

EUROPEAN CURRICULUM VITAE

PERSONAL DATA

TITLE PhD
NAME Immacolata Brigida

RESEARCH EXPERIENCE

May 2018 – April 2019: Vita Salute University

Position: Post-Doctoral Fellow

Vita Salute University, Milan (Prof. A. Aiuti)

Work: Next generation sequencing for the identification of target genes as causative of neurological defects in patients with Wiskott-Aldrich syndrome. Part of the work is based on the molecular analysis of the exome and genotype-phenotype correlations. Functional studies for gene validation.

January 2018 - present: HSR-TIGET

Position: Post-Doctoral Fellow

HSR-TIGET, Milan (Prof. A. Aiuti, Dr. A. Mortellaro)

Work: Study of the pathogenesis of DADA2 deficiency. The project focused on the in depth characterization of the immune system of immunodeficient patients. Part of the work is carried out on cellular models of the disease to understand the molecular pathways governing DADA2 deficiency and the role of *CECR1* gene on the interferon pathway. Management of resources assigned to the project for time-table and budget, as well as team's professional growth.

October 2016- Present

Laboratory study manager to the Telethon Institute for gene therapy (SR-TIGET)

Coordination and supervision of study-related activities conducted in the Clinical Lab in compliance with GCLP principles.

Lab study manager for: ADA-SCID clinical trial (2016-2018); study sponsored by Chiesi farmaceutici group (2017-present).

Acquired skills: referral for clinical laboratory activities; identify technicians \ scientists on the basis of their scientific skills for the assigned project and supervisor; design Analytical Plan; review, evaluate and interpret project Analytical results; writing of the Analytical report (if requested); writing SOPs; liaise with QA in resolving potential issues, answer to queries received from audits; liaise with the Project Leader and the Study PI for all issues and results related to the assigned project.

October 2013 - present: HSR-TIGET

Position: Post-Doctoral Fellow

HSR-TIGET, Milan (Prof. A. Aiuti)

Work: Next generation sequencing for the identification of target genes in patients with unsolved immunodeficiencies. Part of the work is based on the molecular analysis of the exome and genotype-phenotype correlations and to functional studies aimed at validation of genes potentially underlying these diseases. Management of resources assigned to the project for time-table and budget, as well as team's professional growth.

June 2011 - October 2013: HSR-TIGET

Position: Post-Doctoral Fellow

HSR-TIGET, Milan (Prof. A. Aiuti)

Work: "Pathogenesis of autoimmune manifestations in ADA-SCID". The main part of the project was focused at studying the role of regulatory T cells after either PEG-ADA or HSC-gene therapy, with evidence of Treg defects after PEG-ADA treatment. Moreover I was involved in the characterization of B cells in these patients and the possible development of autoreactive B cells in the breakdown of tolerance after different kind of treatments (PEG-ADA, gene therapy or bone marrow transplant). This project was supported by collaboration with GSK industry for the development of a new drug approved from AIFA and EMA (Strimvelis), to treat ADA-SCID patients worldwide.

January 2012 - February 2012: Erasmus MC

Position: Research Fellow (Dr. M. Van der Burg)

Work: I spent two weeks in the laboratory of M. Van der Burg (Rotterdam - Nederland) in order to investigate the development of BM B cells in ADA-SCID patients before any treatment, after PEG-ADA or HSC-gene therapy. The period spent there allowed me to acquire new FACS techniques applicable to SCID patients.

November 2007 - May 2011: HSR-TIGET

Position: PhD Student for "Immunology and Applied Biotechnology",
University of Rome Tor Vergata (Prof. A. Aiuti)

Thesis Title: Immunological reconstitution and peripheral tolerance in ADA-SCID patients after gene therapy or enzyme replacement therapy

Work: PhD program in Immunology and Applied Biotechnology. The principal investigation was done at TIGET (Milan) in the laboratory of Primary Immunodeficiency headed by Prof. Aiuti. I was in charge of the molecular and immunological follow-up of ADA-SCID patients treated with gene therapy, bone marrow transplant or enzyme replacement treatment. Aim of the project was to understand and define the critical factors influencing immune-reconstitution, the mechanisms of antigen-specific responses, the acquisition and maintenance of immunological memory. In addition I studied the perturbations of peripheral tolerance after different treatments, focusing on the phenotype and function of nTreg cells, the reconstitution of the B cell compartment after therapy and their role in autoimmunity.

June 2006 - October 2007: HSR-TIGET

Position: Research Fellow

Work: Research fellow in TIGET (Milan) in the laboratory of Primary Immunodeficiency headed by Prof. Aiuti. I was in charge of the molecular and immunological follow-up of ADA-SCID patients, including those treated with GT. Aim of the project was the long-term follow-up of gene therapy treated patients. I evaluated the presence of gene-corrected cells to assess the correction of metabolic and genetic defects, the immune reconstitution at specific time points after treatment, mechanisms of antigen-specific responses and the acquisition and maintenance of immunological memory.

September 2004 - March 2006: Department of Experimental Medicine, University of Parma

Position: Thesis internship under the supervision of Prof. M. Zuccotti. Basic training in Embryology.

Work: In the laboratory of Experimental Medicine, headed by prof. Zuccotti (Parma) I studied the nuclear architecture of pre-implant mouse embryos, with immunocytochemistry techniques. Aim of the research was the reconstruction of

spatial positions of chromosomic portions, namely the centromeres, chromocenters and nucleoli during the first phases of development, with the final goal to define the 3D nuclear architecture. Part of the thesis was done at University of Pavia, in the laboratory of Developmental Biology, headed by Prof. Redi.

