

BIOGRAPHICAL SKETCH

NAME: **Barbara Cassani**

POSITION TITLE: Tenured Researcher (Primo Ricercatore, Level II) /Junior PI

DATE OF BIRTH/ NATIONALITY: December 13, 1976 / Italian

E-MAIL: Barbara.cassani@irgb.cnr.it; barbara.cassani@cnr.it

Orcid ID: 0000-0002-4115-8109; Google Scholar ID: K-3871-2016

URL for web site: <https://www.humanitas-research.org/groups/cassani-barbara-group/>

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Milan, Italy	B.Sc.	1995 – 2001	Pharmacy
Vita-Salute San Raffaele University, Milan-Open University, London	Ph.D.	2003 – 2007	Molecular and Cellular Biology
HSR-TIGET, Milan, Italy	Postdoctoral Fellow	2007 – 2008	Immunology
Fondazione Humanitas, Milan, Italy	Postdoctoral Fellow	2008 – 2010	Immunology
Massachusetts General Hospital, Harvard Medical School, Boston, MA	Postdoctoral Fellow	2010 – 2012	Mucosal Immunology

CURRENT POSITIONS

2021-Present Tenured Researcher (Primo Ricercatore, Level II) at the Institute of Genetic and Biomedical Research (IRGB) - UOS of Milan, National Research Council (CNR), Milan, Italy

2017-Present Principal Investigator, Humanitas Clinical and Research Center, Rozzano, Italy

PREVIOUS POSITIONS

2016-2020 Tenured Researcher (Ricercatore, Level III) at the Institute of Genetic and Biomedical Research (IRGB) - UOS of Milan, National Research Council (CNR), Milan, Italy

2012-2016 Researcher (RTD) at the Institute of Genetic and Biomedical Research (IRGB) - UOS of Milan, National Research Council (CNR), Milan, Italy

2010-2012 Postdoctoral Fellow, Massachusetts General Hospital, Harvard Medical School, Boston, MA.

2008-2010 Postdoctoral Fellow, Humanitas Clinical Institute (ICH), Rozzano, Italy.

2007-2008 Postdoctoral Fellow, San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET), Milan, Italy.

2003-2007 Ph.D. Student, San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET), Milan, Italy.

2002-2003 Research Fellow, San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET), Milan, Italy.

FELLOWSHIPS AND AWARDS

2021-2023 Recipient of European Food Safety Authority (EFSA) grant (GP/EFSA/SCER/2020/03) Role: PI
2019-2022 Recipient of Italian Ministry of Health grant (GR-2016-02362572) Role: Unit Coordinator
2016 Travel Award Annual FOCIS Meeting (Boston, USA)
2015 -2019 Recipient of Fondazione Telethon grant (GGP15109) Role: PI
2014-2017 Recipient of Italian Ministry of Health grant (GR-2011-02349759) Role: PI
2013-2016 Recipient of Italian Ministry of Education, Universities and Research (MIUR) grant RBFR12I3UB Role: PI
2012 BioEconomy Prize on Rare Disease (Rome, Italy)
2011 Travel Award, Annual Meeting Society of Mucosal Immunology (Paris, France)
2011 Long-term Fellowship, European Molecular Biology Organization (EMBO), International Mobility
2008-2011 Recipient of Fondazione Cariplo per la Ricerca grant (n. 2008.2218). Role: Unit Coordinator
2009 Marie Curie Travel Award, TRiPR III-Genoa, Italy
2006 Travel Award, American Society of Haematology (Orlando, USA)

