacca's research activity is documented by the following bibliometric indicators:

Total article with IF 45

H-index: 19

Total citations: 1324

Ad hoc Reviewer for the following national and international Grant Agencies: MIUR FIRB (IT), Istituto Superiore di Sanità (IT), InBev-Baillet Latour Grants for Medical Research (B), Fondation Jerome Lejeune (F); Federation for Brain Research, FRC (F).

Ad hoc Reviewer for many premier Journals, such as: Science Translational Medicine, Neuroscience & Biobehavioral Reviews, Free radical Medicine and Biology, Molecular Therapy; Molecules; Journal of Cellular and Molecular Medicine; Biochemical Pharmacology etc.

Invited speakers in national and international scientific meeting and held lectures in several scientific institutions and families' associations in Italy.

TEACHING AND TRAINING ACTIVITY

Mentored Trainees of Undergraduate Students for experimental thesis in Biochemistry in Faculty of Sciences, University of Bari

Supervisor of PhD students and post-doctoral fellows

Teacher in PhD and scientific training courses.

Teacher in several theoretical and practical scientific courses in Italy.

Teacher as expert in Biochemistry and Molecular Biology in European projects (PON) for high schools.

MAIN PUBLICATIONS

1. Valenti D, Braidy N, De Rasmio D, Signorile A, Rossi L, Atanasov AG, Volpicella M, Henrion-Caude A, Nabavi SM, **Vacca RA**. (2018) Mitochondria as pharmacological targets in Down syndrome. **Free Radic Biol Med**. 114:69-83.
2. Nabavi SF, Sureda A, Dehpour AR, Shirooie S, Silva AS, Devi KP, Ahmed T, Ishaq N, Hashim R, Sobarzo-Sánchez E, Daglia M, Braidy N, Volpicella M, **Vacca RA**, Nabavi SM. (2017) Regulation of autophagy by polyphenols: Paving the road for treatment of neurodegeneration. *Biotechnol Adv*. 2017 Dec 6. pii: S0734-9750(17)30153-2. doi: 10.1016/j.biotechadv.2017.12.001
3. Tewari D, Nabavi SF, Nabavi SM, Sureda A, Farooqi AA, Atanasov AG, **Vacca RA**, Sethi G, Bishayee A. (2017) Targeting activator protein 1 signaling pathway by bioactive natural agents: Possible therapeutic strategy for cancer prevention and intervention. **Pharmacol Res**. 2017 Sep 23. pii: S1043-6618(17)30692-8.
4. Valenti D, Rossi L, Marzulli D, Bellomo F, De Rasmio D, Signorile A, **Vacca RA**. (2017) Inhibition of Drp1-mediated mitochondrial fission improves mitochondrial dynamics and bioenergetics stimulating neurogenesis in hippocampal progenitor cells from a Down syndrome mouse model. **Biochim Biophys Acta**. 1863(12):3117-3127.
5. Valenti D, de Bari L, Vigli D, Lacivita E, Leopoldo M, Laviola G, **Vacca RA**, De Filippis B. (2017) Stimulation of the brain serotonin receptor 7 rescues mitochondrial dysfunction in female mice from two models of Rett syndrome. **Neuropharmacology** 121:79-88
6. Ajami M, Pazoki-Toroudi H, Amani H, Nabavi SF, Braidy N, **Vacca RA**, Atanasov AG, Mocan A, Nabavi SM. (2017) Therapeutic role of sirtuins in neurodegenerative disease and their modulation by polyphenols. **Neurosci Biobehav Rev**. 73:39-47
7. **Vacca RA**, Valenti D, Caccamese S, Daglia M, Braidy N, Nabavi SM (2016) Plant polyphenols as natural drugs for the management of Down syndrome and related disorders. **Neurosci Biobehav Rev**. 71:865-877.
8. Valenti D, de Bari L, de Rasmio D, Signorile A, Henrion-Caude A, Contestabile A, **Vacca RA**. (2016) The polyphenols resveratrol and epigallocatechin-3-gallate restore the severe impairment of mitochondria in hippocampal progenitor cells from a Down syndrome

mouse model. **Biochim Biophys Acta**. 1862:1093-104.

9. Valenti D, Vacca RA, de Bari L. (2015) 3-Bromopyruvate induces rapid human prostate cancer cell death by affecting cell energy metabolism, GSH pool and the glyoxalase system. **J Bioenerg Biomembr**. 47:493-506.
10. Valenti D, Vacca RA (2015) Green tea EGCG plus fish oil omega-3 dietary supplements rescue mitochondrial dysfunctions and are safe in a Down's syndrome child. **Clin Nutr**. 34:783-4.
11. De Filippis B, Valenti D, de Bari L, De Rasmio D, Musto M, Fabbri A, Ricceri L, Fiorentini C, Laviola G, Vacca RA (2015) Mitochondrial free radical overproduction due to respiratory chain impairment in the brain of a mouse model of Rett syndrome: protective effect of CNF1. **Free Radic Biol Med**. 83:167-177.
12. De Filippis B, Valenti D, Chiodi V, Ferrante A, de Bari L, Fiorentini C, Domenici MR, Ricceri L, Vacca RA, Fabbri A, Laviola G (2015) Modulation of Rho GTPases rescues brain mitochondrial dysfunction, cognitive deficits and aberrant synaptic plasticity in female mice modeling Rett syndrome. **Eur Neuropsychopharmacol** 25:889-901.
13. 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** 46:202-217.
14. 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.
15. 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;
16. 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-kB in the pathogenesis of Down syndrome. **BMC Med Genomics** 6:24.
17. 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.
18. 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 β activation impairs mitochondrial oxidative metabolism and affects malignant mesothelioma cell growth in vitro and in vivo. **Oncogenesis** 2:e72.
19. 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.
20. 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.
21. 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.

22. 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.
23. **Vacca R. A.**, Valenti D., Bobba A., de Pinto M.C., Merafina S., De Gara L., Passerella 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.
24. Valenti D., **Vacca, R.A.**, de Pinto M.C., De Gara L., Marra E., Passerella 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
25. Giannattasio S., Bobba A., Jurgelevičius V., **Vacca R.A.**, Lattanzio P., Merafina R.S., Utkus A., Kučinskis 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.
26. **Vacca R.A.**, Valenti D., Bobba A., Merafina R.S., Passerella 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.
27. **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.
28. **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.
29. **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.
30. 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.
31. **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.
32. 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.
33. 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.
34. 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.
35. **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.

36. **Vacca R.A.**, Giannattasio S., Graber R., Sandmeier E., Marra E., P. Christen (1997) "Active-site Arg→Lys substitution alter reaction and substrate specificity of aspartate aminotransferase" **J. Biol. Chem.** 272: 21932-21937.
37. 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
38. **Vacca R.A.**, Marra E., Passarella S., Petragallo V.A., M. Greco (1996)" Increase in both cytosolic and mitochondria protein synthesis in isolated rat hepatocytes by Helium-Neon irradiation" **J. Photochem. Photobiol. B: Biol.** 34:197-202.
39. **Vacca R.A.**, Christen P., Malashkevich V.N., Jansonius 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.
40. 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.
41. 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
42. **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
43. **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.
44. 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.