March 2003 - September 2003: Department of Viral Immunopathology, Hospital of Parma

Position: Thesis internship under the supervision of Dr. G. Missale (internal tutor Prof. Perris). Basic training in Immunology.

Work: In the laboratory of Viral Immunopathology (Parma) headed by Dr. Missale, I studied the ability of Ag-specific CD8 (CTL cells) to sustain a vigorous and multispecific response in patients chronically co-infected with HCV and acutely with HBV. Results of the study demonstrated a transient and weak response to HCV but not to HBV, due to a selective inhibitory effect of HCV specific CTL function.

SCIENTIFIC EDUCATION

November 2007 - May 2011

PhD program in "Immunology and applied Biotechnology", laboratory of Primary Immunodeficiencies HSR-TIGET (Milan, Italy)
University of Rome Tor Vergata (Prof. A. Aiuti)

Thesis Title: Immunological reconstitution and peripheral tolerance in ADA-SCID patients after gene therapy or enzyme replacement therapy

June 2006: Qualifying examination for Biologists at the University of Parma

September 2003 – April 2006

Medical Biotechnology for human health - Master's Degree
University of Parma - Department of Experimental Medicine
Result - 110/110 cum laude

Thesis title: "Nuclear architecture of murine pre-implant embryo: 3D localization of centromeres, chromocenters and nucleoli".

Thesis internship under the supervision of Prof. M. Zuccotti. Basic training in Embryology (see research experience).

September 2000 – September 2003

Biotechnology – Bachelor's Degree
University of Parma - Department of Viral Immunopathology
Result - 104/110

Thesis title: "Effects of HBV and HCV co-infection on virus specific CD8 cytotoxic activity".

Thesis internship under the supervision of Dr. G. Missale (internal tutor Prof. Perris). Basic training in Immunology (see research experience).

September 1995 – July 2000:

High School – *Liceo Scientifico G. Galilei, Manfredonia*
Final assessment: 100/100

PARTICIPATION TO GLP/GCLP COURSES:

- 24/10/11 Data recording

- 21/11/11 Preparation handling and storage of cv and training records
- 11/11/11 Preparation revision and implementation of standard operating procedure
- 5-6/11/12 Implementing good clinical laboratory practice
- 04/11/13 Immunoterapia antitumorale e terapia genica: regole e sperimentazione
- 20/05/15 GLP principles
- 04/06/15 SOP management
- 04/06/15 Templates forms, TS preparation, revision and implementation
- 11/06/15 Preparation handling and storage of CV and training records
- 11/06/15 Data recording
- 12/02/16 Corso GCP e privacy
- 03/11/16 Good laboratory practice principles
- 09/05/19 ICH Good Clinical Practice course (R2)

TECNICAL SKILLS:

Molecular biology:

- manipulation of nucleic acids (DNA, RNA, cDNA)
- DNA and RNA extraction
- quantitative PCR, RT-PCR
- exome analysis
- preparation of libraries of exome for target sequencing
- sequencing of DNA
- Transformation of bacteria
- Plasmid extraction and evaluation
- Gene therapy techniques
- Basic bioinformatics analysis
- Transduction of hematopoietic stem cells with retroviral vectors
- Western blot
- Preparation of vectors for in vitro transduction

Cellular biology:

- Purification of bone marrow and peripheral blood mononuclear cells
- Isolation of cell subsets by magnetic beads or cell-sorting
- Generation of T/B cell lines
- ³H-Thy incorporation/CFSE assay to assess cell proliferation (T-, B-, nTreg-cells)
- In vitro suppression assays on nTregs in human and in mouse systems
- Immunological assays to test cell function: cytokine beads assay, bioplex, ELISA, ⁵¹Cr-release and CD107a cytotoxic assays on NK and T cells
- Immunofluorescence staining and multiparameter flow cytometry (up to 7 colors) for T, B, NK, nTreg, Monocytes cell subsets
- *In vitro* fertilization, embryo cell culture
- Fluorescence conventional and confocal microscopy.
- Animal handling and care.
- ELISPOT assay
- Protein extraction (BSA assay)
- Spectratyping of major Vbeta chains in mice T cells
- Colony forming unit (CFU) assay on purified CD34+ cells
- Cytoskeletal assays (migration, adhesion, polymerization assay)
- Hematopoietic stem cell transduction and differentiation in vitro

LANGUAGES

ITALIAN – native speaker
ENGLISH – proficiency C2 level

INFORMATICS

- Good use of MAC-OS, Windows
- Office suite
- Adobe Dimension 3.0, Adobe Photoshop 7.0, Adobe Illustrator, GraphPad
- Programs Rasmol
- SwissPdbViewer
- FlowJo
- FCS software

MISCELLANEOUS AND HONORS

GR-2011-02346985: Giovani ricercatori 2011 from Ministero della Salute for the project “Neurological and behavioral abnormalities in Adenosine Deaminase-deficiency and their correction by therapeutical approaches”

November 2008 - January 2009: HSR-TIGET **Laboratory assistant** during the laboratory practice of the “Molecular Pediatrics” Course, University “Vita Salute”-HSR, Milan, Italy

Travel Award for the “4th International Conference on Autoimmunity”, Chania, Crete 2009

Travel Award for the “XIVth meeting of the European society for immunodeficiencies (ESID), Istanbul, Turkey 2010.

European Society of Immunodeficiencies (ESID) Member

European Society of gene and cell therapy (ESGCT) Member

18-19 June 2012: HSR-TIGET **Laboratory assistant** during the laboratory practice of the “Training course on gene transfer in human hematopoietic cells”.

