Giovanni Di Bernardo

Curriculum vitae et studiorum

Name Giovanni Surname Di Bernardo

Place and date of birth 15 Agosto 1969, Caserta ITALY

Degree Master of Science in Biology, PhD in Molecular Biology

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Biology, School of Medicine, University of Campania "Luigi Vanvitelli", Naples,

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PRESENT POSITION

- <u>Associate Professor</u> of Molecular Biology at the School of Medicine, Dept. of Medicina Sperimentale, University of Campania "Luigi Vanvitelli", Naples, Italy.
- Affiliate Professor at the Sbarro Health Research Organization at Temple University

MEMBERSHIP

- ISSCR (International Society for Stem Cell Researches).
- International Society for Cellular Therapy (ISCT).
- National Association of Italian Biologist.
- Founder of Stem Cell Research Italy, scientific association of researchers involved in stem cell studies (http://www.stemcellitaly.it).

STUDIES

- 1994 Master degree in Biological Sciences, *summa cum laude*, University of Naples, Naples, Italy.
- 2003 PhD in Molecular Biology

WORK EXPERIENCES IN ITALY AND ABROAD

- 1994 Post-degree practical training at the School of Medicine, Institute of Biochemistry of Macromolecules, 2nd University of Naples, Naples, Italy
- 1995-1996 Post-doctoral fellowship, P.F. FATMA, National Research Council (C.N.R.), Rome, Italy.
- 1997-1998 Post-doctoral fellowship P. F. Beni Culturali, National Research Council (C.N.R.), Rome, Italy.
- 1999 Post-doctoral fellowship P. F. Beni Culturali, National Research Council (C.N.R.), Rome, Italy.
- 1999-2002 Post-doctoral fellowship at Department of Experimental Medicine, Second University of Napoli, Italy.
- 2000 Visiting Researcher at The Kuvin Centre for the study of infectious and tropical disease", Hebrew University, Hadassah Medical School, Jerusalem-Israele.
- 2003-2007 Post-doctoral fellowship at Department of Experimental Medicine, Second University of Napoli, Italy.
- 2016-2017-2018 Visiting professor at GENKOK, Genome and Stem Cell Center, to supervise the work of student and post-doc researches

HONORS

- 2002: Winner of the Award "Consorzio di Ricerca per lo Sviluppo nella Provincia di Caserta (CRISVICE) for the originality PhD thesis.
- 2007 Selection for Assistant Professor of Molecular Biology, Second University of Napoli, Italy.

ORGANIZING AND REFEREEING ACTIVITY

- Editorial board member of Frontiers in Bioengineering and Biotechnology - Preclinical Cell and Gene Therapy. Topical Advisory Panel Members (Molecular Biology) for International Journal of Molecular Science. In addition, for the same journal, Guest editor of special Issues "Aging and Senescence" and "Aging and Senescence 2.0". Handling Editor of "Current Genomics" Section: Epigenetics. Editorial board of World Journal of Stem Cells. Editorial board of Cell Biology and Development Studies

SCIENTIFIC INTERESTS

Obesity and stem cells

For several years, he has been studying how the condition of obesity or overweight can influence the biology of mesenchymal stromal cells (MSCs). Specifically, in overweight and obese individuals, the dysregulated levels of circulating signaling factors may also affect the differentiation potential of resident MSCs in the bone marrow, altering the balance between adipogenesis and osteogenesis. Furthermore, as a contribution to the fight against obesity, he is evaluating the ability of browning agents to induce white adipogenesis in bone marrow mesenchymal stromal cells. Brown-like adipocytes can be induced in white fat depots through various environmental or drug stimuli, a process known as "browning" or "beiging."

Senescence of stem cells

Mesenchymal stem cells (MSCs) are of particular interest because they are being tested in cell and gene therapy for a number of human diseases. MSCs represent a rare population in tissues. Therefore, it is essential to grow MSCs in vitro before putting them to therapeutic use. This is compromised by senescence, limiting the proliferative capacity of MSCs. He is studying the in vitro senescence of rat and human MSCs: In detail, he is interested in analyzing genes involved in DNA repair, whose expression is downregulated with aging. Senescence was accompanied by downregulation of several genes involved in stem cell self-renewal. He studies also the characteristic changes in the expression patters of Retinoblastoma gene family expression that occur during senescence.

