

BIOGRAPHICAL SKETCH

NAME Rosa Anna Vacca	POSITION TITLE Ibiom-CNR Researcher		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
University "Aldo Moro", Bari, Italy	Doctor in Biological Sciences	02/87	Molecular Biology
National Council of Research (CNR)	Research Fellow	03/1990	Mitochondrial Bioenergetics
National Council of Research (CNR)	Research Fellow	12/1993	Molecular Biology
Department of Biochemistry and Molecular Biology, University "Aldo Moro", Bari, Italy	Ph.D.	02/96	Protein engineering
Department of Biochemistry, University of Zurich, Zurich, Switzerland	Research training	05/97	Protein engineering
National Council of Research (CNR)	Postdoctoral	02/98	Mitochondrial dysfunction in health and disease

A. Personal Statement

During my research activity I have 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 my research has been focused on understanding how cellular signalling networks regulate mitochondrial functions and discover novel compounds for targeted-drug development.

Since 2008 I'm 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. My research studies have allowed to identifying new potential targets for mitochondrial dysfunctions and therapeutic strategies for these neurodevelopmental diseases.

B. 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, Bioenergetics and Molecular Biotechnologies (Ibiom), Bari, Italy

Honors and Professional Memberships

2017-to date	Member of teacher board of Doctoral in Genomics and Functional and Applied Proteomics. Department of Biosciences, Biotechnologies and Biopharmaceuticals, University of Bari Aldo Moro
2017-2023	Certification of Associate Professor of Biochemistry
2017-to date	Member of the Scientific Board of Fondation Jerome Lejeune, Paris, France
2018-to date	Member of Director Board of International Natural Product Sciences Taskforce (INPST)
1998-2013	Member of Italian Society of Biochemistry and Molecular Biology
1996-to date	Member of Reviewer project panel for: French Funding Organization (FRC, Fédération pour la Recherche sur le Cerveau), Paris, France; InBev-Baillet Latour Grants for Medical Research, Belgium; Italian Ministry MIUR
2018	Associate Editor international journal of geriatric psychiatry.
2018-to date	Reviewer Editor in "Frontiers in Molecular Neuroscience"
2015-to date	Ad hoc reviewer for Science; Cell Signaling; Free Radical Biology and Medicine; Biochemical Pharmacology; Neurotoxicity Research; Neuroscience and Biobehavioral Reviews; Molecules; PlosOne

C. Research Support

Selected Grants: PI for Research Projects

2018 - ongoing - Fondation "Amardown" Martina Franca Italy, project: "Nutraceuticals for Down syndrome"

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

2010-2012 - Italian Minister of University and Research, PI of Research Unit, project 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".

2013-2015 - Jérôme Lejeune Foundation, Paris, project (1093-VR2012B) "Oxidative stress and mitochondrial dysfunctions in Down Syndrome".

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"

D. Main publications

1. Ajmone-Cat MA, Spinello C, Valenti D, Franchi F, Macri S, **Vacca RA**, Laviola G. Brain-Immune Alterations and Mitochondrial Dysfunctions in a Mouse Model of Paediatric Autoimmune Disorder Associated with Streptococcus: Exacerbation by Chronic Psychosocial Stress. **J Clin Med.** 2019 Sep 20;8(10). pii: E1514. doi: 10.3390/jcm8101514.