PERSONAL QUALITIES

- Curious, dynamic and ambitious
- Able to work in team, with leadership initiative
- Attitude at problem solving
- Able to work under pressure with strong orientation to results
- Professional and ethical behavior
- Assertiveness, integrity, accuracy, reliability
- Excellent internal and external communication skills
- Open to exchange with other cultures

In compliance with the GDPR (UE 2016/679) and Italian Legislative Decree no. 196 dated 30/06/2003, I hereby authorize the recipient of this document to use and process my personal details for the purpose of recruiting and selecting staff and I confirm to be informed of my rights in accordance to art. 7 of the above-mentioned Decree.

Date
30-12-2019

Signature
Immacolata Brigida


ADDENDUM

LIST OF PUBLICATIONS:

Papers:

1. A novel disorder involving dyshematopoiesis, inflammation, and HLH due to aberrant CDC42 function. Lam MT, Coppola S, Krumbach OHF, Prencipe G, Insalaco A, Cifaldi C, **Brigida I**, Zara E, Scala S, Di Cesare S, Martinelli S, Di Rocco M, Pascarella A, Niceta M, Pantaleoni F, Ciolfi A, Netter P, Carisey AF, Diehl M, Akbarzadeh M, Conti F, Merli P, Pastore A, Levi Mortera S, Camerini S, Farina L, Buchholzer M, Pannone L, Cao TN, Coban-Akdemir ZH, Jhangiani SN, Muzny DM, Gibbs RA, Basso-Ricci L, Chiriaco M, Dvorsky R, Putignani L, Carsetti R, Janning P, Stray-Pedersen A, Erichsen HC, Horne A, Bryceson YT, Torralba-Raga L, Ramme K, Rosti V, Bracaglia C, Messia V, Palma P, Finocchi A, Locatelli F, Chinn IK, Lupski JR, Mace EM, Cancrini C, Aiuti A, Ahmadian MR, Orange JS, De Benedetti F, Tartaglia M. *J Exp Med*. 2019 Dec 2;216(12):2778-2799. doi: 10.1084/jem.20190147. Epub 2019 Oct 10. PMID: 31601675
2. Targeted NGS Platforms for Genetic Screening and Gene Discovery in Primary Immunodeficiencies. Cifaldi C*, **Brigida I***, Barzaghi F*, Zoccolillo M, Ferradini V, Petricone D, Cicalese MP, Lazarevic D, Cittaro D, Omrani M, Attardi E, Conti F, Scarselli A, Chiriaco M, Di Cesare S, Licciardi F, Davide M, Ferrua F, Canessa C, Pignata C, Giliani S, Ferrari S, Fousteri G, Barera G, Merli P, Palma P, Cesaro S, Gattorno M, Trizzino A, Moschese V, Chini L, Villa A, Azzari C, Finocchi A, Locatelli F, Rossi P, Sangiuolo F, Aiuti A, Cancrini C, Di Matteo G. *Front Immunol*. 2019 Apr 11;10:316. doi: 10.3389/fimmu.2019.00316. eCollection 2019. PMID:31031743
3. Lentiviral haemopoietic stem/progenitor cell gene therapy for treatment of Wiskott-Aldrich syndrome: interim results of a non-randomised, open-label, phase 1/2 clinical study. Ferrua F, Cicalese MP, Galimberti S, Giannelli S, Dionisio F, Barzaghi F, Migliavacca M, Bernardo ME, Calbi V, Assanelli AA, Facchini M, Fossati C, Albertazzi E, Scaramuzza S, **Brigida I**, Scala S, Basso-Ricci L, Pajno R, Casiraghi M, Canarutto D, Salerio FA, Albert MH, Bartoli A, Wolf HM, Fiori R, Silvani P, Gattillo S, Villa A, Biasco L, Dott C, Culme-Seymour EJ, van Rossem K, Atkinson G, Valsecchi MG, Roncarolo MG, Ciceri F, Naldini L, Aiuti A. *Lancet Haematol*. 2019 Apr 10. pii: S2352-3026(19)30021-3. doi: 10.1016/S2352-3026(19)30021-3. PMID:30981783
4. First Case of Patient With Two Homozygous Mutations in MYD88 and CARD9 Genes Presenting With Pyogenic Bacterial Infections, Elevated IgE, and Persistent EBV Viremia. Chiriaco M, Di Matteo G, Conti F, Petricone D, De Luca M, Di Cesare S, Cifaldi C, De Vito R, Zoccolillo M, Serafinelli J, Poerio N, Fraziano M, **Brigida I**, Cardinale F, Rossi P, Aiuti A, Cancrini C, Finocchi A. *Front Immunol*. 2019 Feb 14;10:130. doi: 10.3389/fimmu.2019.00130. eCollection 2019. PMID:30837984