Epigenetic regulation of stem cell biology

Chromatin state is fundamental for gene expression. Self-renewal, proliferation and differentiation properties of stem cells are controlled by key transcription factors. However, their activity is modulated by chromatin remodeling factors that operate at the highest hierarchical level. Studies on these factors can be especially important to dissect molecular pathways governing the biology of stem cells.

Histone deacetylase inhibitors (HDACi) have received great attention for their anti-tumoral properties. This anti-cancer action can be obtained by reversion of silenced genes, induction of cell cycle arrest, differentiation and/or apoptosis. HDACi-based therapy can have side effects that impair functions of bone marrow microenvironment, including MSCs. We are studying the biological effects of HDACi on MSCs.

Studies on Retinoblastoma gene family

He is interested in the studies on genes involved in cell cycle regulation, differentiation, apoptosis and senescence such as the Retinoblastoma (RB) family. He has evaluated the role of Retinoblastoma genes in the regulation of cell proliferation, differentiation and apoptosis in cancer and normal stem cells. In detail, his group has analyzed the biology of neural stem cells and mesenchymal stem cells. These studies prompted the attention also on chromatin remodeling factors that interact with RB family members and play a key role in the life of stem cells.

TEACHING

- 2007 to present Teaching in Molecular Biology at School of Medicine, Università della Campania Luigi Vanvitelli, Naples, Italy
- 2007-2010 Teaching in Molecular Biology at School of Dental Medicine, Second University of Naples, Naples, Italy
- 2005 to present Teaching in Molecular Biology at School of Biotechnology, Second University of Naples, Naples, Italy
- 2004-2006 Teaching in Molecular Biology in the diagnosis of infectious diseases, School of Medicine, Second University of Naples, Naples, Italy
- 2007 to present, Teaching in Molecular Biology for Medical students, Bachelor students Science and for Hematology, General Pathology, Clinical Pathology, Oncology, Microbiology, Biochemistry
- 2019 to present, Teacher for PhD students of "SCIENZE MEDICHE CLINICHE E SPERIMENTALI"

PATENT

Patent number 102020000031991 (22/12/2020): UNIVERSITA' DEGLI STUDI DELLA CAMPANIA "LUIGI VANVITELLI". Title: Prevenzione della senescenza cellulare in condizioni di stress. Inventors: Galderisi Umberto, Galano Giovanni, Squillaro Tiziana, Alessio Nicola, Di Bernardo Giovanni, De Rosa Alfredo, De Rosa Roberto.

Patent number RM2001A000087 (2001): Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST). Title: Method to identify cultivar of Olea europaea between RAPD-PCR. Inventors: Luigi De Masi, Galderisi Umberto, Cipollaro Marilena, Di Bernardo Giovanni and Cascino Antonino.

