The Faculty of Medicine of Harvard University

Curriculum Vitae

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Education:

09/2002 - 09/2005	B.Sc. Summa cum laude	Medical Biotechnology Fulvio Mavilio, PhD	University of Modena and Reggio Emilia Modena, Italy
09/2005 - 03/2008	M.Sc. Summa cum laude	Molecular and Cellular Medical Biotechnology Luigi Naldini, MD, PhD	"Vita Salute San Raffaele" University Milan, Italy
11/2009 - 05/2013	Ph.D.	Molecular Medicine - Curriculum of Applied Immunology Luigi Naldini, MD, PhD	"Vita Salute San Raffaele" University Milan, Italy

Postdoctoral Training:

09/2004 - 01/2005	Intern	Molecular Oncology Prof. Bruno Calabretta	University of Modena and Reggio Emilia, Dept. of Biomedical Sciences, Sect. of General Pathology Modena, Italy
02/2005 - 09/2005	Intern	Molecular Biology and Gene Therapy Prof. Fulvio Mavilio	University of Modena and Reggio Emilia, Dept. of Biomedical Sciences, Sect. of Biological Chemistry Modena, Italy
11/2005 - 03/2008	Undergraduate student	Molecular and Cell Biology of Gene Transfer Prof. Luigi Naldini	San Raffaele Telethon Institute for Gene Therapy (HSR-TIGET) Milan, Italy

04/2008 - 01/2009	Research Fellow	Molecular and Cell Biology of Gene Transfer Prof. Luigi Naldini	San Raffaele Telethon Institute for Gene Therapy Milan, Italy
02/2009 - 05/2013	PhD intern	Gene Editing for Adoptive Immunotherapy Prof. Luigi Naldini / Prof. Chiara Bonini	San Raffaele Telethon Institute for Gene Therapy Milan, Italy
06/2013 - 06/2016	Postdoctoral Fellow	Gene Editing of Hematopoietic Stem/Progenitor cells Prof. Luigi Naldini	San Raffaele Telethon Institute for Gene Therapy Milan, Italy

Faculty Academic Appointments:

07/2016 - 06/2019	Director of PhD Study	Medicine	Vita Salute San Raffaele University
07/2019 - Present	Assistant Professor of Pediatrics	Pediatrics	Harvard Medical School

Appointments at Hospitals/Affiliated Institutions:

2016 - 2019	Project Leader	San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)	San Raffaele Scientific Institute
2019 - Present	Faculty member	Hematology/Oncology	Boston Children's Hospital
2019 - Present	Faculty member	Pediatric Oncology	Dana-Farber Cancer Institute
2019 - Present	Assistant Professor	Pediatrics	Harvard Medical School
2020 - Present	Affiliate Faculty	Harvard Stem Cell Institute	Harvard Stem Cell Institute
2021 - Present	Associate Member	Cancer Program	Broad Institute of Harvard and MIT

Other Professional Positions:

2018 - 2019	Scientific consultant	Janssen R&D (pharma R&D organization of Johnson & Johnson)	Up to 30 hours per year
2019	Scientific consultant	San Raffaele Telethon Institute for	1.1 months per year

		Gene Therapy (SR-Tiget)	
2020	Expert consultant	ALGM on behalf of Cellectis	Up to 3 days per year
2020	Founder quota holder	GeneSpire	0
2020 - 2022	Scientific consultant	Dorian Therapeutics	Up to 30 hours per year
2022 - Present	Scientific consultant	Patient Square Capital, L.P.	6 hours per year
2023 - Present	Member of the Scientific Advisory Board	Vor Biosciences	Up to 30 hours per year
2024 - Present	Member of the Scientific Advisory Board	Ensoma, Inc.	Up to 20 hours per year

Major Administrative Leadership Positions:

Local

2021 - Present	Co-organizer of the weekly Floor Meeting of the Division	Boston Children's Hospital Hematology / Oncology

Committee Service:

Local

2013	M.Sc. Thesis defense Molecular and Cellular Medical Biotechnology	Vita Salute San Raffaele University
		Internal Member of the Examiners Panel for Giulia Schiroli
2015	B.Sc. Thesis defense Medical and Pharmaceutical Biotechnology	Vita Salute San Raffaele University
		Internal Member of the Examiners Panel for Samuele Ferrari
2016	M.Sc. Thesis defense Molecular and Cellular Medical Biotechnology	Vita Salute San Raffaele University
		External Member of the Examiners Panel for Mirko Luoni

2016	Ph.D. Examination Ph.D. Program in Translational and Molecular Medicine (Dimet)	Milano Bicocca University
		External Member of the Examination Committee
2017	M.Sc. Thesis defense Molecular and Cellular Medical Biotechnology	Vita Salute San Raffaele University
		Internal Member of the Examiners Panel for Samuele Ferrari and Valentina Vavassori
2019	M.Sc. Thesis defense Molecular and Cellular Medical Biotechnology	Vita Salute San Raffaele University
		External Member of the Examiners Panel for Camilla Sirini
2019	Ph.D. Selection Committee Ph.D. Program in Translational and Molecular Medicine (Dimet)	Milano Bicocca University
		External Member of the Selection Committee
2020 - 2022	Boston Children’s Hospital - Astellas Joint Steering Committee Meeting	Boston Children's Hospital
		Reviewer of proposals for the Astellas award
	2021 - 2022	Scientific supervision of 2 sponsored research agreements

International

2015	Ph.D. Thesis defense committee	Universidad Autónoma de Madrid
		External Member of the Examiners Panel for Begoña Diez Cabezas
2017	EMA expert meeting on genome editing technologies used in medicinal product	European Medicines Agency (EMA), London, UK.
		Invited presentation as expert on hematopoietic stem cell genome editing
2018	Ph.D. Thesis defense committee	Universidad Autónoma de Madrid

		External Examiners for Francisco Roman Rodriguez
2019 - Present	Teaching Body of the DIMET PhD Program	University Milano-Bicocca
		External Member of the Translational and Molecular Medicine (DIMET) Ph.D. Program
2020 - Present	Abstract Reviewer	International Society for Stem Cell Research (ISSCR)
		Abstract Reviewer
2021	"Accelerating Innovations for Sickle Cell Disease with Real-World Evidence"	ASH Research Collaborative
		Member of the discussion panel; Topic Area: Robustness and Persistence
2023 - Present	Organizing Committee	Transatlantic Gene Therapy Consortium
		Member of the organizing Committee of the Stem Cell Clonality and Genome Stability Retreat
2024 - 2026	Ph.D. Thesis Committee	University Hospital of Zürich, University of Zürich
		Member of the Ph.D. Thesis Committee for Dr.Morgane Chambovey
2024 - Present	ALSF Young Investigator Grant - Study session	Alex's Lemonade Stand Foundation
		Reviewer for the 2024 YI grant proposal review cycle
2024 - Present	GOSH Charity Programme Grant - Expert Advisory Group	Great Ormond Street Hospital Children's (GOSH) Charity
		Member of the Expert Advisory Group
2024 - Present	Genome Editing - Scientific Committee	American Society of Gene and Cell Therapy (ASGCT)
		ASGCT Committee Member. Tasks will include developing recommendations for the ASGCT Board of Directors relating to committee focus; providing input into ASGCT program development for future

		annual meetings; and reviewing items for the Society's website.
2024 - Present	Genome and Epigenome Editing - Scientific Committee	Società Italiana di Terapia Genica e Cellulare (SITGEC) SITGEC Committee Member. Tasks will include selecting the speakers and abstracts for the annual conference.
2024 - Present	Immunology and Blood Cell Development (IBCD) - Peer review committee	American Cancer Society Reviewer for the Spring 2024 grant proposal review cycle
2024 - Present	Integrative Vectors - Scientific Committee	European Society of Gene and Cell Therapy (ESGT) ESGCT Committee Member. Tasks will include developing recommendations for the ESGCT Board of Directors relating to committee focus, providing input into ESGCT program development for future annual meetings, and reviewing Abstracts submitted for presentation at the annual meeting.

Professional Societies

2009 - Present	European Society of Gene and Cell Therapy	Associate Member (2009-2018) Full Member (2019-2021)
2009 - Present	The American Society of Gene and Cell Therapy	Associate Member (2009-2018) Transitional Member (2019-2021) Full Member (2022-)
2010 - Present	American Association for Cancer Research (AACR)	Active Member
2018 - Present	International Society for Stem Cell Research (ISSCR)	Full Member
2019 - Present	American Society of Hematology	Associate Member
2022 - Present	American Society for Transplantation and cellular Therapy (ASTCT)	

	Full Member
2024 - Present	Society for Immunotherapy of Cancer (SITC)
	Active Member
2024 - Present	Società Italiana di Terapia Genica e Cellulare (SITGEC)
	Active Member

Grant Review Activities:

2009	Reviewer for International Grant Applications	Dystrophic Epidermolysis Bullosa Research Association (DEBRA) International
		Ad hoc reviewer (2 grant applications)
2009 - 2021	Reviewer for International Grant Applications	French National Research Agency, AgenceNationale de la Recherche (ANR)
		Ad hoc reviewer (3 grant applications)
2020 - 2021	Reviewer of proposals for the Astellas award	Boston Children's Hospital – Astellas Pharma
		Ad hoc reviewer (6 grant applications)
2021	Reviewer for International Grant Applications	Children Cancer Research Fund (CCRF)
		Ad hoc reviewer (5 grant applications)
2021 - 2024	Reviewer for an Advanced ERC Grant proposal	European Research Council
		Ad hoc reviewer (1 grant application per year)
2024	Expert Advisory Group	Great Ormond Street Hospital (GOSH) Charity
		Ad hoc reviewer