5. A combined immunodeficiency with severe infections, inflammation and allergy caused by ARPC1B deficiency. Volpi S, Cicalese MP, Tuijnburg P, Tool ATJ, Cuadrado E, Ahanchian H, Alzyoud R, Akdemir ZC, Barzaghi F, Blank A, Boisson B, Bottino C, Caorsi R, Casanova JL, Chiesa S, Chinn IK, Dückers G, Enders A, Erichsen HC, Forbes LR, Gambin T, Gattorno M, Karimiani EG, Giliani S, Gold MS, Abu-Halaweh M, **Brigida I**, Jacobsen EM, Jansen MH, King JR, Laxer RM, Lupski JR, Mace E, Marcenaro S, Maroofian R, Meijer AB, Niehues T, Notarangelo LD, Orange J, Pannicke U, Pearson C, Picco P, Quinn PJ, Schulz A, Seeborg F, Stray-Pedersen A, Tawamie H, van Leeuwen EMM, Aiuti A, Yeung R, Schwarz K, Kuijpers TW. *J Allergy Clin Immunol*. 2019 Feb 13. pii: S0091-6749(19)30206-4. doi: 10.1016/j.jaci.2019.02.003. [Epub ahead of print] PMID: 30771411
6. ALPS-Like Phenotype Caused by ADA2 Deficiency Rescued by Allogeneic Hematopoietic Stem Cell Transplantation. Barzaghi F, Minniti F, Mauro M, Bortoli M, Balter R, Bonetti E, Zaccaron A, Vitale V, Omrani M, Zoccolillo M, **Brigida I**, Cicalese MP, Degano M, Hershfield MS, Aiuti A, Bondarenko AV, Chinello M, Cesaro S. *Front Immunol*. 2019 Jan 14;9:2767. doi: 10.3389/fimmu.2018.02767. eCollection 2018. PMID:30692987
7. T cell defects in patients with ARPC1B germline mutations account for their combined immunodeficiency. **Brigida I**, Zoccolillo M, Cicalese MP, Pfajfer L, Barzaghi F, Scala S, Oleaga-Quintas C, Álvarez-Álvarez JA, Sereni L, Giannelli S, Sartirana C, Dionisio F, Pavesi L, Benavides-Nieto M, Basso-Ricci L, Capasso P, Mazzi B, Rosain J, Marcus N, Lee YN, Somech R, Degano M, Raiola G, Caorsi R, Picco P, Moncada Velez M, Khourieh J, Arias AA, Bousfiha A, Issekutz T, Issekutz A, Boisson B, Dobbs K, Villa A, Lombardo A, Neven B, Moshous D, Casanova JL, Franco JL, Notarangelo LD, Scielzo C, Volpi S, Dupré L, Bustamante J, Gattorno M, Aiuti A. *Blood*. 2018 Nov 29;132(22):2362-2374. doi: 10.1182/blood-2018-07-863431, comment in *Blood* 2018 132:2316-2317; doi: <https://doi.org/10.1182/blood-2018-10-878603>.
8. Next-Generation Sequencing Reveals A JAGN1 Mutation in a Syndromic Child With Intermittent Neutropenia. Cifaldi C, Serafinelli J, Petricone D, **Brigida I**, Di Cesare S, Di Matteo G, Chiriaco M, De Vito R, Palumbo G, Rossi P, Palma P, Cancrini C, Aiuti A, Finocchi A. *J Pediatr Hematol Oncol*. 2018 Jul 23. doi: 10.1097/MPH.0000000000001256. [Epub ahead of print] PMID:30044346
9. First Occurrence of Plasmablastic Lymphoma in Adenosine Deaminase-Deficient Severe Combined Immunodeficiency Disease Patient and Review of the Literature. Migliavacca M, Assanelli A, Ponzoni M, Pajno R, Barzaghi F, Giglio F, Ferrua F, Frittoli M, **Brigida I**, Dionisio F, Nicoletti R, Casiraghi M, Roncarolo MG, Doglioni C, Peccatori J, Ciceri F, Cicalese MP, Aiuti A. *Front Immunol*. 2018 Feb 2;9:113. doi: 10.3389/fimmu.2018.00113. eCollection 2018. PMID: 29456531.
10. Biological and functional characterization of bone marrow-derived mesenchymal stromal cells from patients affected by primary immunodeficiency. Starc N, Ingo D, Conforti A, Rossella V, Tomao L, Pitisci A, De Mattia F, **Brigida I**, Algeri M, Montanari M, Palumbo G, Merli P, Rossi P, Aiuti A, Locatelli F, Bernardo ME. *Sci Rep*. 2017 Aug 15;7(1):8153. doi: 10.1038/s41598-017-08550-5. PMID: 28811575
11. Large Deletion of MAGT1 Gene in a Patient with Classic Kaposi Sarcoma, CD4 Lymphopenia, and EBV Infection. **Brigida I***, Chiriaco M*, Di Cesare S, Cittaro D, Di Matteo G, Giannelli S, Lazarevic D, Zoccolillo M, Stupka E, Jenkner A, Francalanci P, Livadiotti S, Morawski A, Ravell J, Lenardo M, Cancrini C, Aiuti A, Finocchi A. *J Clin Immunol*. 2017 Jan;37(1):32-35. doi: 10.1007/s10875-016-0341-y. Epub 2016 Oct 21. No abstract available. PMID:

27770395

12. Update on the safety and efficacy of retroviral gene therapy for immunodeficiency due to adenosine deaminase deficiency. Cicalese MP, Ferrua F, Castagnaro L, Pajno R, Barzaghi F, Giannelli S, Dionisio F, **Brigida I**, Bonopane M, Casiraghi M, Tabucchi A, Carlucci F, Grunebaum E, Adeli M, Bredius RG, Puck JM, Stepensky P, Tezcan I, Rolfe K, De Boever E, Reinhardt RR, Appleby J, Ciceri F, Roncarolo MG, Aiuti A. *Blood*. 2016 Jul 7;128(1):45-54. doi: 10.1182/blood-2016-01-688226. Epub 2016 Apr 29. Erratum in: *Blood*. 2017 Jun 15;129(24):3271. PMID: 27129325
13. A novel genomic inversion in Wiskott-Aldrich-associated autoinflammation. **Brigida I***, Scaramuzza S*, Lazarevic D, Cittaro D, Ferrua F, Leonardelli L, Alessio M, Forma O, Lanzani C, Viarengo G, Ciceri F, Jankovic M, Pesce F, Aiuti A, Cicalese MP. *J Allergy Clin Immunol*. 2016 Aug;138(2):619-622.e7. doi: 10.1016/j.jaci.2016.03.007. Epub 2016 Apr 22. No abstract available. PMID: 27113846
14. The case of an APDS patient: Defects in maturation and function and decreased in vitro anti-mycobacterial activity in the myeloid compartment. Chiriaco M*, **Brigida I***, Ariganello P, Di Cesare S, Di Matteo G, Taus F, Cittaro D, Lazarevic D, Scarselli A, Santilli V, Attardi E, Stupka E, Giannelli S, Fraziano M, Finocchi A, Rossi P, Aiuti A, Palma P, Cancrini C. *Clin Immunol*. 2017 May;178:20-28. doi: 10.1016/j.clim.2015.12.008. Epub 2015 Dec 28. PMID: 26732860
15. B-cell reconstitution after lentiviral vector-mediated gene therapy in patients with Wiskott-Aldrich syndrome. Castiello MC, Scaramuzza S, Pala F, Ferrua F, Uva P, **Brigida I**, Sereni L, van der Burg M, Ottaviano G, Albert MH, Grazia Roncarolo M, Naldini L, Aiuti A, Villa A, Bosticardo M. *J Allergy Clin Immunol*. 2015 Sep;136(3):692-702.e2. doi: 10.1016/j.jaci.2015.01.035. Epub 2015 Mar 16. PMID: 25792466
16. B-cell development and functions and therapeutic options in adenosine deaminase-deficient patients. **Brigida I**, Sauer AV, Ferrua F, Giannelli S, Scaramuzza S, Pistoia V, Castiello MC, Barendregt BH, Cicalese MP, Casiraghi M, Brombin C, Puck J, Müller K, Notarangelo LD, Montin D, van Montfrans JM, Roncarolo MG, Traggiai E, van Dongen JJ, van der Burg M, Aiuti A. *J Allergy Clin Immunol*. 2014 Mar;133(3):799-806.e10. doi: 10.1016/j.jaci.2013.12.1043. Epub 2014 Feb 5. PMID: 24506932
17. Human IL2RA null mutation mediates immunodeficiency with lymphoproliferation and autoimmunity. Goudy K, Aydin D, Barzaghi F, Gambineri E, Vignoli M, Ciullini Mannurita S, Doglioni C, Ponzoni M, Cicalese MP, Assanelli A, Tommasini A, **Brigida I**, Dellepiane RM, Martino S, Olek S, Aiuti A, Ciceri F, Roncarolo MG, Bacchetta R. *Clin Immunol*. 2013 Mar;146(3):248-61. doi: 10.1016/j.clim.2013.01.004. Epub 2013 Jan 24. PMID: 23416241
18. Autoimmune dysregulation and purine metabolism in adenosine deaminase deficiency. Sauer AV, **Brigida I**, Carriglio N, Aiuti A. *Front Immunol*. 2012 Aug 27;3:265. doi: 10.3389/fimmu.2012.00265. eCollection 2012. PMID: 22969765
19. T-cell suicide gene therapy prompts thymic renewal in adults after hematopoietic stem cell transplantation. Vago L, Oliveira G, Bondanza A, Novello M, Soldati C, Ghio D, **Brigida I**, Greco R, Lupo Stanghellini MT, Peccatori J, Fracchia S, Del Fiacco M, Traversari C, Aiuti A, Del Maschio A, Bordignon C, Ciceri F, Bonini C. *Blood*. 2012 Aug 30;120(9):1820-30. doi: 10.1182/blood-2012-01-405670. Epub 2012 Jun 18. PMID: 22709689
20. Defective B cell tolerance in adenosine deaminase deficiency is corrected by gene therapy. Sauer AV, Morbach H, **Brigida I**, Ng YS, Aiuti A, Meffre E. *J Clin Invest*. 2012 Jun;122(6):2141-52. doi: 10.1172/JCI61788. Epub 2012