TEACHING ACTIVITIES

2019-2028 Italian National Academic Qualification as Associate Professor in Histology (05/H2)-Professore II Fascia
2019-2028 Italian National Academic Qualification as Associate Professor in General and Clinical Pathology (06/A2)-Professore II Fascia
2014-2023 Italian National Academic Qualification as Associate Professor in Applied Biology (05/F1)-Professore II Fascia
2016-Present Director of Study, PhD program Molecular and Experimental Medicine, Humanitas University, Rozzano, Italy
2014-2018 Director of Study, PhD program Immunology and Immunopathology, ICH-Open University, UK
2010-2012 Students Tutoring, PhD program Immunology, Harvard Medical School, Boston, USA (4 master students)
2004-2007 Assistant, Molecular Pediatrics course, Vita-Salute San Raffaele University, Milan (Italy)

ORGANIZATION OF SCIENTIFIC MEETINGS

2017-Present School of Immunology, Italian Society of Immunology, Clinical Immunology and Allergology (SIICA), Italy
2013-2019 Member Organizer and Scientific committee "Milan Meets Immunology" Meeting (<https://milanimmunology.wordpress.com>), Italy

COMMISSION OF TRUST AND INSTITUTIONAL RESPONSABILITIES

2020 External ad Hoc: United States-Israel Binational Science Foundation

2020 External ad Hoc: Catalan biomedical research funding programme La Marató de TV3 on Rare Diseases

2013 Panel Member, Italian Ministry of Education, Universities and Research Grants (FIR-Grants).

AD-HOC JOURNAL REVIEWER

Journal of Bone and Mineral Research, Journal of Clinical Investigation, Scientific Report, Plos One, Molecular Therapy, Journal of Allergy and Clinical Immunology, Blood, Molecular Immunology.

MEMBERSHIPS OF SCIENTIFIC SOCIETIES

2014-Present Junior Faculty, Society of Immunology, Clinical Immunology and Allergology (SIICA)

2010-Present Assoc. Member, Society of Mucosal Immunology

2008-Present Assoc. Member, European Society for Immunodeficiency (ESID)

PEER-REVIEWED PUBLICATIONS

1. Rigoni R, Fontana E, Dobbs K, Marrella V, Taverniti V, Maina V, Facchetti A, D'Amico G, Al-Herz W, Cruz-Munoz ME, Schuetz C, Gennery AR, Garabedian EK, Giliani S, Draper D, Dbaibo G, Geha RS, Meyts I, Tousseyn T, Neven B, Moshous D, Fischer A, Schulz A, Finocchi A, Kuhns DB, Fink DL, Lionakis MS, Swamydas M, Guglielmetti S, Alejo J, Myles IA, Pittaluga S, Notarangelo LD, Villa A, Cassani B. Cutaneous barrier leakage and gut inflammation drive skin disease in Omenn syndrome. **J Allergy Clin Immunol**. 2020 Apr 18:S0091-6749(20)30492-9. DOI: 10.1016/j.jaci.2020.04.005

2. Cassani B. RalGAP α 2 and NLRP3 Orchestrate Tumor Invasion in Colitis-Associated Cancers. **Cell Mol Gastroenterol Hepatol**. 2020;9(2):339-340. DOI: 10.1016/j.jcmgh.2019.11.004.

3. Menale C, Robinson LJ, Palagano E, Rigoni R, Erreni M, Almarza AJ, Strina D, Mantero S, Lizier M, Forlino A, Besio R, Monari M, Vezzoni P, Cassani B, Blair HC, Villa A, Sobacchi C. Absence of Dipeptidyl Peptidase 3 Increases Oxidative Stress and Causes Bone Loss. **J Bone Miner Res**. 2019 Nov;34(11):2133-2148. DOI: 10.1002/jbmr.3829.

4. Castelli A, Susani L, Menale C, Muggeo S, Caldana E, Strina D, Cassani B, Recordati C, Scanziani E, Ficara F, Villa A, Vezzoni P, Paulis M. Chromosome Transplantation: Correction of the Chronic Granulomatous Disease Defect in Mouse Induced Pluripotent Stem Cells. **Stem Cells**. 2019 Jul;37(7):876-887. DOI: 10.1002/stem.3006.

