BIOGRAPHICAL SKETCH

NAME:	**POSITION TITLE:**
ANGELA GRITTI	**Associate Professor of Human Histology** | Vita-Salute San Raffaele University, Milan, Italy **Group Leader** | Gene/Neural Stem Cell Therapy for Lysosomal Storage Diseases (LSD) | San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) |San Raffaele Scientific Institute, Milan Italy.

EDUCATION/TRAINING

INSTITUTION AND LOCATION	*DEGREE*	*YEAR*	*FIELD OF STUDY*
University of Milan, Italy	Master degree in Biological Sciences (summa cum laude)	1990	Biological Sciences, Pharmacology
Italy	Qualification to practice as a biologist	1991	
University of Milan, Italy	Specialty in Toxicology (70/70)	1996	Toxicology
University of Turin, Italy	PhD in Basic Sciences and Veterinary Biotechnology (XVIII cycle)	2006	Neuroscience, comparative neurogenesis, neural stem cells
Italy	National Academic Qualification as Associate Professor	2018	05/H2 – Histology
Italy	National Academic Qualification as Full Professor	2025	05/H2 - Histology 05/E2 - Molecular Biology

A. Personal Statement

I am a dedicated researcher in neural stem cell (NSC) biology and gene therapy. Over the past 30 years, I have established murine and human NSCs as key tools for modelling CNS development, disease mechanisms, and testing gene and cell therapies.

As Principal Investigator at Ospedale San Raffaele (OSR) and the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) in Milan, I lead a team of 12 in the "Unit of Gene/Neural Stem Cell Therapy for Lysosomal Storage Diseases (LSD)." Our primary focus is on studying and developing treatments for rare genetic CNS disorders, including Lysosomal Storage Disorders such as Metachromatic Leukodystrophy (MLD), Globoid Cell Leukodystrophy (GLD), and Alexander's Disease (AxD), as well as GM2 gangliosidoses, like Sandhoff Disease (SD) and Tay-Sachs Disease (TSD). Our projects combine basic and translational research using murine and human models. We explore various therapeutic strategies, including cell therapy, in vivo and ex vivo gene therapy, gene addition, and genome and epigenome editing. A primary goal is to understand early pathogenic events caused by genetic defects and how therapies can target these stages. This knowledge is essential for improving and implementing our gene therapy techniques. We utilise multiple in vitro systems, including patient-specific induced pluripotent stem cell (iPSC)-derived neural populations in 2D and 3D. These systems replicate disease features and help identify early defects in neuronal and glial cells, which are often underinvestigated. My team has identified critical early abnormalities in these cells, offering new insights into disease mechanisms.

Beyond research, I collaborate with international partners, participate in global expert networks, and engage with patient advocacy groups. My work is supported by prestigious programmes, reflecting a commitment to innovation.

As an associate professor of Human Histology at Vita-Salute San Raffaele University in Milan, I teach courses in Medicine and Surgery, the International MD programme, Biotechnology, and Molecular Biology. I combine lectures with practical sessions and promote active participation through group discussions. I aim to offer a comprehensive overview of tissue types, their development, functions, and roles within organs and systems. I also discuss recent advances in stem cell manipulation, tissue replacement, and regeneration, highlighting current challenges and gaps.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024 -	Associate Professor of Human Histology, Vita-Salute San Raffaele University, Milano
2022 -	Member and Chair (2024), ASGCT Neurologic & Ophthalmic Gene & Cell Therapy committee
2016 - 2024	Adjunt professor, Human Histology, Univ. Vita-Salute San Raffaele, School of Medicine, Master's degree in Medicine and Surgery and International MD Program, Milano
2016 - 2022	Lecturer, course "Organellar Pathology", Univ. Vita-Salute San Raffaele, School of Medicine, Master degree in Medical, Molecular and Cellular Biotechnology, Milano
2015 - 2016	Member, Italian Telethon Foundation, Patent Committee
2015 - 2015	Member, AFM-Telethon, Strategic and Therapeutic Orientation Committee
2011 -	Lecturer, Gene Therapy Course, Univ. Vita Salute San Raffaele, School of Medicine, Master's degree in molecular and cellular medical biotechnology, Milano

2006 -	Group Leader, San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) , Unit of Gene/neural stem cell therapy for lysosomal storage diseases, Milano
2001 - 2005	Research Scientist, San Raffaele Scientific Institute, Stem Cell Research Institute (SCRI), Milano
1997 - 1999	Level I biologist manager, National Neurological Institute "C.Besta", Milano
1995 - 1997	Senior fellow, National Neurological Institute "C.Besta", Neuropharmacology Lab, Milano
1992 - 1992	Visiting Scientist, University of Calgary, Faculty of Medicine, Calgary
1991 - 1994	Junior fellow, National Neurological Institute "C. Besta", Neuropharmacology Lab, Milano