May 24. PMID: 22622038

21. HIV-1 envelope-dependent restriction of CXCR4-using viruses in child but not adult untransformed CD4⁺ T-lymphocyte lines. Mariani SA, **Brigida I**, Kajaste-Rudnitski A, Ghezzi S, Rocchi A, Plebani A, Vicenzi E, Aiuti A, Poli G. *Blood*. 2012 Mar 1;119(9):2013-23. doi: 10.1182/blood-2010-12-325308. Epub 2012 Jan 10. PMID: 22234680
22. Alterations in the adenosine metabolism and CD39/CD73 adenosinergic machinery cause loss of Treg cell function and autoimmunity in ADA-deficient SCID. Sauer AV*, **Brigida I***, Carriglio N, Hernandez RJ, Scaramuzza S, Clavenna D, Sanvito F, Poliani PL, Gagliani N, Carlucci F, Tabucchi A, Roncarolo MG, Traggiai E, Villa A, Aiuti A. *Blood*. 2012 Feb 9;119(6):1428-39. doi: 10.1182/blood-2011-07-366781. Epub 2011 Dec 19. PMID: 22184407
23. Purine metabolism, immune reconstitution, and abdominal adipose tumor after gene therapy for adenosine deaminase deficiency. Grunebaum E, Chung CT, Dadi H, Kim P, **Brigida I**, Ferrua F, Cicalese MP, Aiuti A, Roifman CM. *J Allergy Clin Immunol*. 2011 Jun;127(6):1417-9.e3. doi: 10.1016/j.jaci.2011.04.014. Epub 2011 Apr 29. No abstract available. PMID: 21531016
24. In vivo T-cell dynamics during immune reconstitution after hematopoietic stem cell gene therapy in adenosine deaminase severe combined immune deficiency. Selleri S, **Brigida I**, Casiraghi M, Scaramuzza S, Cappelli B, Cassani B, Ferrua F, Aker M, Slavin S, Scarselli A, Cancrini C, Marktel S, Grazia Roncarolo M, Aiuti A. *J Allergy Clin Immunol*. 2011 Jun;127(6):1368-75.e8. doi: 10.1016/j.jaci.2011.03.004. Epub 2011 Apr 7. PMID: 21477850
25. Integration profile of retroviral vector in gene therapy treated patients is cell-specific according to gene expression and chromatin conformation of target cell. Biasco L, Ambrosi A, Pellin D, Bartholomae C, **Brigida I**, Roncarolo MG, Di Serio C, von Kalle C, Schmidt M, Aiuti A. *EMBO Mol Med*. 2011 Feb;3(2):89-101. doi: 10.1002/emmm.201000108. Epub 2011 Jan 17. PMID: 21243617
26. Update on gene therapy for adenosine deaminase-deficient severe combined immunodeficiency. Ferrua F, Brigida I, Aiuti A. *Curr Opin Allergy Clin Immunol*. 2010 Dec;10(6):551-6. doi: 10.1097/ACI.0b013e32833fea85. Review. PMID: 20966749
27. Role of reduced intensity conditioning in T-cell and B-cell immune reconstitution after HLA-identical bone marrow transplantation in ADA-SCID. Cancrini C, Ferrua F, Scarselli A, **Brigida I**, Romiti ML, Barera G, Finocchi A, Roncarolo MG, Caniglia M, Aiuti A. *Haematologica*. 2010 Oct;95(10):1778-82. doi: 10.3324/haematol.2010.025098. Epub 2010 May 11. PMID: 20460637
28. Hematopoietic stem cell gene therapy for adenosine deaminase deficient-SCID. Aiuti A, **Brigida I**, Ferrua F, Cappelli B, Chiesa R, Marktel S, Roncarolo MG. *Immunol Res*. 2009;44(1-3):150-9. doi: 10.1007/s12026-009-8107-8. PMID: 19224139
29. Gene therapy for immunodeficiency due to adenosine deaminase deficiency. 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, Duppenhaler A, Notarangelo L, Wintergerst U, Buckley RH, Bregni M, Marktel S, Valsecchi MG, Rossi P, Ciceri F, Miniero R, Bordignon C, Roncarolo MG. *N Engl J Med*. 2009 Jan 29;360(5):447-58. doi: 10.1056/NEJMoa0805817. PMID: 19179314

Books:

Recent advances in gene therapy for primary immunodeficiencies.

M.P. Cicalese, F. Barzaghi, **I. Brigida**, M.C. Castiello, G. Ottaviano, R. Bacchetta, A. Aiuti, M.G. Roncarolo. In Hematology Education: the education program for the annual congress of the European Hematology Association 2014;8(1)

Immune reconstitution after gene therapy for adenosine deaminase severe combined immunodeficiency (ADA-SCID).

I. Brigida and A. Aiuti

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List of published abstracts

T cell defects in patients with *arpc1b* germline mutations account for combined immunodeficiency. Immacolata Brigida, Matteo Zoccolillo, Maria Pia Cicalese, Federica Barzaghi, Luca Pavesi, Serena Scala, Carmen Oleaga Quintas, Jesus A. Alvarez, Lucia Sereni, Stefania Giannelli, Claudia Sartirana, Francesca Dionisio, Laurene Pfajfer, Marta Benavides-Nieto, Luca Basso-Ricci, Paola Capasso, Benedetta Mazzi, Nufar Marcus, Yu Nee Lee, Raz Somech, Massimo Degano, Giuseppe Raiola, Roberta Caorsi, Paolo Picco, Marcela Moncada Velez, Aziz Bousfiha, Thomas Issekutz, Andrew Issekutz, Bertrand Boisson, Kerry Dobbs, Anna Villa, Angelo Lombardo, Benedicte Neven, Despina Moshous, Jean-Laurent Casanova, Jose Luis Franco, Loïc Dupre, Luigi D Notarangelo, Cristina Scielzo, Stefano Volpi, Jacinta Bustamante, Marco Gattorno and Alessandro Aiuti. (Oral presentation at ESID meeting 2018)

Gene therapy for adenosine deaminase 2 deficiency. **I. Brigida**, M. Zoccolillo, C. Sartirana, Giulia Milardi, R.J. Hernandez, S. Scala, L. Basso-Ricci, F. Barzaghi, M. P. Cicalese, A. Mortellaro and A. Aiuti. (Selected poster for Oral presentation at ESGCT meeting 2018)

Targeted exome sequencing for primary immune deficiencies leads to identification of ARPC1B as the cause of a novel combined immune deficiency.

I. Brigida, M.P. Cicalese, M. Zoccolillo, F. Barzaghi, G. Di Matteo, S. Giannelli, C. Sartirana, D. Lazarevic, D. Cittaro, L. Pavesi, L. Sereni, P. Capasso, M. Degano, A. Villa, A. Lombardo, C. Scielzo, C. Cancrini, L.D. Notarangelo, S. Volpi, M. Gattorno, A. Aiuti. (Oral presentation at ESID meeting 2017)

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Long-Term Safety and Efficacy of Retroviral-Mediated Gene Therapy for ADA-SCID.