Editorial Activities:

- **Ad hoc Reviewer**

Blood
Blood Advanced
Clinical and Translational Medicine

Current Stem Cell Research & Therapy
Frontiers in Genome Editing
Frontiers in Molecular Medicine
Gene Therapy
Molecular Therapy
Molecular Therapy - Methods & Clinical Development
Nature Communications
Nature Reviews Immunology
Scientific Reports

- **Other Editorial Roles**

2019 - Present	Associate Editor	Frontiers in Genome Editing Journal
2020	Co-coordinator of a Research Topic(eBook): Mutation Specific Gene Editing for Blood Disorders	Frontiers in Genome Editing Journal (section: Genome Editing in Blood Disorders)

Honors and Prizes:

2010	Leslie Fairbairn Runner Up Award	Persisting Transgenesis (PERSIST) European Research Consortium	Best presentation from young scientist at the Second PERSIST Meeting
2012	Van Bekkum Award	European Society for Blood and Marrow Transplantation (EBMT)	the best abstract submitted to the physician's program at the EBMT annual congress
2012	Jon Van Rood Award	European Federation for Immunogenetics (EFI)	Best Abstract submitted to the EFI annual congress
2014	Meritorious Travel Grant Award	American Society of Gene and Cell Therapy (ASGCT)	Best Abstract submitted to the ASGCT meeting (Awardee in the years: 2010, 2012, 2013 and 2014)
2014	Cecilia Cioffrese Award	Fondazione Carlo Erba	the best research followed by Italian young graduates on the field of cancer
2014	Meritorious Travel Grant Award	European Society of Gene and Cell Therapy (ESGCT)	Best Abstract submitted to the ESGCT meeting (Awardee in the years: 2011, 2013 and 2014)

2014	NicolòCopernico Award for Biomedical Science	the Promoting Committee of the Awards «Giulio Natta and NicolòCopernico for the Scientific Research and Technology Innovation of Ferrara	Best publication from an Italian young researcher in a Scientific Journal with an impact factor over 10
2016	2016 Young Investigator Award	European Society of Gene and Cell Therapy (ESGCT)	Recognition for the valuable contribution in the field of cell & gene therapy
2019 - 2023	Excellence in Research Awards	American Society of Gene and Cell Therapy (ASGCT)	Best Abstracts of the ASGCT meeting (Mentor of the winning Awardees in 2019, 2020, 2021, 2022 and 2023)
2020	Merit Abstract Award	International Society for Stem Cell Research (ISSCR)	Best Abstracts of the ISSCR meeting (Mentor of the winning Awardee)
2021	Emerging Scientist Award	Children's Cancer Research Fund (CCRF)	Support for the project "Empowering specificity of AML immunotherapy by HSC engineering"
2021	Pilot Research Award	Research Executive council, Boston Children's Hospital	Support for the project "Generation of "stealth" tyrosine kinases for an immunotherapy resistant hematopoiesis"
2023	Translation to CURE Award (T2C)	CURE Childhood Cancer	Support for the project "Empowering pediatric immunotherapies by HSC engineering"
2023	Scholar Award aabb Foundation	Advancement of Blood & Biotherapies (aabb) Foundation	Successfully completed research project founded by the aabb Foundation
2024	Outstanding New Investigator Award	American Society of Gene and Cell Therapy (ASGCT)	Recognition for the valuable contribution in the field of cell & gene therapy

Report of Funded and Unfunded Projects

Past

2013 - 2016	Towards clinical translation of new gene targeting technologies for correcting inherited mutations and empowering adoptive immunotherapy of cancer

	European Union FP7-HEALTH ID:601958- SUPERSIST Key Personnel (PI: Luigi Naldini)
2015 - 2020	Targeted genome editing of the CD40LG gene for the treatment of X-linked hyper-IgM immunodeficiency ItalianMinistry of Health Giovani Ricercatori GR-2013-02358956 PI ($450,000)
2016 - 2018	Exploiting CRISPR/Cas technology for gene editing in T cell and HSPC EDITAS Medicine Sponsored Research Agreement Co-PI (PI: Luigi Naldini) ($385,000)
2016 - 2021	Towards clinical testing of HSC gene editing in SCID-X1 Telethon Foundation SR-Tiget Core Grant Project E1 PI
2016 - 2021	Gene correction of CD40LG gene in T cells and HSPC for the treatment of X-linked hyper-IgM immunodeficiency Telethon Foundation SR-Tiget Core Grant Project E3 PI (Co-PI: Anna Villa) ($205,000)
2018 - 2021	Gene Edited Lymphoid Progenitors for Adoptive Transfer as Treatment of Primary Immunodeficiency Italian Ministry of Health ERA-Net Grant for Research on Rare Diseases Project Leader (PI: Luigi Naldini)
2018 - 2021	Targeted gene editing in Hematopoietic Stem Cells for the correction of SCID-X1 and RAG1 Immunodeficiencies Italian Ministry of Health Italian researcher abroad PE-2016-02363691 Project Leader (PI: Luigi Naldini)
2018 - 2021	Exploiting cutting edge technologies to hunt T cell receptor for TCR gene editing of acute myeloid leukemia ItalianMinistry of Health, Giovani Ricercatori GR-2016-02364847 Multiple-PI (PI: Eliana Ruggero) ($100,000)
2019 - 2021	Advanced genetic engineering to study and treat monogenic diseases Italian Ministry of Instruction, University and Research PRIN 2017 – (Research Projects of Relevant National Interest) Project Leader (PI: Luigi Naldini)
2019 - 2023	Unlocking Precision Gene Therapy European Union H2020 SC1-BHC-09-2018 - UPGRADE Project Leader (PI: Luigi Naldini)
2019 - 2024	Start-Up Funding Boston Children's Hospital Start-up Funding PI ($2,460,000)
2020 - 2021	Empowering specificity of AML immunotherapies by HSC engineering Children’s Cancer Research Fund Emerging Scientist Award PI ($100,000)
2020 - 2021	Fixing HSC lymphoid differentiation by in situ correction of RAG1 mutations Immune Deficiency Foundation (IDF) IDF Research Grant Program PI ($50,000)

2020 - 2022	RAG1 deficiency: From pathophysiology to precise gene correction NIH-NIAD Bench-to-Bedside Program Co-Investigator (PI: Notarangelo) ($37,000)
2020 - 2023 NCE	Targeted gene addition at a relevant microglia locus for the treatment of inherited neuro metabolic diseases Orchard Therapeutics Sponsored Research Agreement Co-Investigator (PI: Biffi) ($75,000)
2020 - 2023	Gene editing for adoptive immunotherapy of breast cancer Takeda Oncology Sponsored Research Agreement PI ($973,005)
2021 - 2022	Generation of "stealth" tyrosine kinase receptors for an immunotherapy resistant hematopoiesis Research Executive council - Boston Children's Hospital Pilot Research Grant PI ($50,000)
2021 - 2022	Engineering immunotherapy resistant hematopoiesis to treat high-risk acute myeloid leukemia National Blood Foundation (NBF) Research Grant PI ($75,000)
2021 - 2022	Generation of "stealth" antigens for an immunotherapy resistant hematopoiesis Leukemia Research Foundation New Investigator Blood Cancer Research Grant PI ($100,000)
2022	Request for Equipment: RNA chromatography column Equipment and Core Resource Allocation Committee (ECRAC) - Boston Children's Hospital Equipment Funding Opportunity Cycle 12 PI ($18,000)
2022	Hematopoietic stem cell gene therapy for infantile neuronal ceroid lipofuscinosis NIH - NICHD RO1 HD095935-05 Co-Investigator (PI: David A. Williams) ($50,000)

Current

2021 - 2026	Development, Optimization and Preclinical Modeling of Hematopoietic Stem Cell Gene Editing for the Treatment of RAG1 Immunodeficiency NIH - NIAID RO1 RO1 AI155796-01A1 PI ($1,250,000)
06/2023 - 06/2025	Empowering pediatric immunotherapies by HSC engineering CURE Childhood Cancer Translation to CURE Award (T2C) 1070087 PI ($300,000)
07/2023 - 06/2025	Immunotherapy-resistant hematopoiesis to treat acute myeloid leukemia American Cancer Society Discovery Boost Grant DBG-23-1039598-01-IBCD PI ($300,000)
07/2023 - 06/2026	Towards clinical testing of epitope editing to enable novel adoptive immunotherapies Leukemia & Lymphoma Society (LLS) Translational Research Program 6669-24 PI ($750,000)

08/2023 - 07/2028	Chemotherapy-free cure of hemoglobin disorders through base editing NIH - NHLBI RO1 HL170629 Multiple-PI (PI: Daniel E Bauer) ($2,500,000)
01/2024 - 01/2026	Empowering specificity of AML immunotherapies by HSC engineering Alex Lemonade's Stand Foundation Research Catalyst Grant # 1266935 PI ($250,000)
07/2024 - 06/2029	Multiplex Epitope Editing to Enable Novel Immunotherapies for Acute Myeloid Leukemia NIH / NCI RO1 R01 CA286036 PI ($2,000,000)
09/2024 - 08/2027	Base Editing to Improve Conditioning and Transplant of Bone Marrow Failure Patients Department of Defense (DOD) DoD Bone Marrow Failure Investigator-Initiated Research Award BM230066 PI ($675,000)
01/2025 - 12/2026	B cell receptor gene eding for a combined humoral and cellular adopve immunotherapy American Cancer Society (ACS) Discovery Boost Grant PI ($300,000)
01/2025 - 12/2026	Advanced Genetic Engineering to Unravel Tumor-Specific B Cell Responses NIH / NCI R21 R21CA296527 PI ($275,000)
01/2025 - 12/2026	Enhancing Epitope Editing for Enabling Multiplex Tumor-Specific Immunotherapy SWIM Across America (SAA) Gene Editing Innovation Grant PI ($450,000)
2025 - 2026	Redirecting B cell specificity to improve immunotherapy of breast cancer Breast Cancer Alliance 2025 Exceptional Project Award Grant Agreement PI ($100,000)

Projects Submitted for Funding

Pending	Building the Next Generation Gene Therapy for X-linked Adrenoleukodystrophy NIH / NICHD RO1 Role: MPI (PI: David A. Williams) ($425,000) Impact score: 39; Percentile: 28

Training Grants and Mentored Trainee Grants

2017 - 2021	Enrichment and Clonal Tracking of Gene Edited Hematopoietic Stem/Progenitor Cells Italian Ministry of Instruction, University and Research Ph.D. Fellowship Director of Studies of Samuele Ferrari, M.Sc.
2019 - 2020	Generation of long-living engineered cells for adoptive cancer immunotherapy American-Italian Cancer Foundation (AICF) Post-Doctoral Research Fellowship Post-doctoral fellowship Mentor of Lucia Sereni, Ph.D.