2. Bawari S, Tewari D, Argüelles S, Sah AN, Fazel Nabavi S, Xu S, **Vacca RA**, Nabavi SM, Shirooie S. Targeting BDNF signaling by natural products: novel synaptic repair therapeutics for neurodegeneration and behavior disorders. **Pharmacol Res.** 2019 Sep 20:104458. doi: 10.1016/j.phrs.2019.104458.
3. Nabavi SF, Sureda A, Sanches-Silva A, Pandima Devi K, Ahmed T, Shahid M, Sobarzo-Sánchez E, Dacrema M, Daglia M, Braidy N, **Vacca RA**, Berindan-Neagoe I, Gulei D, Barreca D, Banach M, Nabavi SM, Dehpour AR, Shirooie Novel therapeutic strategies for stroke: The role of autophagy. **Crit Rev Clin Lab Sci.** 2019 May;56(3):182-199. doi: 10.1080/10408363.2019.1575333.
4. **Vacca RA**, Bawari S, Valenti D, Tewari D, Nabavi SF, Shirooie S, Sah AN, Volpicella M, Braidy N, Nabavi SM. Down syndrome: Neurobiological alterations and therapeutic targets. **Neurosci Biobehav Rev.** 2019 Mar;98:234-255. doi: 10.1016/j.neubiorev.2019.01.001.
5. Nabavi SM, Ahmed T, Nawaz M, Devi KP, Balan DJ, Pittalà V, Argüelles-Castilla S, Testai L, Khan H, Sureda A, de Oliveira MR, **Vacca RA**, Xu S, Yousefi B, Curti V, Daglia M, Sobarzo-Sánchez E, Filosa R, Nabavi SF, Majidinia M, Dehpour AR, Shirooie S. Targeting STATs in neuroinflammation: The road less traveled! **Pharmacol Res.** 2019 Mar;141:73-84. doi: 10.1016/j.phrs.2018.12.004..
6. Vigli D, Rusconi L, Valenti D, La Montanara P, Cosentino L, Lacivita E, Leopoldo M, Amendola E, Gross C, Landsberger N, Laviola G, Kilstrup-Nielsen C, **Vacca RA**, De Filippis B. Rescue of prepulse inhibition deficit and brain mitochondrial dysfunction by pharmacological stimulation of the central serotonin receptor 7 in a mouse model of CDKL5 Deficiency Disorder. **Neuropharmacology.** 2019 Jan;144:104-114. doi:10.1016/j.neuropharm.2018.10.018.
7. Balzotti A, Filograsso M, Altamura C, Fairfield B, Bellomo A, Daddato F, **Vacca RA**, Altamura M. Comparison of the efficacy of gesture-verbal treatment and doll therapy for managing neuropsychiatric symptoms in older patients with dementia. **Int J Geriatr Psychiatry.** 2018 Aug 23. doi: 10.1002/gps.4961. [Epub ahead of print]
8. Nabavi SF, Atanasov AG, Khan H, Barreca D, Trombetta D, Testai L, Sureda A, Tejada S, **Vacca RA**, Pittalà V, Gulei D, Berindan-Neagoe I, Shirooie S, Nabavi SM. Targeting ubiquitin-proteasome pathway by natural, in particular polyphenols, anticancer agents: Lessons learned from clinical trials. **Cancer Lett.** 2018 Oct 10;434:101-113. doi: 10.1016/j.canlet.2018.07.018.
9. Caracausi M, Ghini V, Locatelli C, Mericio M, Piovesan A, Antonaros F, Pelleri MC, Vitale L, **Vacca RA**, Bedetti F, Mimmi MC, Luchinat C, Turano P, Strippoli P, Cocchi G. Plasma and urinary metabolomic profiles of Down syndrome correlate with alteration of mitochondrial metabolism. **Sci Rep.** 2018 Feb 14;8(1):2977. doi: 10.1038/s41598-018-20834-y.
10. 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. Regulation of autophagy by polyphenols: Paving the road for treatment of neurodegeneration. **Biotechnol Adv.** 2018 Nov 1;36(6):1768-1778. doi: 10.1016/j.biotechadv.2017.12.001.
11. Tewari D, Nabavi SF, Nabavi SM, Sureda A, Farooqi AA, Atanasov AG, Vacca RA, Sethi G, Bishayee A. Targeting activator protein 1 signaling pathway by bioactive natural agents: Possible therapeutic strategy for cancer prevention and intervention. **Pharmacol Res.** 2018 Feb;128:366-375. doi: 10.1016/j.phrs.2017.09.014.
12. 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.
13. 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.
14. 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
15. 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
16. 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.
 17. 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.
 18. 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.
 19. 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.
 20. 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.
 21. 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.
 22. 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.
 23. 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.
 24. 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;
 25. 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- κ B in the pathogenesis of Down syndrome. **BMC Med Genomics** 6:24.
 26. 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.
 27. 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.
 28. 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.
 29. 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.

30. **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.
31. 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.
32. **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.
33. 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
34. 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.
35. **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.
36. **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.
37. **Vacca R.A.**, Moro L., Maiorano E., Selvaggi L., Marra E., Perlino E. (2004) "Alternatively Spliced Variants of β 1 Integrin Are Involved in the Modulation of Human Endometrial Transformation in Different Physiological/Pathological Conditions" **Recent Res Devel Proteins**, 2: 25-47 Review.
38. **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.
39. Lovecchio M., Maiorano E., **Vacca R.A.**, Loverro G., Fanelli M., Resta L., Stefanelli S., Selvaggi L., Marra E., E. Perlino (2003). " β 1C integrin expression in human endometrial proliferative diseases" **Am. J. Pathol.** 163: 2543-2553.
40. **Vacca R.A.**, Marra E, Loverro G., Maiorano E., Napoli A., Lovecchio M., Selvaggi L., Perlino E. (2003). "Differential expression of β 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.
41. 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.
42. 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 β 1 integrin variants in human prostate carcinoma" **Am. J. Pathol.** 157: 1727-1733.
43. 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.
44. **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.

45. **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.
46. 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
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47. **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.
48. **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.
49. 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.
50. 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.
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51. **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
52. **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.
53. 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.