5. Pellicciotta M, Rigoni R, Falcone EL, Holland SM, Villa A, Cassani B. The microbiome and immunodeficiencies: Lessons from rare diseases. **J Autoimmun**. 2019 Jan 28. pii: S0896-8411(18)30649-8. DOI: 10.1016/j.jaut.2019.01.008. Invited Review

6. Capo V, Castiello MC, Fontana E, Penna S, Bosticardo M, Draghici E, Poliani LP, Sergi LS, Rigoni R, Cassani B, Zanussi M, Carrera P, Uva P, Dobbs K, Sacchetti N,

Notarangelo LD, van Til NP, Wagemaker G, Villa A. Efficacy of lentiviral mediated gene therapy in an Omenn syndrome Rag2 mouse model is not hindered by inflammation and immune dysregulation. **J Allergy Clin Immunol**. 2018 Sep;142(3):928-941.e8. DOI: 10.1016/j.jaci.2017.11.015.

7. Faggioli F, Palagano E, Di Tommaso L, Donadon M, Marrella V, Recordati C, Mantero S, Villa A, Vezzoni P, Cassani B. B lymphocytes limit senescence-driven fibrosis resolution and favor hepatocarcinogenesis in mouse liver injury. **Hepatology**. 2018 May;67(5):1970-1985. DOI: 10.1002/hep.29636.

8. Cassani B, Castriconi R., Mazzoni A., Piconese S., Sciume G. The SIICA School of Immunology 2017: a gathering for NGS (next generation scientists). **Eur J Immunol** 2017 DOI: 10.1002/eji.201770095. Invited Comment

9. Rigoni R, Grassi F, Villa A, Cassani B. RAGs and BUGS: An alliance for autoimmunity. **Gut Microbes**. 2016 Nov;7(6):503-511. DOI: 10.1080/19490976.2016.1228517. Invited Review

10. Farini A, Sitzia C, Cassani B, Cassinelli L, Rigoni R, Colleoni F, Fusco N, Gatti S, Bella P, Villa C, Napolitano F, Maiavacca R, Bosari S, Villa A, Torrente Y. Therapeutic Potential of Immunoproteasome Inhibition in Duchenne Muscular Dystrophy. **Mol Ther**. 2016 Nov;24(11):1898-1912. DOI: 10.1038/MT.2016.162

11. R. Rigoni, E. Fontana, S. Guglielmetti, B. Fosso, A.M. D'Erchia, V. Maina, V. Taverniti, M.C. Castiello, S. Mantero, G. Pacchiana, S. Musio, R. Pedotti, J.R. Mora, G. Pesole, P. Vezzoni, P.L. Poliani, F. Grassi, A. Villa and B. Cassani. Intestinal microbiota sustains inflammation and autoimmunity induced by hypomorphic RAG defects. 2016 **J Exp Med**. 213(3):355-75. DOI: 10.1084/jem.20151116

12. Pala F, Morbach H, Castiello MC, Schickel JN, Scaramuzza S, Chamberlain N, Cassani B, Glauzy S, Romberg N, Candotti F, Aiuti A, Bosticardo M, Villa A, Meffre E. Lentiviral-mediated gene therapy restores B cell tolerance in Wiskott-Aldrich syndrome patients. 2015 **J Clin Invest**. 125(10):3941-51. DOI: 10.1172/JCI82249

13. Marrella V, Lo Iacono N, Fontana E, Sobacchi C, Sic H, Schena F, Sereni L, Castiello MC, Poliani PL, Vezzoni P, Cassani B, Traggiai E, Villa A. IL-10 critically modulates B cell responsiveness in Rankl^{-/-} mice. 2015 **J Immunol**. 194(9):4144-53. DOI: 10.4049/jimmunol.1401977

14. van Til NP, Cortes P, Danos O, Cassani B, Poliani PL, Villa A, Wagemaker G. Reply: To PMID 24332219. 2014 **J Allergy Clin Immunol**. 134(1):243-4.