2020 - 2022	Increase safety and efficacy of cancer adoptive immunotherapy American-Italian Cancer Foundation (AICF) Post-Doctoral Research Fellowship Post-doctoral fellowship Mentor of Gabriele Casirati, M.D.
2021	Hematopoietic Stem Cell Gene Editing to Improve Safety and Efficacy of Cancer Adoptive Immunotherapy German Academic Exchange Service (DAAD) PROMOS scholarship Mentor of Iratxe Ugarte Zabala, B.Sc.
2021	Improving targeted gene editing in hematopoietic stem cells for clinical translation Central Department of Missions – Ministry of Higher Education - Egypt Scientific Mission Mentor of Mohammed Salah Mahmoud, Ph.D.
2021	Summer Fellowship Program Armenise Harvard Foundation Undergraduate Fellowship Mentor of Silvia Rizzato, B.Sc.
2022	Gene editing to improve safety and efficacy of cancer adoptive immunotherapy European Union ERASMUS+ Mentor of Brenda Besemer, B.Sc.
2022	Fellowship Program University of Trento Short-term Fellowship Mentor of Arianna Martinuzzi, B.Sc.
2022 - 2024	Epitope Engineered Hematopoiesis to Enable CAR-T Cell Immunotherapy for Multiple Myeloma American-Italian Cancer Foundation (AICF) Post-Doctoral Research Fellowship Post-doctoral fellowship Mentor of Andrea Cosentino, M.D.
2023	Dissecting the Role of Tumor-Specific B cells in Breast Cancer German Academic Exchange Service (DAAD) PROMOS scholarship Mentor of Nicara Parr, B.Sc.
2023	Towards gene therapy for CTLA4 deficiency University College London (UCL) Bogue Fellowship Mentor of Thomas A. Fox, M.D., Ph.D.
2023 - 2024	Novel Base Editors with Single Base Selectivity to Minimize Bystander and Off-target Effects American Society of Gene and cell Therapy Career Development Award Mentor of Gabriele Casirati, M.D., Ph.D.
2023 - 2024	CD244 targeted CAR-T cells for high-risk pediatric leukemias Pedals for Pediatrics Research Grant Mentor of Gabriele Casirati, M.D., Ph.D.
2023 - 2025	Epitope engineered hematopoiesis to enable safer non-genotoxic conditioning American Society for Transplantation and cellular Therapy (ASTCT) New Investigator Award Mentor of Gabriele Casirati, M.D., Ph.D.
2023 - 2025	Epitope-edited HSPCs to enable CD244 immunotherapies for acute leukemias

	PTCTC Jeff Gordon Children's Foundation New Investigator Award Mentor of Gabriele Casirati, M.D., Ph.D.
2024	Harnessing Self-Amplyfing RNA for Gene and Cell Therapy Applications German Academic Exchange Service (DAAD) PROMOS scholarship Mentor of Annika Strauss, B.Sc.
2024 - 2025	Epitope edited Hematopoietic Stem Cells to eliminate on-target/off-tumor toxicity Society for the Immunotherapy of Cancer (SITC) Mallinckrodt Adverse Events in Cancer Immunotherapy Mentor of Gabriele Casirati, M.D., Ph.D.
2025	Epitope Edited Stem Cells to Enable Next-Generation Non-Genotoxic Transplant Protocols Cell Discovery Network (CDN) NextGen Accelerator Grant 2025 Mentor of Gabriele Casirati, M.D., Ph.D.
2025 - 2026	Gene therapy approach for SCID-X1 using non-genotoxic conditioning via epitope editing Clinical Immunology Society (CIS) 2025 Vicki Modell I-CIS Innovation Grant Award Mentor of Enrico Drago, M.D.
2025 - 2027	Overcoming AML Resistance to Targeted Cellular Immunotherapies American Society of Hematology (ASH) ASH Scholar Award Mentor of Gabriele Casirati, M.D., Ph.D.
2025 - 2028	Next-generation CAR-T cell immunotherapies for pediatric tumors Alex's Lemonade Stand Foundation Young Investigator Mentor of Gabriele Casirati, M.D., Ph.D.
2025 - 2028	Epitope Editing to Enable Next-generation Non-genotoxic Conditioning Regimens for Hematopoietic Stem Cell Transplantation Deutsche Knochenmarkspenderdatei (DKMS) John Hansen Research Grant 2025 Mentor of Gabriele Casirati, M.D., Ph.D.

Report of Local Teaching and Training

Teaching of Students in Courses:

2017	Molecular Therapy - Therapy for genetic diseases PhD Students	Telethon Institute of Genetic and Medicine, Naples, Italy 4-hr lecture
2019	Gene Therapy and Ethics M.Sc. Students	Massachusett General Hospital, Boston, MA 2-hr lecture
2019	Spring School PhD Students	European Society of Gene and Cell Therapy, Naples, Italy 1-hr lecture
2020	Precision Medicine in the Era of Targeted Genome Editing	Ph.D. Program in Translational and Molecular Medicine (Dimet),

	PhD Students	Milano-Bicocca University, Milan, Italy Organization of a 2-day PhD Course
2022 - 2025	Cell Therapy Course M.Sc. and M.D. students	School of Medicine - University of Pittsburgh, Pittsburgh, PA One 90-minute lecture per year
2024	Cancer Immunotherapy M.Sc. and M.D. Students	Harvard Medical School, Boston, MA 2-hr lecture

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs):

2022 - 2024	Data Blitz Hematology/Oncology Fellows	Boston Children's Hospital, Boston, MA One lecture per year

Research Supervisory and Training Responsibilities:

2016 - 2019	Supervisor M.Sc. and M.D. students (1-2 per year)	Vita Salute San Raffaele University, Milan, Italy Two-hour individual 1:1 meeting each week; Thesis preparation
2016 - 2019	Director of PhD studies Ph.D. students (2-3 per year)	Vita Salute San Raffaele University, Milan, Italy Two-hour individual 1:1 meeting each week; Thesis preparation
2016 - 2019	Research supervision and training Postdoctoral Fellows (1 per year)	San Raffaele Telethon Institute for Gene Therapy, Milan, Italy Two-hour individual 1:1 meeting each week
2019 - Present	Research supervision and training Postdoctoral Fellows (2-3 per year)	Boston Children's Hospital, Boston, MA Two-hour lab meeting and one hour individual 1:1 meeting each week
2019 - Present	Director of PhD studies Ph.D. students (2-3 per year)	Milan-Bicocca University, Milan, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2021 - Present	External Supervisor M.Sc. students (1-2 per year)	German Cancer Research Center (DKFZ), Heidelberg, Germany Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2021 - Present	External Supervisor M.Sc. students (1-2 per year)	Hannover Medical School, Hannover, Germany

		Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2022 - Present	Member of Faculty Advisor Committee Faculty Advisor Committee for Cedric Louvet, Ph.D., Instructor in Medicine	Dana-Farber Cancer Institute, Boston, MA One 90-minute FAC meeting and ad hoc 1:1 meeting each year
2024	External Supervisor Resident in Paediatrics	University of Genoa, Genoa, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly
2024	External Supervisor Ph.D. student	University College of London (UCL), London, United Kingdom Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly;
2024 - 2025	External Supervisor Hematology Resident	University of Pavia, Pavia, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2024 - 2025	External Supervisor M.Sc. student	University of Vienna, Vienna, Austria Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2025	External Supervisor Residents in Paediatrics (2 per year)	University of Milano-Bicocca, Milan, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2025	External Supervisor M.Sc. student	Swiss Federal Technology Institute of Lausanne (EPFL), Lausanne, Switzerland Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly
2025	External Supervisor Hematology Resident	Humanitas University, Milan, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation
2025 - 2027	External Supervisor Ph.D. student	University of Genoa, Genoa, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly
2025 - Present	External Supervisor M.Sc. students (2 per year)	University Vita-salute San Rafaele, Milan, Italy Two-hour lab meeting, weekly; one hour individual 1:1 meeting, monthly; Thesis preparation

Other Mentored Trainees and Faculty:

2013 - 2018	Giulia Schiroli, Ph.D. / Senior Scientist, Tessera Therapeutics Career Stage: Post Doctoral Fellow. Mentoring Role: Director of Studies. Accomplishments: Successfully completed master thesis with top grades; Ph.D. studies and first Post-Doctoral studies, and published 2 first-author papers in top scientific journals
2014 - 2020	Samuele Ferrari, Ph.D. / Project Leader, San Raffaele Telethon Institute for Gene Therapy Career Stage: PhD Student. Mentoring Role: Director of Study. Accomplishments: Successfully completed both Bachelor's and Master's thesis with top grades, Ph.D. studies in Molecular Medicine, and published 2 first-author papers in top scientific journals
2016	Mark Hendriks, MS / Coassistent / PhD Student at UMCG Career Stage: Masters Student. Mentoring Role: Research Mentor. Accomplishments: Successfully completed master thesis with top grades
2016 - 2019	Luisa Albano, MS / Senior Lab technician Career Stage: Research Technician. Mentoring Role: Supervisor. Accomplishments: acquired unique expertise in performing complex in vivo procedures and analysis on murine models, received a permanent employment position within the Institute, and is recognized as an author in multiple publications.
2016 - 2020	Aurelien Jacob, PhD / Gene Therapy Scientist and Group Leader, Next Generation Medicines Career Stage: PhD Student. Mentoring Role: Director of Study. Accomplishments: Successfully completed Ph.D. studies in Molecular Medicine and published a first-author paper in a top scientific journal
2016 - 2020	Valentina Vavassori, Ph.D. / Science Communicator Career Stage: PhD Student. Mentoring Role: Director of Study. Accomplishments: Successfully completed master's thesis with top grades, Ph.D. studies in Molecular Medicine, and published a first-author paper in a top scientific journal
2018 - 2020	Martina Fiumara, BS / Ph.D. student, Vita Salute San Raffaele University Career Stage: M.Sc. Student. Mentoring Role: Director of Study. Accomplishments: Successfully completed master thesis with top grades
2018 - 2020	Elisabetta Mercuri, Ph.D. / Scientific Project Coordinator, Robert Koch Institute Career Stage: PhD Student. Mentoring Role: Director of Study. Accomplishments: Successfully completed Ph.D. studies in Molecular Medicine and published a first-author paper in a top scientific journal
2018 - 2020	Lucrezia Bertaggia, M.D. / M.D. student Career Stage: 3rd year MD Student. Mentoring Role: Research Supervisor. Accomplishments: Successfully completed two research internships and acquired basic research skills that will allow her to perform an experimental research Thesis for her MD graduation
2019 - 2020	Giulia Ceglie, MD / Physician, "Bambin Gesù" Children's Research Hospital

	Career Stage: Resident in pediatrics; Harvard trainees. Mentoring Role: Research Supervisor. Accomplishments: Successfully completed her residency in pediatrics with full honor and enrolled in an international PhD program
2019 - Present	Lucia Sereni, PhD / Postdoctoral Fellow, Boston Children's Hospital Career Stage: Postdoctoral fellow; Harvard trainees. Mentoring Role: Supervisor. Accomplishments: Successfully started a new area of investigation and was awarded a Post-Doctoral Research Fellowship from the American-Italian Cancer Foundation (AICF)
2019 - Present	Andrea Bianchi, M.Sc. / Ph.D. Student, Boston Children's Hospital Career Stage: Ph.D. student. Mentoring Role: Supervisor. Accomplishments: Successfully started a new area of investigation on gene editing for cancer immunotherapy and enrolled in an international Ph.D. program in Molecular Medicine
2019 - Present	Gabriele Casirati, MD, Ph.D. / Postdoctoral Fellow, Boston Children's Hospital Career Stage: Postdoctoral Fellow. Mentoring Role: Supervisor. Accomplishments: Successfully started a new area of investigation, published a first-author paper in a top scientific journal, completed his Ph.D. studies, and was awarded several fellowships and junior research grants.
2020 - 2021	Arianna Martinuzzi, B.Sc. / Master Student, University of Trento Career Stage: Undergraduate student. Mentoring Role: Supervisor. Accomplishments: Successfully completed bachelor thesis with top grades and was awarded a short-term fellowship from the University of Trento, Italy
2020 - 2022	Silvia Rizzato, M.Sc. / Ph.D. Student Career Stage: Undergraduate student. Mentoring Role: Supervisor. Accomplishments: Successfully started a new area of investigation on gene editing for cancer immunotherapy and was awarded a short-term fellowship from the University of Trento, Italy
2020 - 2022	Marina Theodorou, PhD / Scientist, TRON Mainz-Clinical Cancer Research Career Stage: Postdoctoral fellow; Harvard trainees. Mentoring Role: Supervisor. Accomplishments: Successfully started a new area of investigation on gene editing for cancer immunotherapy
2021	Iratxe Ugarte Zabala, MSc / Ph.D. Student, CIMA Research Center, Spain Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship with top grades, was awarded a short-term fellowship from the German Academic Exchange Service, and is listed as an author on a publication in a top scientific journal
2021	Vincenzo Cinella, M.Sc. / Research Technician, Dana-Farber Cancer Institute Career Stage: Research Technician. Mentoring Role: Supervisor. Accomplishments: acquired unique expertise in performing complex gene editing experiments and is listed as an author in a research manuscript submitted for publication
2021 - Present	Andrea Cosentino, M.D. / Ph.D. student, Boston Children's Hospital Career Stage: Ph.D. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed hematology residency Thesis, enrolled in an international Ph.D. program in Molecular Medicine, published a paper as second-author in a

	top scientific journal, and was awarded 2 Research Fellowships from the American-Italian Cancer Foundation (AICF)
2021 - Present	Mohammed Salah Mahmoud, Ph.D. / Research Associate, Boston Children's Hospital Career Stage: Research Associate. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship, was awarded a short-term fellowship from the Egyptian Ministry of Higher Education, and is listed as an author on a publication in a top scientific journal
2022	Brenda Besemer, B.Sc. / M.Sc. student, German Cancer Research Center (DKFZ) Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship with top grades, was awarded a short-term fellowship from the European Union
2022 - Present	Marta Freschi, M.Sc. / Ph.D. Student, Boston Children's Hospital Career Stage: Ph.D. student. Mentoring Role: Supervisor. Accomplishments: Successfully started a new area of investigation on gene editing for cancer immunotherapy and enrolled in an international Ph.D. program in Molecular Medicine
2023	Nicara Parr, B.Sc. / M.Sc. Student, Hannover Medical School Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship with top grades, was awarded a short-term fellowship from the German Academic Exchange Service
2023	Thomas A. Fox, M.D., Ph.D. / Postdoctoral fellow, University College London (UCL) Career Stage: Postdoctoral Fellow. Mentoring Role: Host Supervisor. Accomplishments: Successfully completed a research internship and was awarded a short-term fellowship from the University College London (UCL)
2023 - 2024	Jan-Phillipp Gerhards, BSc / M.Sc. Student, Hannover Medical School Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship with top grades, was awarded a short-term fellowship from the German Academic Exchange Service
2024	Robert Torrance, M.Sc. / Ph.D. student, University College London Career Stage: Ph.D. student. Mentoring Role: External Supervisor. Accomplishments: Successfully completed a research internship with top grades
2024 - 2025	Francesco Romano, M.D. / Resident in Hematology, University of Pavia Career Stage: Resident in hematology. Mentoring Role: Supervisor. Accomplishments: Successfully completed hematology residency Thesis
2024 - 2025	Andreas Brandauer, B.Sc. / M.Sc. student, University of Vienna Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a M.Sc. thesis with top grades
2024 - Present	Giada Zambonini, M.Sc. / Research technician Career Stage: Research Technician. Mentoring Role: Supervisor. Accomplishments: acquired unique expertise in performing complex gene editing experiments and acquired the role of lab manager
2025	Enzo Espinosa, B.Sc. / M.Sc. student, Swiss Federal Technology Institute of Lausanne (EPFL)

	Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship with top grades
2025	Ciro Improta, M.D. / Resident in hematology, Humanitas University Career Stage: Resident in hematology. Mentoring Role: Supervisor. Accomplishments: Successfully completed hematology residency Thesis
2025	Sofiya Vinogradova, B.Sc. / M.Sc. student, German Cancer Research Center (DKFZ) Career Stage: M.Sc. student. Mentoring Role: Supervisor. Accomplishments: Successfully completed a research internship with top grades, was awarded a short-term fellowship from the European Union

Local Invited Presentations:

☒ *No presentations below were sponsored by 3rd parties/outside entities*

☐ *Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.*

2021	Gene Editing of Hematopoietic Stem cells and T cells for the Treatment of Primary Immunodeficiencies / Invited Seminar Fetal Research Seminar, Boston Children's Hospital, Boston, MA
2021	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Human Diseases / Invited Seminar Department of Pediatrics – Hematology/Oncology Seminar series, BCH/DFCI. Boston, Boston, MA
2024	Epitope Editing Enables Novel Immunotherapies for Acute Myeloid Leukemia / Invited Seminar Gene Therapy Conference, Boston Children's Hospital

Report of Regional, National and International Invited Teaching and Presentations

☒ *No presentations below were sponsored by 3rd parties/outside entities*

☐ *Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.*

National

2016	Towards Clinical Translation of Hematopoietic Stem Cell Gene Editing for the Correction of Inherited Mutations / Invited Presentation Telethon Tri-Retreat, Rome, Italy
2016	Towards Clinical Translation of Hematopoietic Stem Cell Gene Editing for the Correction of Inherited Mutations / Invited Seminar Genome Editing Science Club, Gaslini Children’s Hospital, Genoa, Italy
2017	Gene correction of CD40LG gene in T cells and HSPC for the treatment of X-linked hyper-IgM immunodeficiency (HIGM1) / Invited Presentation Annual Meeting -Gruppo di Studio sulle Immunodeficienze Primitive AIEOP-IPINET, Turin, Italy