M.P. Cicalese, F. Ferrua, R. Pajno, F. Barzaghi, M. Frittoli, L. Castagnaro, S. Giannelli, F. Dionisio, **I. Brigida**, A. Tabucchi, F. Carlucci, A. Hogg, K. Singh, A. Campanile, R. Philipson, J. Appleby, M.G. Roncarolo, A. Aiuti. (Journal of Clinical Immunology, Volume 34, p. S311, 2014)

Defects in thymic central tolerance and T cell development contribute to autoimmunity in Adenosine Deaminase (ADA)-deficiency.

Di Lorenzo B, Sauer AV, Bosticardo M, **Brigida I**, Carriglio N, Jofra Hernandez R, Giannelli S, Poliani PL, Hollander GA, Aiuti A. (Journal of Clinical Immunology, Volume 34, p. S442, 2014)

B cell reconstitution after lentiviral vector-mediated gene therapy in Wiskott-Aldrich syndrome patients

Castiello MC, Bosticardo M, Scaramuzza S, Pala F, **Brigida I**, Sereni L, van der Burg M, Ottaviano G, Ferrua F, Naldini L, Aiuti A, Villa A.
(Mol ther, Vol22 (1) 2014)

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(Front. Immunol. Conference Abstract: 15th International Congress of Immunology (ICI), 2013)

Altered B cell development and function in ADA deficiency and their correction after gene therapy.

Brigida I, Sauer AV, Ferrua F, Pistoia V, Giannelli S, Scaramuzza S, Castiello MC, Casiraghi M, Traggiai E, Van der Burg M, Aiuti A. (Journal of Clinical Immunology, Volume 32, Supplement 1, p. 126, 2012)

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Vago L, Oliveira G, Bondanza A, Noviello M, Soldati C, Ghio D, **Brigida I**, Greco R, Lupo Stanghellini MT, Peccatori J, Fracchia S, Del Fiacco M, Traversari C, Aiuti A, Lambiase A, Del Maschio A, Bordignon C, Ciceri F, Bonini C.
(Blood (ASH Annual Meeting Abstracts) 2011 118: Abstract 1968)

The infusion of suicide gene-modified donor T cells after hematopoietic stem cell transplantation prompts thymic renewal in adult patients by an IL7 dependent mechanism

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(ESGCT 2011; Human Gene Therapy 19(1): abstract #264)

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Oliveira G., Vago L., Noviello M., Soldati C., Ghio D., Nicoletti R., **Brigida I.**, Aiuti A., Lupo Stanghellini M.T., Peccatori J., Bondanza A., Fleischhauer K., Bordignon C., Ciceri F., Bonini C.
(ESGCT 2010; Human Gene Therapy 21(10): abstract #O48)

Defective Regulatory T Cells in ADA-/- Mice and ADA-SCID Patients After

Enzyme Replacement Therapy.

Sauer AV, **Brigida I**, Carriglio N, Jofra Hernandez R, Selleri S, Scaramuzza S, Clavenna D, Sanvito F, Schena F, Traggiai E, Poliani L, Aiuti A.
(Clinical Immunology, Volume 135, Issue 2, p.284, 2010)

Study of peripheral tolerance in ADA SCID patients after different treatments.

Brigida I, Sauer AV, Selleri S, Scaramuzza S, Ripamonti A, Casiraghi M, Ferrua F, Olek S, Roncarolo MG, Aiuti A.
(Journal of Immunology, Volume 184, S143.36, 2010)

Thymic Renewal and Anti-Leukemic Effect in Adults after Haploidentical Transplantation and Suicide Gene Therapy

Vago L., Oliveira G., Noviello M., Soldati C., Ghio D., Nicoletti R., **Brigida I.**, Aiuti A., Lupo Stanghellini M.T., Peccatori J., Bondanza A., Fleischhauer K., Bordignon C., Ciceri F., Bonini C.
(ASGT 2010; Molecular Therapy 18 (1): abstract #295)

Expression Profile and Epigenetic Landscape Influence in a Cell-Specific Fashion Integration Site Selection and In Vivo Distribution of MLV-Vector in Patients

Biasco L., Ambrosi A., Pellin D., Bartholomae C., **Brigida I.**, Roncarolo M.G., Di Serio C., Von Kalle C., Schmidt M., Aiuti A.
(ASGT 2010; Molecular Therapy 18 (1): abstract #345)

A glimpse into the in vivo dynamics during immune reconstitution in ADA-SCID patients after gene therapy treatment

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(Combined Meeting of the ESGCT, GSZ, DG-GT and ISC 2009, Human Gene Therapy 20(11): abstract #P65)

Comparative Study of Retroviral Insertions in ADA-SCID Patients Treated with PBL-GT and HSC-GT Unveils a Cell Specific Integration Profile

Biasco L, **Brigida I**, Cassani B, Lo Perfido M, Ambrosi A, Bartholomä C, Schmidt M, von Kalle C, Roncarolo MG, Aiuti A.
(ASGT 2009; Molecular Therapy 17(1):S143 abstract #366)

Immune reconstitution in ADA-SCID patients treated with hematopoietic stem cell gene therapy

Brigida I, Cassani B, Ferrua F, Scaramuzza S, Selleri S, Casiraghi M, Callegaro L, Frugnoli I, Biral E, Chiesa R, Marktel S, Roncarolo MG, Aiuti A.
(Clinical and Experimental Immunology 2008, 154 (S1), OIII-3)

Reconstitution of thymic function after gene therapy for ADA-SCID: preliminary observations by imaging and immunological studies

Ferrua F, **Brigida I**, Cassani B, Casiraghi M, De Iorgi V, Paesano PL, Roncarolo MG, Aiuti A.
(Clinical and Experimental Immunology 2008, 154 (S1), ED6)

Cells specific integration profile with no in vivo skewing in mature T cells following PBL gene therapy for ADA-SCID

Biasco L, Cassani B, **Brigida I**, Roncarolo MG, Aiuti A.
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Vector integration analysis in mature T cells following PBL gene therapy in

ADA-SCID reveals a cell-type specific insertion profile

Biasco L, Cassani B, Mirolo M, Andolfi G, **Brigida I**, Recchia A, Mavilio F, Roncarolo MG, Bordignon C and Aiuti A.