15. van Til NP, Sarwari R, Visser TP, Hauer J, Lagresle-Peyrou C, van der Velden G, Malshetty V, Cortes P, Jollet A, Danos O, Cassani B, Zhang F, Thrasher AJ, Fontana E, Poliani PL, Cavazzana M, Verstegen MM, Villa A, Wagemaker G. Recombination-activating gene 1 (Rag1)-deficient mice with severe combined immunodeficiency treated with lentiviral gene therapy demonstrate autoimmune Omenn-like syndrome. 2014 **J Allergy Clin Immunol**. 133(4):1116-23. DOI: 10.1016/j.jaci.2013.10.009

16. Maina V, Marrella V, Mantero S, Cassani B, Fontana E, Anselmo A, Del Prete A, Sozzani S, Vezzoni P, Poliani PL, Villa A. Hypomorphic mutation in the RAG2 gene

affects dendritic cell distribution and migration. 2013 **J Leukoc Biol.** 94(6):1221-30. DOI: 10.1189/jlb.0713365

17. Villablanca EJ, De Calisto J, Torregrosa Paredes P, Cassani B, Nguyen DD, Gabrielsson S, Mora JR. $\beta 7$ integrins are required to give rise to intestinal mononuclear phagocytes with tolerogenic potential. 2013 **Gut** 63(9):1431-40. DOI: 10.1136/gutjnl-2013-305386

18. van Til NP, de Boer H, Mashamba N, Wabik A, Huston M, Visser TP, Fontana E, Poliani PL, Cassani B, Zhang F, Thrasher AJ, Villa A, Wagemaker G. Correction of Murine Rag2 Severe Combined Immunodeficiency by Lentiviral Gene Therapy Using a Codon-optimized RAG2 Therapeutic Transgene. 2012 **Mol Ther.** 20(10):1968-80. DOI: 10.1038/mt.2012.110

19. Lo Iacono N, Blair HC, Poliani PL, Marrella V, Ficara F, Cassani B, Facchetti F, Fontana E, Guerrini MM, Traggiai E, Schena F, Paulis M, Mantero S, Inforzato A, Valaperta S, Pangrazio A, Crisafulli L, Maina V, Kostenuik P, Vezzoni P, Villa A, Sobacchi C. Osteopetrosis rescue upon RANKL administration to Rankl(-/-) mice: A new therapy for human RANKL-dependent ARO. 2012 **J Bone Miner Res.** 27(12):2501. DOI: 10.1002/jbmr.1712

20. Marrella V, Poliani PL, Fontana E, Casati A, Maina V, Cassani B, Ficara F, Cominelli M, Schena F, Paulis M, Traggiai E, Vezzoni P, Grassi F, Villa A. Anti-CD3{varepsilon} mAb improves thymic architecture and prevents autoimmune manifestations in a mouse model of Omenn syndrome: therapeutic implications. 2012 **Blood.** 120(5):1005-14. DOI: 10.1182/blood-2012-01-406827

21. Cassani B, Villablanca EJ, De Calisto J, Wang S, Mora JR. Vitamin A and immune regulation: Role of retinoic acid in gut-associated dendritic cell education, immune protection and tolerance. 2012 **Mol Aspects Med.** 33(1):63-76. DOI: 10.1016/j.mam.2011.11.001

22. Pangrazio A*, Cassani B*, Guerrini MM, Crockett JC, Marrella V, Zammataro L, Strina D, Schulz A, Schlack C, Kornak U, Mellis DJ, Duthie A, Helfrich MH, Durandy A, Moshous D, Vellodi A, Chiesa R, Veys P, Iacono NL, Vezzoni P, Fischer A, Villa A, Sobacchi C. RANK-dependent autosomal recessive osteopetrosis: characterisation of 5 new cases with novel mutations.* equal contribution. 2012 **J Bone Miner Res.** 27(2):342-51. DOI: 10.1002/jbmr.559