2017	Targeted Genome Editing in Hematopoietic Stem/Progenitor Cells and T cells for the Treatment of Inherited Diseases / Invited Seminar Telethon Institute of Genetics and Medicine (TIGEM), Naples, Italy
2018	Hematopoietic Stem Cells Gene Editing for the Treatment of Human Inherited Diseases / Invited Presentation XXI SIGU National Congress – Società Italiana Genetica Umana (SIGU), Catania, Italy
2019	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Human Diseases / Invited Presentation "Gene Editing" Seminars for the PhD Course in Life Science and Biotechnologies – Insubria University, Varese, Italy
2020	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Human Diseases / Invited Presentation Retreat of the Transatlantic Gene Therapy Consortium., Boston, MA
02/2024	Epitope Editing Enables Novel Immunotherapies for Acute Myeloid Leukemia / Invited Seminar VOR Biopharma, Boston, MA
2024	Developing Genome Editing Tools to Improve Safety and Efficacy of Adoptive Immunotherapy / Invited Presentation Festival of Genomics, Boston, MA

International

2015	Site-Specific Genome Modification of Human Primary T Lymphocytes and Hematopoietic Stem/Progenitor Cells / Invited Seminar Glaxosmithkline, Stevenage, UK
2015	Site-Specific Genome Modification of Human Hematopoietic Stem/Progenitor Cells / Invited Presentation 18th Annual Meeting of the American Society of Gene and Cell Therapy (ASGCT), New Orleans, LA
2015	Towards Clinical Translation of New Gene Targeting Technologies for Empowering Adoptive Immunotherapy and Correcting Inherited Mutations / Invited Seminar St. Jude Children's Research Hospital, Memphis, TN
2016	Towards Clinical Translation of Hematopoietic Stem Cell Gene Editing for the Correction of Inherited Mutations / Invited Presentation 1st Annual Symposium on Cell and Gene Therapy, Vellore, India
2016	Towards Clinical Translation of Hematopoietic Stem Cell Gene Editing for the Correction of Inherited Mutations / Invited Presentation 5th International Conference of the Cyprus Society of Human Genetics, Nicosia, Cyprus
2016	Toward Clinical Translation of Hematopoietic Stem Cell Gene Editing for the Treatment of Inherited Diseases / Invited Presentation FUTURE MEDICINE / Innovation in Health Sciences, Berlin, Germany
2016	Towards Clinical Translation of Hematopoietic Stem Cell Gene Editing for the Correction of Inherited Mutations / Invited Presentation

	Annual Meeting of the French society of cellular and gene therapy (SFTCG), Marseilles, France
2016	Towards clinical translation of gene editing technologies for empowering adoptive immunotherapy or correcting inherited mutations / Invited Presentation The ESGCT/ISSCR/ABCD Collaborative Congress, Florence, Italy
2017	Targeted genome editing in hematopoietic stem/progenitor cells for the treatment of inherited diseases / Invited Presentation XXV Anniversary Congress of the European Society of Gene and Cell Therapy (ESGCT), Berlin, Germany
2018	Hematopoietic Stem Cell Gene editing for the treatment of inherited diseases / Invited Presentation Ski Retreat of COVAGEN AG, Laax, Switzerland
2018	Exploiting the Therapeutic Potential of Hematopoietic Stem Cell Gene Editing for the Treatment of Inherited Diseases / Invited Presentation 9th Biennial Congress of the Spanish Society for Gene and Cell Therapy, Palma de Mallorca, Spain
2018	Towards Clinical Translation of Gene Editing Technologies / Invited Presentation 2nd Congress of Gene Therapy and Regenerative Medicine, Athens, Greece
2018	Hematopoietic Stem Cell Gene editing in human rare diseases / Invited Presentation International Symposium: Applications of gene editing on research and therapy of human - Fundacion Ramon Areces, Madrid, Spain
2018	Preclinical Modelling of Gene Editing in Hematopoietic Stem/Progenitor Cells for the Treatment of Primary Immunodeficiencies / Invited Presentation International Mouse Phenotyping Consortium (IMPC) Stakeholder, Munich, Germany
2018	Precise Genetic Engineering of Hematopoiesis for Treating Inherited Diseases / Invited Seminar Special Seminar in the Infection, Immunity and Inflammation Program - University College London, London, UK
2018	Gene Editing of CD40L for the treatment of X-Linked Hyper-IgM Syndrome / Invited Presentation Annual Meeting - Inborn Errors Working Party (IEWP) of the European Society of Blood and Marrow Transplantation (EBMT), Leiden, Netherlands
2019	Oral presentation of 15 selected abstracts at international meeting including the Annual Meetings of the American Society of Gene and Cell Therapy (ASGCT; 2012, 2013, 2014, 2016), the European Society of Gene and Cell Therapy (ESGCT; 2009, 2011, 2013, 2014), the CELL-PID & PERSIST (2010, 2011, 2013), the American Association for Cancer Research (AACR, 2010), FASEB meeting (2018), ICLE meeting (2019).
2019	Improved HSC Gene Editing Protocol Allows Establishing Polyclonal Hematopoiesis. / Invited Presentation Stem Cell Clonality and Genotoxicity Retreat, Barcelona, Spain

2019	“One Size Fits All" Strategy for T Cell Correction, Selection and Depletion as New Treatment for HIGM1 Syndrome. / Invited Presentation Annual Meeting of the European Society of Cell and Gene Therapy (ESGCT), Barcelona, Spain
2019	Gene editing: Towards clinical applications. / Invited Lecture Annual Meeting of the European Society of Cell and Gene Therapy (ESGCT), Barcelona, Spain
2019	Precise Genetic Engineering of T Lymphocytes and Hematopoietic Stem Cells for the Treatment of Human Diseases / Invited Seminar University of Nantes, Nantes, France
2019	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Inherited Diseases / Invited Presentation Gene Editing Workshop of the ASGCT annual meeting, Washington DC, US
2019	T cell and HSPC Gene Editing in CD40 Ligand Deficiency / Invited Presentation 45th Meeting of the European Society of Blood and Marrow Transplantation (EBMT), Frankfurt, Germany
2020	“One Size Fits All” Strategy for T Cell Correction, Selection and Depletion as New Treatment for HIGM1 Syndrome. / Invited Presentation FASEB Conference on “Genome Engineering: Cutting Edge Research and Applications”, Lisbon, Portugal - CANCELLED DUE TO COVID-19 EMERGENCY
2021	Sections: CAR Modified Cellular Therapies / Session Moderator/Chair American Society of Gene and Cell Therapy (ASGCT), Virtual
2021	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Inherited Diseases / Invited Seminar The Institute of Molecular Medicine – UTHealth – University of Texas, Houston, Texas
2021	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Human Diseases / Invited Presentation Department of Pediatrics – Innovative Therapies Seminar series, University of Padova, Padova, Italy
2021	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Inherited Diseases / Invited Presentation 6th Annual Cell and Gene Therapy Symposium, Vellore, India
2022	Engineering Immunotherapy Resistant Hematopoiesis to Treat High-Risk Acute Myeloid Leukemia / Selected Presentation International Conference of Lymphocyte Engineering, Munich, Germany.
2022	Epitope Engineered HSPC to Enable CAR-T Cell Immunotherapy of Acute Myeloid Leukemia / Selected Presentation FASEB Genome Engineering: Cutting Edge Research and Applications, Lisbon, Portugal
2022	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Inherited Diseases Oral Presentation / Invited Seminar MiltenyiBiotec - Internal Seminar, BergischGladbach, Germany.

2022	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Human Diseases / Invited Presentation Clinical Immunology Society, Charlotte, NC
2023	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Seminar The Jackson Laboratory for Genomic Medicine, Farmington, CT
2023	Epitope Engineering for an Immunotherapy “Stealth” Hematopoiesis / Invited Plenary Talk Annual Meeting of the European Society of Gene and Cell Therapy, Brussels, Belgium
2023	Editing of Hematopoietic Stem Cells for Treating Inherited Blood Disorders and Improving Adoptive Immunotherapy of Leukemia / Invited Seminar Penn-CHOP Blood Center for Patient Care and Discovery Seminar Series, The Children’s Hospital of Philadelphia, Philadelphia, PA
2023	Epitope Editing of Hematopoietic Stem Cells to Enable Adoptive Immunotherapies for Acute Myeloid Leukemia / Invited Presentation ASGCT Spotlight on Immuno-Oncology, Seattle, WA
2023	Section: Ex vivo Gene Edited Cell Therapies / Session Moderator/Chair Keystone Symposia - Precision Genome Engineering & Genomic Instability and DNA Repair, Whistler, BC, Canada
2023	Advanced Genetic Engineering of Hematopoiesis for the Treatment of Human Diseases / Invited Seminar Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC
2024	Epitope Editing for an Immunotherapy “Stealth” Hematopoiesis / Invited Seminar NCI Pediatric Oncology Branch - Center for Cancer Research, Bethesda, MD
2024	Base Editing to Improve Conditioning and Transplant of Sickle Cell Patients / Invited Presentation NHLBI Cure Sickle Cell Initiative, Virtual
2024	Base Editing of Hematopoietic Sm Cells / Invited Presentation Tandem Meetings -Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR, San Antonio, TX
2024	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Presentation Tandem Meetings -Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR, San Antonio, TX
2024	Epitope Editing Enables Novel Immunotherapies for Acute Myeloid Leukemia / Invited Presentation EBMT-EHA 6th European CAR T-cell Meeting, Valencia, Spain
2024	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Presentation 2nd annual Fred Hutch international symposium, Seattle, WA
2024	Editing of Hematopoietic Stem Cells for Treating Inherited Blood Disorders and Improving Adoptive Immunotherapy of Leukemia / Invited Seminar Mayo Clinic - Department of Molecular Medicine, Rochester, MN

