



## Debora Bencivenga

RTD A  
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### Education

2011 Board in Clinical Biochemistry (Specialty School), Second University of Naples.  
2009 PhD in Cellular Biochemistry, Second University of Naples.  
2005 Professional Qualification as Biologist, University of Naples "Federico II".  
2005 Degree in Biological Science, University of Naples "Federico II".

### Current Accademical Position

Since 2018 Researcher (RTD A) S.S.D. BIO/10, Department of Precision Medicine, School of Medicine, University of Campania "Luigi Vanvitelli".

### Professional Appointments and Former Research Experiences

2004-2006

Pre-graduate and post-graduate student at the Department of Biochemistry and Biophysics, Second University of Naples".

2005-2006

Training course (1200 h) "Creazione di operatori di innovazione di prodotto e di processo PMI" (POR 2000/2006 – Regione Campania);

2006-2009

PhD Student in Cellular Biochemistry, Department of Biochemistry and Biophysics, Second University of Naples. PhD Thesis Title: "Serine 10 phosphorylation role in p27Kip1 metabolism and effects on cell proliferation";

2005-2006/2009-2011

Post-graduate fellow, Department of Biochemistry and Biophysics, Second University of Naples. In this period, she attended the Board in Clinical Biochemistry;

2013-2015/ 2016-2017

n. 3 post-doctoral fellowship, Department of Biochemistry and Biophysics, Second University of Naples;

2018-2021

Researcher to determined time (RTDA), art. 24, co 3, l. a, L. 240/2010, VALERE Program, (S.C. 05/E1- S.S.S. BIO/10 - Biochemistry) D.R. n. 767, 14.11.2017- Department of Precision Medicine, University of Campania "L. Vanvitelli".

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## Teaching activities:

University of Campania "Luigi Vanvitelli", Italy

2013/2014 Teaching support activities, through lectures and/or e-learning - BIOCHEMISTRY module (C4.A1.M1.U2) - 50 hours;

2015-2018 Connoisseur of the subject "Biochemistry" (S.S.D. BIO / 10), University of Campania "L. Vanvitelli" - School of Medicine and Surgery.

2019-2020

A6501B – Biochemistry - A65 - FISIOTERAPIA (ABILITANTE ALLA PROFESSIONE SANITARIA DI FISIOTERAPISTA).

## Scientific Society Memberships

Member of the Italian Society of Biochemistry and Molecular Biology (SIB).

## Research Grants

Since 2005 Dr. Bencivenga has been participant of research units supported by AIRC (Italian Association for Cancer Research), Ministry of Health and MIUR on the basis of peer-reviewing processes, listed below:

2015-18 3 years AIRC research grant. Title: "p27 and p57 interactors and cancer: role in cell growth, cytoskeleton dynamics, metastasization and tumor therapy";

2011-2013 3 years AIRC research grant. Title: "Mechanisms of p27 and p57 level modulation: relevance in cell growth, differentiation and cancer treatment";

2007-2009 3 years AIRC research grant. Title: "Novel mechanisms of p27 and p57 level modulation: relevance in cell phenotype and cancer therapy";

2007 1 year Ministry of Health research grant in the framework of "*Programma di ricerca 2007 sui farmaci, sulle sostanze e pratiche mediche utilizzabili a fini di doping nelle attività sportive*", titled "*La policitemia congenita come malattia modello per la caratterizzazione degli effetti molecolari e clinici del trattamento cronico con eritropoietina*";

2006 1 year AIRC research grant. Title: "Novel mechanisms of p21, p27 and p57 level modulation: their relevance in cell phenotype and cancer therapy";

2006-2007 – 2 years National PRIN (Project of National Relevant Interest) research grant. Title: "*Meccanismi di controllo dell'eritropoiesi e policitemie congenite e familiari: ruolo delle vie di risposta alla pressione di ossigeno*";

2005-2007 – 3 years AIRC research grant. Title: "Prostate cancer: molecular bases of invasiveness and identification of novel targets for therapy";

2005 1 year AIRC grant. Title: "Novel mechanisms of p21, p27 and p57 level modulation: their relevance in cell phenotype and cancer therapy".

## Scientific Interests

Dr. Bencivenga main scientific interests fall in the field of basic biochemistry, cellular and molecular biology.