C. Contribution to Science

Main scientific output

1. After earning my master's in biological sciences, I joined a leading adult NSC research group in Italy. Working in Dr. Weiss's Calgary lab strengthened my commitment to this field. As a research fellow and later a PhD student, I studied growth factor regulation of murine NSCs and helped establish human fetal-derived NSC lines for research and translational work. In 2001, I founded my own research group at Ospedale San Raffaele in Milan, and in 2004, I secured a tenure-track position through successful grants. My research on murine and human NSCs established these cells as models for CNS development and neurodegeneration. Collaborations led to breakthroughs, including preclinical evidence supporting NSC-based therapies for multiple sclerosis, now in Phase I/II trials.
   a) *Pluchino S*, **Gritti A***, Blezer E, Amadio S, Brambilla E, Borsellino G, Cossetti C, Del Carro U, Comi G, 't Hart B, Vescovi A, Martino G. Human neural stem cells ameliorate autoimmune encephalomyelitis in non-human primates. **Ann Neurol. 2009** Sep;66(3):343-54. *equal contribution*
   b) ***Gritti A**, Galli R, Vescovi AL. Clonal analyses and cryopreservation of neural stem cell cultures. **Methods Mol Biol. 2008**;438:173-84.*
   c) *Pluchino S, Quattrini A, Brambilla E, **Gritti A**, Salani G, Dina G, Galli R, Del Carro U, Amadio S, Bergami A, Furlan R, Comi G, Vescovi AL, Martino G. Injection of adult neurospheres induces recovery in a chronic model of multiple sclerosis. **Nature. 2003** Apr 17;422(6933):688-94.*
   d) ***Gritti A**, Bonfanti L, Doetsch F, Caille I, Alvarez-Buylla A, Lim DA, Galli R, Verdugo JM, Herrera DG, Vescovi AL. Multipotent neural stem cells reside into the rostral extension and olfactory bulb of adult rodents. **J Neurosci. 2002** Jan 15;22(2):437-45.*
2. As a group leader at the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget), I focus on gene- and NSC-based approaches for lysosomal storage diseases (LSDs), particularly Globoid Cell Leukodystrophy (GLD) and GM2-gangliosidosis. My team demonstrated the feasibility and efficacy of these therapies in preclinical models. We also developed engineering enzymes with improved production, secretion, and cross-correction capacity.
   a) *Cascino F, Ricca A, Picciotti I, Valeri E, Unali G, Saporito V, Freschi M, Morena F, Martino S, Kajaste-Rudnitski A, **Gritti A**. Chimeric enzymes enhance treatment potential for globoid cell leukodystrophy through hematopoietic stem cell gene therapy. **Mol Ther. 2025** Sep 22.*
   b) *Sala D, Ornaghi F, Morena F, Argentati C, Valsecchi M, Alberizzi V, Di Guardo R, Bolino A, Aureli M, Martino S, **Gritti A**. Therapeutic advantages of combined gene/cell therapy strategies in a murine model of GM2 gangliosidosis. **Mol Ther Methods Clin Dev. 2022** Jun 9;25:170-189.*
   c) *Ricca A, Cascino F, Morena F, Martino S, **Gritti A**. In vitro Validation of Chimeric β-Galactosylceramidase Enzymes With Improved Enzymatic Activity and Increased Secretion. **Front Mol Biosci. 2020**;7:167.*
   d) *Ornaghi F, Sala D, Tedeschi F, Maffia MC, Bazzucchi M, Morena F, Valsecchi M, Aureli M, Martino S, **Gritti A**. Novel bicistronic lentiviral vectors correct β-Hexosaminidase deficiency in neural and hematopoietic stem cells and progeny: implications for in vivo and ex vivo gene therapy of GM2 gangliosidosis. **Neurobiol Dis. 2020** Feb;134:104667*
3. Our pioneering rodent and non-human primate study validated lentiviral vector-mediated intracerebral gene therapy as a CNS-targeting strategy for clinical translation. We are actively working to develop the first-in-human LV-mediated intracerebral gene therapy targeting MLD patients who are not eligible to receive HSC GT, thus broadening the therapeutic options for this severe LSD.
   a) *Meneghini V, Lattanzi A, Tiradani L, Bravo G, Morena F, Sanvito F, Calabria A, Bringas J, Fisher-Perkins JM, Dufour JP, Baker KC, Doglioni C, Montini E, Bunnell BA, Bankiewicz K, Martino S, Naldini L, **Gritti A.** Pervasive supply of therapeutic lysosomal enzymes in the CNS of normal and Krabbe-affected non-human primates by intracerebral lentiviral gene therapy. **EMBO Mol Med. 2016** May;8(5):489-510.*
   b) *Lattanzi A, Salvagno C, Maderna C, Benedicenti F, Morena F, Kulik W, Naldini L, Montini E, Martino S, **Gritti A**. Therapeutic benefit of lentiviral-mediated neonatal intracerebral gene therapy in a mouse model of globoid cell leukodystrophy. **Hum Mol Genet. 2014** Jun 15;23(12):3250-68.*
   c) *Lattanzi A, Neri M, Maderna C, di Girolamo I, Martino S, Orlacchio A, Amendola M, Naldini L**, Gritti A**. Widespread enzymatic correction of CNS tissues by a single intracerebral injection of therapeutic lentiviral vector in leukodystrophy mouse models. **Hum Mol Genet. 2010** Jun 1;19(11):2208-27.*