2024	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Presentation 9th Annual Cell and Gene Therapy Symposium, Vellore, India
2024	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Seminar Tettamanti Foundation, Milan, Italy
2024	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Seminar University Vita-Salute San Raffaele, Milan, Italy
2024	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Presentation Annual Meeting of the American Society of Hematology (ASH), San Diego, CA
02/2025	Epitope Editing Enables Novel Immunotherapies for Acute Myeloid Leukemia / Invited Presentation 13th AACR-JCA Joint Conference: From Cancer Discovery Science to Therapeutic Innovation, Maui, HI
02/2025	Advanced Genetic Engineering of Hematopoiesis for the Development of Novel Therapeutic Strategies / Invited Seminar Fred Hutchinson Cancer Center, Seattle, WA
03/2025	Immuno-Epitope Shielding / Invited Presentation 9th Zurich Immuno-Oncology Symposium - Comprehensive Cancer Center Zurich, Zurich, Switzerland
03/2025	Epitope Editing for an Immunotherapy "Stealth" Hematopoiesis / Invited Presentation Keystone Symposium - Precision Genome Engineering: Translating the Human Genome to the Clinic, Killarney, Ireland

Report of Technological and Other Scientific Innovations

Targeted disruption of T cell receptor genes using engineered zinc finger protein (2009)	Patent - Active Disclosed herein are methods and compositions for inactivating TCR genes, using zinc finger nucleases (ZFNs) comprising a zinc finger protein and a cleavage domain or cleavage half-domain in conditions able to preserve cell viability. US US8956828B2 Priority 2009-11-10 • Filed 2010-11-10 • Granted 2015-02-17 • Published 2015-02-17
Targeted disruption of T cell receptor genes using TALEN (2013)	Patent - Active Disclosed herein are methods and compositions for modifying TCR genes, using nucleases (zinc finger nucleases or TAL nucleases) to modify TCR genes. WO EP US CN JP AU CA HK IL US20180214485A1 Priority 2013-03-21 • Filed 2018-03-26 • Published 2018-08-02

Delivery methods and compositions for nuclease-mediated genome engineering in hematopoietic stem cells (2014)	Patent - Active The present disclosure is in the field of genome engineering, particularly targeted modification of the genome of a hematopoietic cell. WO EP US CA US10117899B2 Priority 2013-10-17 • Filed 2014-10-16 • Granted 2018-11-06 • Published 2018-11-06
Systems and methods for treating hyper-IgM syndrome (2017)	Patent Disclosed herein are genome editing systems and related methods which allow for treatment of Hyper IgM Syndrome, a group of disorders characterized by defective CD40 signaling. WO EP US CN JP CA IL WO2019084168A1 Priority 2017-10-24 • Filed 2018-10-24 • Published 2019-05-02
Cyclosporin improves lentiviral transduction and gene targeting efficiencies in hematopoietic stem and progenitor cells alone and in combination with other compounds (2017)	Patent - Use of cyclosporin H (CsH) or a derivative thereof for increasing the efficiency of transduction of an isolated population of cells by a viral vector and/or increasing the efficiency of gene editing of an isolated population of cells when transduced by a viral vector. US20210121579A1 Priority 2017-04-20 - Filed 2018-04-20 - Published 2022-02-28
Selection of edited cells by means of artificial transactivators (2018)	Patent - A method for selecting genome-edited cells and/or for enrichment of genome-edited cells. WO EP US CN JP AU CA IL SG AU2019358519A1 Priority 2018-10-11 • Filed 2019-10-11 • Published 2021-05-27
Development of a truncated epidermal growth factor receptor (EGFRt) with enhanced stability and cell surface expression to select and deplete engineered cells (2020)	Patent - Pending A polynucleotide comprising a nucleotide sequence encoding an epidermal growth factor receptor (EGFR) extracellular epitope operably linked to: (a) a NGFR or GMS SFR alpha signal peptide; (b) a EGFR or NGFR transmembrane domain; and/or (c) a NGFR or EGFR cytosplasmic tail. WO EP US CN JP AU CA GB IL WO2021229075A2 Priority 2020-05-14 • Filed 2021-05-14 • Published 2021-11-18
Methods and compositions for editing the RAG1 gene as treatment	Patent - The present invention relates to an isolated polynucleotide comprising from 5' to 3': a first homology region, a splice acceptor sequence, a nucleotide sequence

for severe combined immunodeficiency (2020)	encoding a RAG1 polypeptide, and a second homology region for use in treating a RAG-deficient immunodeficiency. WO AU IL WO2022079054A1 Priority 2020-10-12 • Filed 2021-10-12 • Published 2022-04-21
Methods and compositions for editing the CTLA4 gene as treatment for CTLA4 immunodeficiency (2021)	Patent - Describe methods and compositions for treating CTLA4 deficiency with autologous gene edited T cells or HSC
Epitope Engineering of Cell-Surface Receptors (2022)	Patent - Describe methods and compositions for editing cell-surface proteins on hematopoietic stem cells, that can be used in combination with immunotherapies
Epitope Engineering of Cell-Surface Receptors (2023)	Patent - Describe methods and compositions for editing cell-surface proteins on hematopoietic stem cells, that can be used in combination with immunotherapies
MODIFIED B CELLS AND METHODS FOR USE THEREOF (2024)	Patent - The present disclosure is in the field of genome engineering, particularly targeted modification of B cells for cancer immunotherapy strategies. Filed 2024-05-05
CD52 epitope editing (2025)	Patent - Describe methods and compositions for CD52 epitope editing to facilitate non-cytotoxic lymphodepletion and in vivo cell therapies involving chimeric antigen receptor and T cell receptor therapies in mature haematopoietic cells, such as T and NK cells

Report of Education of Patients and Service to the Community

☒No presentations below were sponsored by 3rd parties/outside entities.

☐Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.

Activities

2020	Espanoles Cientificos en USA (ECUSA) / Invited Speaker Title of the presentation: Gene Editing of Hematopoietic Stem Cells and T Cells for the Treatment of Primary Immunodeficiencies

Educational Material for Patients and the Lay Community:

Books, articles, and presentations in other media

2016	Researcher description	Highlight of the research Grant on HIGM1 gene editing from the Telethon Foundation	https://www.telethon.it/cosa-facciamo/ricerca/ricercatori/pietro-genovese/
2017	SR-Tiget: piccoli geni crescono	Interview for the Telethon Foundation	https://www.telethon.it/storie-e-news/storie/ricercatori/sr-tiget-piccoli-geni-crescono/
2021	Leukemia Research Foundation aims to fight AML using CAR T-cell therapy	Highlight of the research Grant on AML immunotherapy from the Leukemia Research Foundation	article on page 7: https://www.dana-farber.org/uploadedFiles/Newsroom/Publications/impact-summer-2022.pdf
2021	Engineering better treatments for AML	Interview for the Children Cancer Research Foundation	https://childrenscancer.org/engineering-better-treatments-for-aml/
2021	Editing genetico, vicini all'applicazione clinica	Highlight of the research manuscript on EMBO Mol Med, 2021, by the Telethon Foundation	https://www.telethon.it/storie-e-news/news/dalla-ricerca/editing-genetico-vicini-allapplicazione-clinica/

Report of Scholarship

* denotes equal authorship contribution

** denotes mentored trainee.

Peer-Reviewed Scholarship in print or other media:

Research Investigations

1. Lombardo A, **Genovese P**, Beausejour CM, Colleoni S, Lee YL, Kim KA, Ando D, Urnov FD, Galli C, Gregory PD, Holmes MC, Naldini L. Gene editing in human stem cells using zinc finger nucleases and integrase-defective lentiviral vector delivery. Nat Biotechnol. 2007 Nov; 25(11):1298-306. PMID: 17965707
2. Mátrai J, Cantore A, Bartholomae CC, Annoni A, Wang W, Acosta-Sanchez A, Samara-Kuko E, De Waele L, Ma L, **Genovese P**, Damo M, Arens A, Goudy K, Nichols TC, von Kalle C, L Chuah MK, Roncarolo MG, Schmidt M, Vandendriessche T, Naldini L. Hepatocyte-targeted expression by integrase-defective lentiviral vectors induces antigen-specific tolerance in mice with low genotoxic risk. Hepatology. 2011 May; 53(5):1696-707. PMID: 21520180
3. Gabriel R, Lombardo A, Arens A, Miller JC, **Genovese P**, Kaeppel C, Nowrouzi A, Bartholomae CC, Wang J, Friedman G, Holmes MC, Gregory PD, Glimm H, Schmidt M, Naldini L, von Kalle C. An unbiased genome-wide analysis of zinc-finger nuclease specificity. Nat Biotechnol. 2011 Aug 07; 29(9):816-23. PMID: 21822255
4. Lombardo A, Cesana D, **Genovese P**, Di Stefano B, Provasi E, Colombo DF, Neri M, Magnani Z, Cantore A, Lo Riso P, Damo M, Pello OM, Holmes MC, Gregory PD, Gritti A, Broccoli V,