23. Cassani B, Villablanca EJ, Quintana FJ, Love PE, Lacy-Hulbert A, Blaner WS, Sparwasser T, Snapper SB, Weiner HL, Mora JR. Gut-Tropic T Cells That Express Integrin $\alpha 4\beta 7$ and CCR9 Are Required for Induction of Oral Immune Tolerance in Mice. 2011 **Gastroenterology.** 141(6):2109-18. DOI: 10.1053/j.gastro.2011.09.015

24. Deichmann A, Brugman MH, Bartholomae CC, Schwarzwaelder K, Verstegen MM, Howe SJ, Arens A, Ott MG, Hoelzer D, Seger R, Grez M, Hacein-Bey-Abina S, Cavazzana-Calvo M, Fischer A, Paruzynski A, Gabriel R, Glimm H, Abel U, Cattoglio C, Mavilio F, Cassani B, Aiuti A, Dunbar CE, Baum C, Gaspar HB, Thrasher AJ, von Kalle C, Schmidt M, Wagemaker G. Insertion sites in engrafted cells cluster within a limited repertoire of genomic areas after gammaretroviral vector gene therapy. 2011 **Mol Ther.** 19(11):2031-9. DOI: 10.1038/mt.2011.178

25. EJ. Villablanca*, B. Cassani*, UH. von Andrian and JR. Mora. Blocking Lymphocyte Localization to the Gastrointestinal Mucosa as a Therapeutic Strategy for Inflammatory Bowel Diseases. *equal contribution. 2011 **Gastroenterology** 140(6):1776-84. DOI: 10.1053/j.gastro.2011.02.015

26. S. Selleri, I. Brigida, M. Casiraghi, S. Scaramuzza, B. Cappelli, B. Cassani, A. Scarselli, C. Cancrini, S. Markt, M.G. Roncarolo and A. Aiuti. In vivo hematopoietic cell dynamics during immune reconstitution after hematopoietic stem cell gene therapy in ADA-SCID. 2011 **J Allergy Clin Immunol.** 127(6):1368-75.e8. DOI: 10.1016/j.jaci.2011.03.004

27. Cassani B, Poliani PL, Marrella V, Schena F, Sauer AV, Ravanini M, Strina D, Busse CE, Regenass S, Wardemann H, Martini A, Facchetti F, van der Burg M, Rolink AG, Vezzoni P, Grassi F, Traggiai E, Villa A. Homeostatic expansion of autoreactive immunoglobulin-secreting cells in the Rag2 mouse model of Omenn syndrome. 2010 **J Exp Med.** 207(7):1525-40. DOI: 10.1084/jem.20091928

28. Cassani B, Poliani PL, Moratto D, Sobacchi C, Marrella V, Imperatori L, Vairo D, Plebani A, Giliani S, Vezzoni P, Facchetti F, Porta F, Notarangelo LD, Villa A, Badolato R. Defect of regulatory T cells in patients with Omenn syndrome. 2010 **J Allergy Clin Immunol.** 125(1):209-16. DOI: 10.1016/j.jaci.2009.10.023

29. Cassani B, Montini E, Maruggi G, Ambrosi A, Mirolo M, Selleri S, Biral E, Frugnoli I, Hernandez-Trujillo V, Di Serio C, Roncarolo MG, Naldini L, Mavilio F, Aiuti A. Integration of retroviral vectors induces minor changes in the transcriptional activity of T cells from ADA-SCID patients treated with gene therapy. 2009 **Blood.** 114(17):3546-56. DOI: 10.1182/blood-2009-02-202085

*Comment in Blood 2009 114: 3507-3508

30. Tondelli B, Blair HC, Guerrini M, Patrene KD, Cassani B, Vezzoni P, Lucchini F. Fetal liver cells transplanted in utero rescue the osteopetrotic phenotype in the oc/oc mouse. 2009 **Am J Pathol.** 174(3):727-35. DOI: 10.2353/ajpath.2009.080688