4. Inspired by the discovery of induced pluripotent stem cells (iPSCs), I expanded my research to model early CNS development and generate renewable human NSC populations for disease modelling and cell therapy. My group showed that iPSC-derived neural progeny from MLD and GLD retain key pathological hallmarks, also enabling us to uncover early neuronal and glial defects. Additionally, we studied DNA damage responses and innate immune mechanisms of vector sensing in the CNS that could potentially contribute to AAV-associated neurotoxicity (collaborative study).
   a) *Costa-Verdera H, Meneghini V, Fitzpatrick Z, Abou Alezz M, Fabyanic E, Huang X, Dzhashiashvili Y, Ahiya A, Mangiameli E, Valeri E, Crivicich G, Piccolo S, Cuccovillo I, Caccia R, Chan YK, Bertin B, Ronzitti G, Engel EA, Merelli I, Mingozzi F,* ***Gritti A****, Kuranda K, Kajaste-Rudnitski A. AAV vectors trigger DNA damage response-dependent pro-inflammatory signalling in human iPSC-derived CNS models and mouse brain.* ***Nat Commun. 2025*** *Apr 18;16(1):3694.*
   b) *Giordano AMS, Luciani M, Gatto F, Abou Alezz M, Beghè C, Della Volpe L, Migliara A, Valsoni S, Genua M, Dzieciatkowska M, Frati G, Tahraoui-Bories J, Giliani SC, Orcesi S, Fazzi E, Ostuni R, D'Alessandro A, Di Micco R, Merelli I, Lombardo A, Reijns MAM, Gromak N,* ***Gritti A****, Kajaste-Rudnitski A. DNA damage contributes to neurotoxic inflammation in Aicardi-Goutières syndrome astrocytes.* ***J Exp Med. 2022*** *Apr 4;219(4)*
   c) *Mangiameli E, Cecchele A, Morena F, Sanvito F, Matafora V, Cattaneo A, Della Volpe L, Gnani D, Paulis M, Susani L, Martino S, Di Micco R, Bachi A,* ***Gritti A.*** *Human iPSC-based neurodevelopmental models of globoid cell leukodystrophy uncover patient- and cell type-specific disease phenotypes.* ***Stem Cell Reports. 2021*** *Jun 8;16(6):1478-1495.*
   d) *Frati G, Luciani M, Meneghini V, De Cicco S, Ståhlman M, Blomqvist M, Grossi S, Filocamo M, Morena F, Menegon A, Martino S,* ***Gritti A.*** *Human iPSC-based models highlight defective glial and neuronal differentiation from neural progenitor cells in metachromatic leukodystrophy.* ***Cell Death Dis. 2018*** *Jun 13;9(6):698.*
5. In addition to using hiPSC-derived neural progeny for mechanistic studies, my group has extensively characterised the heterogeneity within hiPSC-derived neural stem cell populations in a side-by-side comparison with somatic fetal-derived NSCs, and has demonstrated their long-term safety following intracerebral transplantation in mice.
   a) *Luciani M, Garsia C, Beretta S, Cifola I, Peano C, Merelli I, Petiti L, Miccio A, Meneghini V,* ***Gritti A.*** *Human iPSC-derived neural stem cells displaying radial glia signature exhibit long-term safety in mice.* ***Nat Commun. 2024*** *Nov 1;15(1):9433..*
   b) *Luciani M, Garsia C, Mangiameli E, Meneghini V, Gritti A. Intracerebroventricular transplantation of human iPSC-derived neural stem cells (hiPSC-NSCs) into neonatal mice.* ***Methods Cell Biol. 2022****;171:127-147.*
   c) *Luciani M,* ***Gritti A****, Meneghini V. Human iPSC-Based Models for the Development of Therapeutics Targeting Neurodegenerative Lysosomal Storage Diseases.* ***Front Mol Biosci. 2020****;7:224.*
   d) *Meneghini V, Frati G, Sala D, De Cicco S, Luciani M, Cavazzin C, Paulis M, Mentzen W, Morena F, Giannelli S, Sanvito F, Villa A, Bulfone A, Broccoli V, Martino S,* ***Gritti A.*** *Generation of Human Induced Pluripotent Stem Cell-Derived Bona Fide Neural Stem Cells for Ex Vivo Gene Therapy of Metachromatic Leukodystrophy.* ***Stem Cells Transl Med. 2017*** *Feb;6(2):352-368.*