Bonini C, Naldini L. Site-specific integration and tailoring of cassette design for sustainable gene transfer. Nat Methods. 2011 Aug 21; 8(10):861-9. PMID: 21857672

5. Provasi E*, **Genovese P***, Lombardo A, Magnani Z, Liu PQ, Reik A, Chu V, Paschon DE, Zhang L, Kuball J, Camisa B, Bondanza A, Casorati G, Ponzoni M, Ciceri F, Bordignon C, Greenberg PD, Holmes MC, Gregory PD, Naldini L, Bonini C. Editing T cell specificity towards leukemia by zinc finger nucleases and lentiviral gene transfer. Nat Med. 2012 May; 18(5):807-815. (*denotes co-first authors) PMID: 22466705
6. Casucci M, Nicolis di Robilant B, Falcone L, Camisa B, Norelli M, **Genovese P**, Gentner B, Gullotta F, Ponzoni M, Bernardi M, Marcatti M, Saudemont A, Bordignon C, Savoldo B, Ciceri F, Naldini L, Dotti G, Bonini C, Bondanza A. CD44v6-targeted T cells mediate potent antitumor effects against acute myeloid leukemia and multiple myeloma. Blood. 2013 Nov 14; 122(20):3461-72. PMID: 24016461
7. Rio P, Baños R, Lombardo A, Quintana-Bustamante O, Alvarez L, Garate Z, **Genovese P**, Almarza E, Valeri A, Díez B, Navarro S, Torres Y, Trujillo JP, Murillas R, Segovia JC, Samper E, Surralles J, Gregory PD, Holmes MC, Naldini L, Bueren JA. Targeted gene therapy and cell reprogramming in Fanconi anemia. EMBO Mol Med. 2014 Jun; 6(6):835-48. PMID: 24859981
8. **Genovese P**, Schiroli G, Escobar G, Tomaso TD, Firrito C, Calabria A, Moi D, Mazzieri R, Bonini C, Holmes MC, Gregory PD, van der Burg M, Gentner B, Montini E, Lombardo A, Naldini L. Targeted genome editing in human repopulating haematopoietic stem cells. Nature. 2014 Jun 12; 510(7504):235-240. PMID: 24870228
9. Elia AR, Circosta P, Sangiolo D, Bonini C, Gammaitoni L, Mastaglio S, **Genovese P**, Geuna M, Avolio F, Inghirami G, Tarella C, Cignetti A. Cytokine-induced killer cells engineered with exogenous T-cell receptors directed against melanoma antigens: enhanced efficacy of effector cells endowed with a double mechanism of tumor recognition. Hum Gene Ther. 2015 Apr; 26(4):220-31. PMID: 25758764
10. Mastaglio S, **Genovese P**, Magnani Z, Ruggiero E, Landoni E, Camisa B, Schiroli G, Provasi E, Lombardo A, Reik A, Cieri N, Rocchi M, Oliveira G, Escobar G, Casucci M, Gentner B, Spinelli A, Mondino A, Bondanza A, Vago L, Ponzoni M, Ciceri F, Holmes MC, Naldini L, Bonini C. NY-ESO-1 TCR single edited stem and central memory T cells to treat multiple myeloma without graft-versus-host disease. Blood. 2017 08 03; 130(5):606-618. PMID: 28637663
11. Schiroli G, Ferrari S, Conway A, Jacob A, Capo V, Albano L, Plati T, Castiello MC, Sanvito F, Gennery AR, Bovolenta C, Palchaudhuri R, Scadden DT, Holmes MC, Villa A, Sitia G, Lombardo A, **Genovese P**, Naldini L. Preclinical modeling highlights the therapeutic potential of hematopoietic stem cell gene editing for correction of SCID-X1. Sci Transl Med. 2017 Oct 11; 9(411). PMID: 29021165
12. Diez B, **Genovese P**, Roman-Rodriguez FJ, Alvarez L, Schiroli G, Ugalde L, Rodriguez-Perales S, Sevilla J, Diaz de Heredia C, Holmes MC, Lombardo A, Naldini L, Bueren JA, Rio P. Therapeutic gene editing in CD34+ hematopoietic progenitors from Fanconi anemia patients. EMBO Mol Med. 2017 11; 9(11):1574-1588. PMID: 28899930
13. Petrillo C, Thorne LG, Unali G, Schiroli G, Giordano AMS, Piras F, Cuccovillo I, Petit SJ, Ahsan F, Noursadeghi M, Clare S, **Genovese P**, Gentner B, Naldini L, Towers GJ, Kajaste-Rudnitski A. Cyclosporine H Overcomes Innate Immune Restrictions to Improve Lentiviral Transduction and Gene Editing In Human Hematopoietic Stem Cells. Cell Stem Cell. 2018 12 06; 23(6):820-832.e9. PMID: 30416070
14. Schiroli G, Conti A, Ferrari S, Della Volpe L, Jacob A, Albano L, Beretta S, Calabria A, Vavassori V, Gasparini P, Salataj E, Ndiaye-Lobry D, Brombin C, Chaumeil J, Montini E,

Merelli I, **Genovese P**, Naldini L, Di Micco R. Precise Gene Editing Preserves Hematopoietic Stem Cell Function following Transient p53-Mediated DNA Damage Response. Cell Stem Cell. 2019 04 04; 24(4):551-565.e8. PMID: 30905619

15. Ferrari S*, Jacob A*, Beretta S, Unali G, Albano L, Vavassori V, Cittaro D, Lazarevic D, Brombin C, Cugnata F, Kajaste-Rudnitski A, Merelli I, **Genovese P**, Naldini L. Efficient gene editing of human long-term hematopoietic stem cells validated by clonal tracking. Nat Biotechnol. 2020 11; 38(11):1298-1308. (*denotes co-first authors) PMID: 32601433
16. Vavassori V, Mercuri E, Marcovecchio GE, Castiello MC, Schiroli G, Albano L, Margulies C, Buquicchio F, Fontana E, Beretta S, Merelli I, Cappelleri A, Rancoita PM, Lougaris V, Plebani A, Kanariou M, Lankester A, Ferrua F, Scanziani E, Cotta-Ramusino C, Villa A, Naldini L, **Genovese P**. Modeling, optimization, and comparable efficacy of T cell and hematopoietic stem cell gene editing for treating hyper-IgM syndrome. EMBO Mol Med. 2021 03 05; 13(3):e13545. PMID: 33475257
17. Ferrari S, Vavassori V, Canarutto D, Jacob A, Castiello MC, Javed AO, **Genovese P**. Gene Editing of Hematopoietic Stem Cells: Hopes and Hurdles Toward Clinical Translation. Front Genome Ed. 2021; 3:618378. PMID: 34713250
18. Ferrari S*, Beretta S*, Jacob A, Cittaro D, Albano L, Merelli I, Naldini L, **Genovese P**. BAR-Seq clonal tracking of gene-edited cells. Nat Protoc. 2021 06; 16(6):2991-3025. (*denotes co-first authors) PMID: 34031609
19. Cesana D, Calabria A, Rudilosso L, Gallina P, Benedicenti F, Spinozzi G, Schiroli G, Magnani A, Acquati S, Fumagalli F, Calbi V, Witzel M, Bushman FD, Cantore A, **Genovese P**, Klein C, Fischer A, Cavazzana M, Six E, Aiuti A, Naldini L, Montini E. Retrieval of vector integration sites from cell-free DNA. Nat Med. 2021 08; 27(8):1458-1470. PMID: 34140705
20. Crippa S, Conti A, Vavassori V, Ferrari S, Beretta S, Rivis S, Bosotti R, Scala S, Pirroni S, Jofra-Hernandez R, Santi L, Basso-Ricci L, Merelli I, **Genovese P**, Aiuti A, Naldini L, Di Micco R, Bernardo ME. Mesenchymal stromal cells improve the transplantation outcome of CRISPR-Cas9 gene-edited human HSPCs. Mol Ther. 2022 Oct 05; 30(10):3333. PMID: 36096132
21. Crippa S, Conti A, Vavassori V, Ferrari S, Beretta S, Rivis S, Bosotti R, Scala S, Pirroni S, Jofra-Hernandez R, Santi L, Basso-Ricci L, Merelli I, **Genovese P**, Aiuti A, Naldini L, Di Micco R, Bernardo ME. Mesenchymal stromal cells improve the transplantation outcome of CRISPR-Cas9 gene-edited human HSPCs. Mol Ther. 2023 01 04; 31(1):230-248. PMID: 35982622
22. Fox TA, Houghton BC, Petersone L, Waters E, Edner NM, McKenna A, Preham O, Hinze C, Williams C, de Albuquerque AS, Kennedy A, Pesenacker AM, **Genovese P**, Walker LSK, Burns SO, Sansom DM, Booth C, Morris EC. Therapeutic gene editing of T cells to correct CTLA-4 insufficiency. Sci Transl Med. 2022 10 26; 14(668):eabn5811. PMID: 36288278
23. Casirati G, Cosentino A, Mucci A, Salah Mahmoud M, Ugarte Zabala I, Zeng J, Ficarro SB, Klatt D, Brendel C, Rambaldi A, Ritz J, Marto JA, Pellin D, Bauer DE, Armstrong SA, Genovese P. Epitope editing enables targeted immunotherapy of acute myeloid leukaemia. Nature. 2023 Sep; 621(7978):404-414. PMID: 37648862
24. Landoni E, Woodcock MG, Barragan G, Casirati G, Cinella V, Stucchi S, Flick LM, Withers TA, Hudson H, Casorati G, Dellabona P, Genovese P, Savoldo B, Metelitsa LS, Dotti G. IL-12 reprograms CAR-expressing natural killer T cells to long-lived Th1-polarized cells with potent antitumor activity. Nat Commun. 2024 01 02; 15(1):89. PMID: 38167707
25. Castiello MC, Brandas C, Ferrari S, Porcellini S, Sacchetti N, Canarutto D, Draghici E, Merelli I, Barcella M, Pelosi G, Vavassori V, Varesi A, Jacob A, Scala S, Basso Ricci L, Paulis M, Strina D, Di Verniere M, Sergi Sergi L, Serafini M, Holland SM, Bergerson JRE, De Ravin SS, Malech