(ASGT 2007, Molecular Therapy 15(1):S90 abstract #238)

PARTICIPATION TO LECTURE COURSES AND SCIENTIFIC MEETINGS:

31/3-3/4/2019 Meeting of the ISSAID (Genova).

24-27/10/2018 Meeting of the European society for immunodeficiencies (ESID, Lisbon).

15-20/10/2018 Meeting of the European society for gene and cell therapy (ESGCT, Lausanne).

10-14/09/2017 KICK OFF meeting of the European society for immunodeficiencies (ESID, Edinburgh).

21-25/09/2016 XVIIth meeting of the European society for immunodeficiencies (ESID, Barcelona).

30/09/15: IEWP Newborn screening meeting, London (UK)

14-15/09/15: Aieop in Lab, oral communication. Naples, Italy.

11/6/15: Preparation, handling and storage of CV and training records; Data recording. GLP seminar series, Milan

4/06/15: SOP management and Templates, Forms, TS preparation, revision and implementation. GLP seminar series, Milan

20/05/15: GLP principles. GLP seminar series, Milan

29/10-1/11/14: XVIth meeting of the European society for immunodeficiencies (ESID, Prague).

24-4-2014 participation to workshop on New-born screening (Amsterdam, the Netherlands)

21-03-2014 Participation to workshop on Next Generation Sequencing (Amsterdam, the Netherlands)

22-26/08/13: XVth International Congress of Immunology (ICI, Milan) [Poster presentation: Altered B cell development and functions in Adenosine Deaminase deficient patients]

17-19/06/13: 2nd Workshop on Diagnostics of Immunodeficiencies (ESID, Freiburg). oral presentation.

5-6/11/12: Implementing Good Clinical Laboratory Practice training course (BARQA training course)

3-6/10/12: XVth meeting of the European society for immunodeficiencies (ESID, Florence). [Poster presentation: Altered B cell development and function in ADA deficiency and their correction after gene therapy].

13-16/5/12: ESID Junior Workshop "Methods in Primary Immunodeficiency" oral presentation: Altered B cell development and function in ADA-SCID patients and their correction after gene therapy.

6-9/10/2010: XIVth meeting of the European society for immunodeficiencies (ESID, Istanbul) [poster presentation: B cell reconstitution in ADA-SCID patients after gene

or enzyme replacement therapy]

7-11/05/2010: Immunology 010 (Baltimore, Maryland) [poster presentation: Study of peripheral tolerance in ADA SCID patients after different treatments]

11-12/01/2010: ESID Junior Workshop (Florence, Italy) [oral presentation: Study of peripheral tolerance in ADA-SCID patients treated with enzyme replacement of gene therapy]

4-9/10/2009: 4th International Conference on Autoimmunity: Mechanisms and Novel Treatments (Crete, Greece) [poster: Analysis of peripheral tolerance in ADA SCID patients treated with enzyme replacement or gene therapy, abstract#44]

19-21/02/2009: HSR SCIENTIFIC RETREAT (Stresa, Italy) [posters: Insertion sites comparison on T cells derived from transduced lymphocytes or stem cell unveils a cell-specific integration profile of retroviral vectors abstract #159C; Autoimmunity in ADA deficiency- New insights from human and mouse studies abstract #143T]

16-19/10/2008 XIII Meeting of the European Society of Immunodeficiencies ('s-Hertogenbosch, the Netherlands) [oral presentations: Immune reconstitution in ADA-SCID patients treated with hematopoietic stem cell gene therapy; Reconstitution of thymic function after gene therapy for ADA-SCID: preliminary observations by imaging and immunological studies]

20-21/09/2007 HSR-TIGET Retreat (HSR, Milano, Italy)

28/2/07: Multiparameter Flow and Compensation Course (Milano, Italy)

11-13/02/2007: HSR SCIENTIFIC RETREAT (Bardolino, Italy) [poster: Long-Term Safety and Efficacy of Stem Cell Gene Therapy for ADA-SCID abstract #32; Role of altered purine metabolism in immunological defects of ADA-SCID pag.145]

08/01/2007: Course "Analisi con FACSDivaSoftware" (Buccinasco, Italy)

19-12-2006: seminar "Real Time PCR: aggiornamento e troubleshooting", (HSR, Milano, Italy)

18-22/9/06: PhD Lecture Course "Signal Transduction in T and B cell activation, development and differentiation" (Milano, Italy)

22-24/6/06: HSR-TIGET Retreat (Sestri Levante, Italy)

20-21/04/2006: congress "Attualità in Ematologia 2006 – Il trapianto di cellule staminali" (Casa sollievo della Sofferenza, Istituto di Ricovero e Cura a carattere scientifico - Opera di San Pio da Pietrelcina, San Giovanni Rotondo, Italy)

12/05/05: seminar "Fast seminar tour - protocolli rapidi per l'estrazione di acidi nucleici per PCR e PCR Real Time", (facoltà di Medicina e Chirurgia dell'Università degli Studi di Modena e Reggio Emilia; Modena, Italy).