SELECTED PUBLICATIONS

- Nicola Alessio, Alessia Ambrosino, Andrea Boggi, Iole Pinto, Giovanni Galano, Umberto Galderisi, and Giovanni Di Bernardo. Germicidal lamps using UV-C radiation may pose health safety issues: a biomolecular analysis of their effects on apoptosis and senescence. **Aging Us**. 2024 In press
- Nicola Alessio, Domenico Aprile, Gianfranco Peluso, Valeria Mazzone, Deanira Patrone, Giovanni Di Bernardo, Umberto Galderisi. IGFBP5 is released by senescent cells and is internalized by healthy cells, promoting their senescence through interaction with retinoic receptors. **Cell Communication and Signaling**. DOI 10.1186/s12964-024-01469-1. In press
- Yo Oguma, Nicola Alessio, Domenico Aprile, Mari Dezawa, Gianfranco Peluso, Giovanni Di Bernardo, Umberto Galderisi. Meta-analysis of senescent cell secretomes to identify common and specific features of the different senescent phenotypes: a tool for developing new senotherapeutics. **Cell Commun Signal**. 2023 Sep 28;21(1):262 doi: 10.1186/s12964-023-01280-4.
- Al Sammarraie SHA, Aprile D, Meloni I, Alessio N, Mari F, Manata M, Lo Rizzo C, Di Bernardo G, Peluso G, Renieri A, Galderisi U. An Example of Neuro-Glial Commitment and Differentiation of Muse Stem Cells Obtained from Patients with IQSEC2-Related Neural Disorder: A Possible New Cell-Based Disease Model. **Cells**. 2023 Mar 23;12(7):977. doi: 10.3390/cells12070977.
- Alessio N, Acar MB, Squillaro T, Aprile D, Ayaz-Güner Ş, Di Bernardo G, Peluso G, Özcan S, Galderisi U. Progression of irradiated mesenchymal stromal cells from early to late senescence: Changes in SASP composition and anti-tumour properties. **Cell Prolif.** 2023 Mar 22:e13401. doi: 10.1111/cpr.13401.
- Aprile D, Alessio N, Squillaro T, Di Bernardo G, Peluso G, Galderisi U. Role of glycosphingolipid SSEA-3 and FGF2 in the stemness and lineage commitment of multilineage differentiating stress enduring (MUSE) cells. **Cell Prolif.** 2023 Jan;56(1):e13345. doi: 10.1111/cpr.13345.
- Di Maio G, Alessio N, Peluso G, Perrotta S, Monda M, Di Bernardo G. Molecular and Physiological Effects of Browning Agents on White Adipocytes from Bone Marrow Mesenchymal Stromal Cells. Int J Mol Sci. 2022 Oct 12;23(20):12151. doi:10.3390/ijms232012151.
- Najahi H, Alessio N, Squillaro T, Conti GO, Ferrante M, Di Bernardo G, Galderisi U, Messaoudi I, Minucci S, Banni M. Environmental microplastics (EMPs) exposure alter the differentiation potential of mesenchymal stromal cells. **Environ Res.** 2022 Nov;214(Pt 4):114088. doi: 10.1016/j.envres.2022.114088.
- Galderisi, U, Peluso, G, Di Bernardo, G. Clinical Trials Based on Mesenchymal Stromal Cells are Exponentially Increasing: Where are We in Recent Years? **Stem Cell Reviews and Reports**, 2021 Aug 16:1-14. doi: 10.1007/s12015-021-10231-w.
- Alessio N, Squillaro T, Lettiero I, Galano G, De Rosa R, Peluso G, Galderisi U and Di Bernardo G. Biomolecular Evaluation of Piceatannol's Effects in Counteracting the Senescence of Mesenchymal Stromal Cells: A New Candidate for Senotherapeutics? Int J Mol Sci. 2021, 22 11619. doi.org/10.3390/ijms222111619.
- Galderisi, U, Peluso, G, Di Bernardo, G. Clinical Trials Based on Mesenchymal Stromal Cells are Exponentially Increasing:
 Where are We in Recent Years? Stem Cell Reviews and Reports, 2021 Aug 16:1-14. doi: 10.1007/s12015-021-10231-w.