She has long been interested at the mechanisms of regulation of the division cycle in normal and transformed cells. In an initial phase of her studies (2005-2006), he devoted himself to the study of the retinoic acid on neuroblastoma cell line proliferation and differentiation. Subsequently, she focused on the fundamental mechanisms of transcriptional, translational and post-translational control of cyclin-dependent kinase inhibitors of the Cip / Kip family, p27Kip1 and p57Kip2, and the relevance of these processes in the proliferation and differentiation of normal and cancer cells. Particular attention was focused on the identification and characterization of post-synthetic modifications, in particular phosphorylation, and their role in the fundamental processes for the cell. From 2014 to date, it deals with the characterization of mutations of the CDKN1B gene found in human tumours and the consequences of these gene aberrations (mostly missense mutations) on metabolism, post-synthetic modifications and function of the p27Kip1 protein. She works also in:

- Effects of resveratrol, butyrate and other non-nutritive compounds on cell proliferation and differentiation. Study of the mechanism of action of these molecules. Analysis of their effect on proteins that regulate cell cycle progression, apoptosis and signal transduction. Identification of the possible target genes and effectors of the antiproliferative action of resveratrol and butyrate;

- Genetic alterations and molecular bases of congenital polycythemia and pathologies of altered hypoxia response. Erythroid differentiation mechanisms related to the cell division cycle. Biochemical mechanisms of congenital polycythemia. Molecular mechanisms of processes regulated by oxygen pressure.

-In vitro preparation and propagation of bone marrow mesenchymal stromal cells. Effects of drugs and/or natural molecules

on osteogenic and/or adipogenic proliferation and differentiation. Effects of resveratrol and other dietary molecules on the proliferation and differentiation of human mesenchymal stromal cells. Biochemical mechanisms of regulation of adipogenesis and osteogenesis.

### **Job-related skills**

Chemistry of Proteins (cellular extract preparation (total extracts, cytoplasmic and nuclear extracts, microtubules purification, centrosomes purification), SDS-PAGE 1D and 2D, in vitro enzymatic assays

Molecular Biology (Nucleic acid extraction, PCR, RT-PCR, qRT-PCR, Cloning, Mutagenesis)

Cellular Biology (primary and cell line propagation, Transfection, human dermal Fibroblast and MSCs isolation)

Microscopy (live imaging analysis, fixed tissues and cells –Time Laps and confocal microscopy)

Immunological techniques (immunoblotting, immunoprecipitation, immunofluorescence, Cytofluorimetry)

### **Speaker at International Events**

XIV congress of the Italian Federation of Life Sciences (FISV), Rome 2016 – title: “Biochemical and functional characterization of cancer-associated p27Kip1 mutants”;

SIB 2017 59th Congress / Caserta 2017 – title: “CDKN1B alterations and human cancer: mechanistic investigations on G9R missense mutation”.

### **Peer Reviewing Activities**

Referee for the following journals:

- Journal of Cellular Physiology

- Merit research journal of agricultural science and soil sciences

### **PUBLICATIONS**

1) Borriello A., Cucciolla V., Criscuolo M., Indaco S., Oliva A., Giovane A., Bencivenga D., Iolascon A., Zappia V., and Della Ragione F. Retinoic Acid induces p27Kip1 nuclear accumulation by modulating its phosphorylation. *Cancer research* 2006; 66: (8). April 15, 2006. I.F. 9,284

2) Cucciolla V., Borriello A., Criscuolo M., Sinisi AA., Bencivenga D., Tramontano A., Scudieri AC., Oliva A., Zappia V., Della Ragione F. Histone deacetylase inhibitors upregulate p57Kip2 level by enhancing its expression through Sp1 transcription factor. *Carcinogenesis*. 2008 Mar;29(3):560-7. I.F. 5,266

3) Borriello A, Caldarelli I, Bencivenga D, Cucciolla V, Oliva A, Usala E, Danise P, Ronzoni L, Perrotta S, Della Ragione F. p57Kip2 is a downstream effector of BCR-ABL kinase inhibitors in chronic myelogenous leukemia cells. *Carcinogenesis*. 2010. I.F. 5,266

4) Borriello A, Bencivenga D, Criscuolo M, Caldarelli I, Cucciolla V, Tramontano A, Borgia A, Spina A, Oliva A, Naviglio S, Della Ragione F. Targeting p27(Kip1) protein: its relevance in the therapy of human cancer. *Expert Opin Ther Targets*. 2011. I.F. 4,901

5) Borriello A, Caldarelli I, Bencivenga D, Criscuolo M, Cucciolla V, Tramontano A, Oliva A, Perrotta S, Della Ragione F. p57(Kip2) and cancer: time for a critical appraisal. *Mol Cancer Res*. 2011 Oct;9(10):1269-84. Epub 2011 Aug 4. PMID:21816904 I.F. 4,453

6) Borriello A, Caldarelli I, Basile MA, Bencivenga D, Tramontano A, Perrotta S, Della Ragione F, Oliva A. The tyrosine kinase inhibitor dasatinib induces a marked adipogenic differentiation of human multipotent mesenchymal stromal cells. *PLoS One*. 2011;6(12):e28555. Epub 2011 Dec 2. PMID:22164306 I.F. 3,534