HL, Pala F, Bosticardo M, Brombin C, Cugnata F, Calzoni E, Crooks GM, Notarangelo LD, Genovese P, Naldini L, Villa A. Exonic knockout and knockin gene editing in hematopoietic stem and progenitor cells rescues RAG1 immunodeficiency. Sci Transl Med. 2024 Feb 07; 16(733):eadh8162. PMID: 38324638

26. Cianciotti BC, Magnani ZI, Ugolini A, Camisa B, Merelli I, Vavassori V, Potenza A, Imparato A, Manfredi F, Abbati D, Perani L, Spinelli A, Shifrut E, Ciceri F, Vago L, Di Micco R, Naldini L, Genovese P, Ruggiero E*, Bonini C*. TIM-3, LAG-3, or 2B4 gene disruptions increase the anti-tumor response of engineered T cells. Front Immunol. 2024; 15:1315283. (*denotes co-senior authors) PMID: 38510235
27. Levesque S, Cosentino A, Verma A, Genovese P, Bauer DE. Enhancing prime editing in hematopoietic stem and progenitor cells by modulating nucleotide metabolism. Nat Biotechnol. 2024 May 28. PMID: 38806736
28. Klatt D, Sereni L, Liu B, Genovese P, Schambach A, Verhoeyen E, Williams DA, Brendel C. Engineered packaging cell line for the enhanced production of baboon-enveloped retroviral vectors. Mol Ther Nucleic Acids. 2024 Dec 10; 35(4):102389. PMID: 39679008
29. Montepeloso A, Mattioli D, Pellin D, Peviani M, Genovese P, Biffi A. Haploinsufficiency at the CX3CR1 locus of hematopoietic stem cells favors the appearance of microglia-like cells in the central nervous system of transplant recipients. Nat Commun. 2024 Nov 25; 15(1):10192. PMID: 39587072

Non-peer reviewed scholarship in print or other media:

Reviews, chapters, and editorials

1. Lederer CW, **Genovese P**, Miccio A, Philipsen S. Editorial: Mutation-Specific Gene Editing for Blood Disorders. Front Genome Ed. 2021; 3:761771. PMID: 34713270
2. Zeng J, Casirati G, Nguyen MA, **Genovese P**, Bauer DE. Base Editing of Human Hematopoietic Stem Cells. Methods Mol Biol. 2023; 2606:43-62. PMID: 36592307

Thesis:

1. International Ph.D. School in Molecular Medicine, Program in Basic and Applied Immunology, Vita-Salute San Raffaele University. Site-Specific Genome Modification of Human Primary T Lymphocytes and Hematopoietic Stem/Progenitor Cells. Pietro Genovese, M.Sc.. Identification number: 004066. Cycle of studies: XXIV. Director of Studies: Prof. Luigi Naldini. Second Supervisor: Prof. Toni Cathomen.

Abstracts, Poster Presentations, and Exhibits Presented at Professional Meetings:

1. Martina Fiumara, Samuele Ferrari, Elisabetta Mercuri, Aurelien Jacob, Luisa Albano, Angelo Lombardo, **Pietro Genovese**#, Luigi Naldini#. Efficient Ex-Vivo Selection of Gene Edited Human Hematopoietic Stem/Progenitor Cells. ASGCT 2021.
2. Safa F. Mohamad, Meaghan McGuiness, Gabriele Casirati, Alejo Rodriguez-Fraticelli, Chad Harris, Fernando Camargo, **Pietro Genovese**, Eric J. Allenspach, David A. Williams. Septin-6 regulates murine and human hematopoiesis, and its dysregulation is associated with pediatric myelodysplasia. ASH 2022

3. Gabriele Casirati, Andrea Cosentino, Adele Mucci, Mohammed S. Mahmoud, Marta Freschi, Jing Zeng, Christian Brendel, Daniel Bauer, **Pietro Genovese**. Epitope Edited Hematopoietic Stem Cells Allow Immune-Based In Vivo Selection of Genome-Engineered Cells. ASGCT 2023
4. Lucia Sereni, Andrea Bianchi, Marta Freschi, Silvia Rizzato, Giulia Escobar, Nicara Chantal Parr, Marina Theodorou, Adele Mucci, Denise Klatt, Trine Ahn Kristiansen, Christian Brendel, **Pietro Genovese**. *Engineered B-cells show anti-tumor activity in preclinical model of HER2+ breast cancer*. SITC annual meeting. 2024
5. Robert Torrance, Kate Orf, Nathan White, Alexander McKenna, Claire Booth, Adrian Thrasher, Thomas Fox, **Pietro Genovese**, Siobhan Burns, Emma Morris. *Functional Restoration of Immune Defects in STAT1 Gain-of-Function Immunodeficiency Following Gene Editing*. ASGCT annual meeting. 2025

Narrative Report

My main research interest is to exploit gene engineering technologies to study biological functions and solve problems with a direct impact on human health. During my academic studies, I matured my scientific interests working on innovative projects aimed to develop a new gene editing technology that allows site-specific manipulation of the human genome. In 2007, within the group of Prof. Luigi Naldini, I contributed to a break-through work where we demonstrated for the first time the power of the artificial nucleases technology to direct the integration of exogenous DNA sequences into a predetermined genomic locus of several human cell types (Lombardo, Genovese et al., Nat. Biotech. 2007). During my Ph.D. studies, I extended my knowledge and skills on this technology exploiting it for the development of a new cancer adoptive immunotherapy approach. In collaboration with the group of Prof. Chiara Bonini and with Sangamo Therapeutics, the stakeholder biotech company leader in development of Zinc Finger Nucleases (ZFNs), we exploited the use of these artificial nucleases to genetically re-write the endogenous antigen specificity of cytotoxic T cells and re-direct them against a tumor-associated antigen. By avoiding competition for surface expression between exogenous and endogenous TCR chains, and by abrogating the risk of inappropriate TCR pairing, the TCR editing approach permanently overcomes some of the major limitations of TCR gene transfer immunotherapy (Provasi* - Genovese* et al., Nat. Med. 2012). As post-doctoral associate, I decided to engage an ambitious study aimed to develop an effective gene targeting strategy for the correction of inherited mutations in human hematopoietic stem cells (HSC). Here I coordinated a work team of scientists with the aim to overcome the biologic barriers that specifically constrain gene targeting in the most primitive subset of hematopoietic progenitors. By tailoring culture conditions and gene delivery vehicles we developed a protocol that allows targeted integration of a transgene expression cassette into a “safe harbor” site or direct correction of the IL2RG gene of HSCs from healthy donors and X-linked severe combined immunodeficiency (SCID-X1) patients (Genovese et al., Nature 2014).Then, I assumed the more senior role of Project Leader and, focused my research on pre-clinical development and proof of feasibility of these novel medical treatments based on gene correction or TCR editing for two diseases, chosen as paradigmatic for testing their therapeutic potential: SCID-X1 and myeloid leukemia. For the first target, we improved the protocol for efficient gene editing of HSCs and exploited suitable preclinical models to establish the key parameters underlying safe and effective rescue of the SCID-X1 disease phenotype (Schiroli, …, Genovese* & Naldini*, Science Transl. Med. 2017). To simplify the TCR gene editing procedure in view of clinical development, we developed the TCR single editing approach which enables rapid generation of highly performing tumor specific T cells (Mastaglio, Genovese et al., Blood 2017). My expertise in genome engineering, T cell manipulation and stem cell transplantation,

together with my ability to supervise the work of a team of scientists, allowed me to conduct as principal investigator a successful project aimed to exploit gene editing to correct mutations of the *CD40LG* gene, a tightly regulated gene active on cell proliferation that causes the X-linked immunodeficiency with hyper-IgM (HIGM1). This research line was then partnered in collaboration with Editas Medicine, a biotech stakeholder in the field of genome editing. I leaded this investigational research line aimed to exploit the Editas' pipeline of CRISPR/Cas-based nuclease reagents to develop effective gene correction of the mutated gene in both T cells and HSCs. In collaboration with MolMed, a biotech company specialized in clinical manufacturing of gene therapy products, and with the support of the GLP facility of the SR-Tiget, we scaled up the gene editing procedures and established clinical-grade processes in preparation for a first of this kind clinical trial (recruitment of 1st patient expected in 2023).

Recently, I have established my own independent laboratory at the Dana-Farber/Boston Children's Cancer and Blood Disorder Center, and been appointed assistant professor at Harvard Medical School. As an early stage investigator, I am keenly interested in overcoming obstacles currently hampering full exploitation of HDR-driven editing in human lymphocytes and HSPC, and apply these innovative tools for developing new therapeutics. This extended scope matches well my prior scientific training in cancer immunotherapy and T cell and HSC engineering. My impression is that now that the HSC gene editing technology is approaching clinical testing for relatively straightforward problems like monogenic blood diseases, scientists have to higher the bar to reach new solution for more complex disorders, such as common blood disorders or hematologic malignancies.