- Acar MB, Ayaz-Guner S., Gunaydin Z, Karakukcu M, Peluso G, Di Bernardo G, Ozcan S, Galderisi U. Proteomic and Biological Analysis of the Effects of Metformin Senomorphics on the Mesenchymal Stromal Cells. Front Bioeng Biotechnol. 2021 Oct 5;9:730813. doi: 10.3389/fbioe.2021.730813.
- Alessio N, Stellavato A, Aprile D, Cimini D, Vassallo V, Di Bernardo G., Galderisi U, Schiraldi C. Timely Supplementation of Hydrogels Containing Sulfated or Unsulfated Chondroitin and Hyaluronic Acid Affects Mesenchymal Stromal Cells Commitment Toward Chondrogenic Differentiation. Front Cell Dev Biol. 2021 Apr 12;9:641529. doi: 10.3389/fcell.2021.641529.
- Aprile D, Alessio N, Demirsoy IH, Squillaro T, Peluso G, Di Bernardo G, Galderisi U. MUSE Stem Cells Can Be Isolated from Stromal Compartment of Mouse Bone Marrow, Adipose Tissue, and Ear Connective Tissue: A Comparative Study of Their In Vitro Properties. Cells. 2021 Mar 30;10(4):761. doi: 10.3390/cells10040761.
- Alessio N, Aprile D, Cappabianca S, Peluso G, Di Bernardo G, Galderisi U. Different Stages of Quiescence, Senescence, and Cell Stress Identified by Molecular Algorithm Based on the Expression of Ki67, RPS6, and Beta-Galactosidase Activity. Int J Mol Sci. 2021 Mar 18;22(6):3102. doi: 10.3390/ijms22063102.
- Acar MB, Aprile D, Ayaz-Guner S, Guner H, Tez C, Di Bernardo G, Peluso G, Ozcan S, Galderisi U. Why Do Muse Stem Cells Present an Enduring Stress Capacity? Hints from a Comparative Proteome Analysis. Int J Mol Sci. 2021 Feb 19;22(4):2064. doi: 10.3390/ijms22042064.
- Di Maio G, Alessio N, Demirsoy IH, Peluso G, Perrotta S, Monda M, Di Bernardo G. Evaluation of Browning Agents on the White Adipogenesis of Bone Marrow Mesenchymal Stromal Cells: A Contribution to Fighting Obesity. Cells. 2021 Feb 16;10(2):403. doi: 10.3390/cells10020403.
- Squillaro, T.; Peluso, G.; Galderisi, U.; Di Bernardo, G. Long non-coding RNAs in regulation of adipogenesis and adipose tissue function. eLife, 2020, 9, pp. 1-15, e59053
- Acar MB, Ayaz-Guner S, Di Bernardo G, Guner H, Murat A, Peluso G, Ozcan S, Galderisi U. Obesity induced by high-fat diet is associated with critical changes in biological and molecular functions of mesenchymal stromal cells present in visceral adipose tissue. Aging (Albany NY). 2020 Dec 27;12(24):24894-24913. doi: 10.18632/aging.202423.
- Ayaz-Guner S., Alessio, Nicola, Acar M. B., Aprile D., Ozcan S., Di Bernardo, G., Peluso G., Galderisi U. A comparative study on normal and obese mice indicates that the secretome of mesenchymal stromal cells is influenced by tissue environment and physiopathological conditions. Cell Commun Signal. 2020 Jul 29;18(1):118. doi: 10.1186/s12964-020-00614-w.
- Alessio, N., Squillaro, T., Di Bernardo G., Galano G., De Rosa R., Melone M.B., Peluso, G., Galderisi, U. Increase of circulating IGFBP-4 following genotoxic stress and its implication for senescence eLife. 2020 Mar 30;9:e54523. doi: 10.7554/eLife.54523.
- Alessio N, Squillaro T, Monda V, Peluso G, Monda M, Melone MA, Galderisi U, Di Bernardo G. Circulating factors present in the sera of naturally skinny people may influence cell commitment and adipocyte differentiation of mesenchymal stromal cells. World J Stem Cells. 2019 Mar 26;11(3):180-195. doi: 10.4252/wjsc.v11.i3.180.
- Alessio N, Aprile D, Squillaro T, Di Bernardo G, Finicelli M, Melone MA, Peluso G, Galderisi U. The senescence-associated secretory phenotype (SASP) from mesenchymal stromal cells impairs growth of immortalized prostate cells but has no effect on metastatic prostatic cancer cells. Aging 2019 Aug 14;11(15):5817-5828. doi: 10.18632/aging.102172
- Squillaro T, Alessio N, Di Bernardo G, Özcan S, Peluso G, Galderisi U. Stem Cells and DNA Repair Capacity: Muse
 Stem Cells Are Among the Best Performers. Adv Exp Med Biol. 2018;1103:103-113. doi: 10.1007/978-4-431-56847-6_5.
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- Alessio N, Squillaro T, Özcan S, Di Bernardo G, Venditti M, Melone M, Peluso G, Galderisi U. Stress and stem cells: adult Muse cells tolerate extensive genotoxic stimuli better than mesenchymal stromal cells. Oncotarget. 2018 Apr 10;9(27):19328-19341. doi: 10.18632/oncotarget.25039.

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- Alessio N, Capasso S, Di Bernardo G, Cappabianca S, Casale F, Calarco A, Cipollaro M, Peluso G, Galderisi U.
 Mesenchymal stromal cells having inactivated RB1 survive following low irradiation and accumulate damaged DNA: Hints for side effects following radiotherapy. Cell Cycle. 2017 Feb;16(3):251-258. doi:10.1080/15384101.2016.1175798.
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- Di Bernardo G, Alessio N, Dell'Aversana C, Casale F, Teti D, Cipollaro M, Altucci L, Galderisi U. Impact of histone deacetylase inhibitors SAHA and MS-275 on DNA repair pathways in human mesenchymal stem cells. J Cell Physiol. 2010 Nov;225(2):537-44. doi: 10.1002/jcp.22236.
- Di Bernardo G, Galderisi U, Fiorito C, Squillaro T, Cito L, Cipollaro M, Giordano A, Napoli C. Dual role of parathyroid hormone in endothelial progenitor cells and marrow stromal mesenchymal stem cells. J Cell Physiol. 2010 Feb;222(2):474-80. doi: 10.1002/jcp.21976.

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