7) Borriello A, Bencivenga D, Caldarelli I, Tramontano A, Borgia A, Pirozzi AV, Oliva A, Della Ragione F. Resveratrol and cancer treatment: is hormesis a yet unsolved matter? *Curr Pharm Des*. 2013;19(30):5384-93. Review. PMID:23394084 I.F. 3,288

8) Perrotta S1, Stiehl DP, Punzo F, Scianguetta S, Borriello A, Bencivenga D, Casale M, Nobili B, Fasoli S, Balduzzi A, Cro L, Nytko KJ, Wenger RH, Della Ragione F. Congenital erythrocytosis associated with gain-of-function HIF2A gene mutations and erythropoietin levels in the normal range. *Haematologica*. 2013 Oct;98(10):1624-32. doi: 10.3324/haematol.2013.088369. Epub 2013 May 28. PMID: 23716564 I.F. 5,868

9) Borriello A, Bencivenga D, Caldarelli I, Tramontano A, Borgia A, Zappia V, Della Ragione F. Resveratrol: from basic studies to bedside. *Cancer Treat Res*. 2014;159:167-84. doi: 10.1007/978-3-642-38007-5\_10. Review. PMID: 24114480

10) Caldarelli I, Speranza MC, Bencivenga D, Tramontano A, Borgia A, Pirozzi AV, Perrotta S, Oliva A, Della Ragione F, Borriello A. Resveratrol mimics insulin activity in the adipogenic commitment of human bone marrow mesenchymal stromal cells. *Int J Biochem Cell Biol*. 2015 Jan 3;60C:60-72; I.F. 4,240

- 11) Bencivenga D, Tramontano A, Borgia A, Negri A, Caldarelli I, Oliva A, Perrotta S, Della Ragione F, Borriello A. p27Kip1 serine 10 phosphorylation determines its metabolism and interaction with cyclin-dependent kinases. *Cell Cycle*. 2014;13(23):3768-82.; I.F. 4,565
- 12) Borriello A, Bencivenga D, Della Ragione F. The unpredictable consequences of CDKN1B/p27Kip1 mutations in cancer. *Cell Cycle*. 2015 Sep 17;14(18):2865-6. doi: 10.1080/15384101.2015.1076302. Epub 2015 Jul 29; I.F. 3,952
- 13) A. Borriello, S. Naviglio, D. Bencivenga, I. Caldarelli, A. Tramontano, M. Speranza, E. Stampone, L. Sapio, A. Negri, A. Oliva, A. A. Sinisi, A. Spina, and F. Della Ragione. Histone Deacetylase Inhibitors Increase p27Kip1 by Affecting Its Ubiquitin-Dependent Degradation through Skp2 Downregulation. *Oxidative Medicine and Cellular Longevity*. 2016;2016:2481865. doi: 10.1155/2016/2481865. Epub 2015 Nov 22; I.F. 4,344
- 14) Borriello A, Caldarelli I, Speranza MC, Scianguetta S, Tramontano A, Bencivenga D, Stampone E, Negri A, Nobili B, Locatelli F, Perrotta S, Oliva A, Della Ragione F.  
Iron overload enhances human mesenchymal stromal cell growth and hampers matrix calcification. *Biochim Biophys Acta*. 2016 Jun;1860(6):1211-23. doi: 10.1016/j.bbagen.2016.01.025. Epub 2016 Feb 3. I.F. 5,34
- 15) Borriello A, Caldarelli I, Bencivenga D, Stampone E, Perrotta S, Oliva A, Della Ragione F. Tyrosine kinase inhibitors and mesenchymal stromal cells: effects on self-renewal, commitment and functions. *Oncotarget*. 2017 Jan 17;8(3):5540-5565. doi: 10.18632/oncotarget.12649. Review I.F. 5,168
- 16) Bencivenga D, Caldarelli I, Stampone E, Mancini FP, Balestrieri ML, Della Ragione F, Borriello A. p27Kip1 and human cancers: A reappraisal of a still enigmatic protein. *Cancer Lett*. 2017 Sep 10;403:354-365. doi: 10.1016/j.canlet.2017.06.031. Review I.F. 6,375
- 17) Casale M, Borriello A, Scianguetta S, Roberti D, Caiazza M, Bencivenga D, Tartaglione I, Ladogana S, Maruzzi M, Della Ragione F, Perrotta S. Hereditary hypochromic microcytic anemia associated with loss-of-function DMT1 gene mutations and absence of liver iron overload. *Am J Hematol*. 2017 Nov 27. doi: 10.1002/ajh.24988. I.F. 5,275
- 18) Stampone E, Caldarelli I, Zullo A, Bencivenga D, Mancini FP, Della Ragione F, Borriello A. Genetic and Epigenetic Control of CDKN1C Expression: Importance in Cell Commitment and Differentiation, Tissue Homeostasis and Human Diseases. *Int J Mol Sci*. 2018 Apr 2;19(4). pii: E1055. doi: 10.3390/ijms19041055. Review I.F. 3,687