31. Villa A, Guerrini MM, Cassani B, Pangrazio A, Sobacchi C. Infantile malignant, autosomal recessive osteopetrosis: the rich and the poor. 2009 **Calcif Tissue Int.** 84(1):1-12. DOI: 10.1007/s00223-008-9196-4

32. Aiuti A, Cattaneo F, Galimberti S, Benninghoff U, Cassani B, Callegaro L, Scaramuzza S, Andolfi G, Mirolo M, Brigida I, Tabucchi A, Carlucci F, Eibl M, Aker M, Slavin S, Al-Mousa H, Al Ghonaium A, Ferster A, Duppenthaler A, Notarangelo L, Wintergerst U, Buckley RH, Bregni M, Markt S, Valsecchi MG, Rossi P, Ciceri F, Miniero R, Bordignon C, Roncarolo MG. Gene therapy for immunodeficiency due to adenosine deaminase deficiency. 2009 **N Engl J Med.** 360(5):447-58. DOI: 10.1056/NEJMoa0805817

33. Guerrini MM, Sobacchi C, Cassani B, Abinun M, Kilic SS, Pangrazio A, Moratto D, Mazzolari E, Clayton-Smith J, Orchard P, Coxon FP, Helfrich MH, Crockett JC, Mellis D, Vellodi A, Tezcan I, Notarangelo LD, Rogers MJ, Vezzoni P, Villa A, Frattini A. Human osteoclast-poor osteopetrosis with hypogammaglobulinemia due to TNFRSF11A

(RANK) mutations. 2008 **Am J Hum Genet.** 83(1):64-76. DOI: 10.1016/j.ajhg.2008.06.015

34. Cassani B, Mirolo M, Cattaneo F, Benninghoff U, Hershfield M, Carlucci F, Tabucchi A, Bordignon C, Roncarolo MG, Aiuti A. Altered intracellular and extracellular signaling leads to impaired T-cell functions in ADA-SCID patients. 2008 **Blood.** 111(8):4209-19. DOI: 10.1182/blood-2007-05-092429

35. Aiuti A, Cassani B, Andolfi G, Mirolo M, Biasco L, Recchia A, Urbinati F, Valacca C, Scaramuzza S, Aker M, Slavin S, Cazzola M, Sartori D, Ambrosi A, Di Serio C, Roncarolo MG, Mavilio F, Bordignon C. Multilineage hematopoietic reconstitution without clonal selection in ADA-SCID patients treated with stem cell gene therapy. 2007 **J Clin Invest.** 117(8):2233-40. DOI: 10.1172/JCI31666

36. Cattoglio C, Facchini G, Sartori D, Antonelli A, Miccio A, Cassani B, Schmidt M, von Kalle C, Howe S, Thrasher AJ, Aiuti A, Ferrari G, Recchia A, Mavilio F. Hot spots of retroviral integration in human CD34+ hematopoietic cells. 2007 **Blood.** 110(6):1770-8. DOI: 10.1182/blood-2007-01-068759

37. Isgrò A, Marziali M, Mezzaroma I, Luzi G, Mazzone AM, Guazzi V, Andolfi G, Cassani B, Aiuti A, Aiuti F. Bone marrow clonogenic capability, cytokine production, and thymic output in patients with common variable immunodeficiency. 2005 **J Immunol.** 174(8):5074-81. DOI: 10.4049/jimmunol.174.8.5074

RESEARCH MONOGRAPHS

1. Gene therapy for primary immunodeficiency. A. Sauer, B. Cassani and A. Aiuti. "A guide to human gene therapy" Ed. RW Herzog and S Zolotukhin, World Scientific Publishing Company; 2010. ISBN-13: 978-9814280907

CAREER BREAKS

2012 Maternity Leave

2017 Maternity Leave