Total publications: 85; Total citations: 9,838; h-Index: 37 (Source: Scopus, Nov 2025)
Scopus Author ID: 7004129522; ORCID ID: 0000-0002-9845-0370; Researcher ID: K-2729-2016

Complete list of publications at: https://www.ncbi.nlm.nih.gov/myncbi/1ls4kKbQ6tb/bibliography/public/

Professional activities.

I contribute to the scientific community by:

- Serving on **academic promotions, graduation, and PhD committees**
- Participating in **scientific committees**: Panel discussion, International Krabbe Think Tank London (UK) Session 3: Preclinical Data and Animal Models (2019); Panel discussion and invited speaker, ELA/MLD Research Group: Pathophysiology of Metachromatic Leukodystrophy (2019); AFM-Telethon, Strategic and Therapeutic Orientation Committee (2015); Italian Telethon Foundation, Patent Committee (2015-2016); ASGCT Neurologic & Ophthalmic Gene & Cell Therapy Committee (2022-2025; Chair in 2024).
- Reviewing **grant proposals** for national and international funding agencies: ERC starting grants, LS7 panel member (2022-2024); Italian Multiple Sclerosis Association; European Leukodystrophy Association (ELA); The Netherlands Organisation for Scientific Research (NWO); Health Research Board (HRB), Ireland; Sparks Children Medical Research, UK; Austrian Science Fund; Vaincre les maladies lysosomales (VLM), France; AFM Telethon, France; Istituto Superiore di Sanità (ISS), Italy. (e.g., ELA, INSERM, GOSH, NWO, UKRI, VLM)
- Reviewing **abstract submissions** for and scientific societies (ASGCT, ESGCT, ISSCR)
- **Editorial activity** - Editor of Research Topic: Neurodegenerative Lysosomal Storage Diseases (LSDs): Between Biology and Innovative Therapeutic Approaches (Frontiers in Molecular Biosciences)(2020)
- Serving as a **reviewer for international peer-reviewed journals**, including **Science, Cell Stem Cell, PNAS, Brain, GLIA, Cell Reports Medicine, Molecular Therapy, and other leading publications.**
- **Organizing meetings:** Course "The role of *glial cells in neurodegeneration*", Doctoral School in Molecular Medicine, May 5-8, 2026, Vita-Salute San Raffaele University, Milan, Italy; Course "Cellular and animal models in Neuroscience Research", Doctoral School in Molecular Medicine, Vita-Salute San Raffaele University Milan, Italy (2014); SR-Tiget Scientific Retreat,

Camogli (GE), Italy (2017); ELRIG Drug Discovery Meeting, Telford, UK, responsible for Track 3 - Cell & Gene Therapy (2015).

- **Communicating science:** In the period 2020-25, I have delivered 10 invited lectures, five of which took place outside Italy, on topics including neural stem cells and gene and cell therapy.
- **Promoting public engagement** by communicating research to lay audiences (e.g., **Annual Telethon Marathon),** discussing with high school students about gene therapy and the societal role of science, contributing video interviews and editorial content, and engaging with patient communities (e.g**., European Leukodystrophy Association and National Tay-Sachs and Allied Diseases Family Meetings).**

Funding

Since 2010, I have been the principal or co-principal investigator of grants from the Italian Telethon Foundation, Italian Ministry of Health, Italian Multiple Sclerosis Association, European Leukodystrophy Association (ELA), National Tay-Sachs and Allied Disease Association (NTSAD), European Joint Program for Rare Diseases, Vaincre les Maladies Lisosomiales (VML), Bespoke Gene Therapy Consortium (BGTC), and AFM-Telethon.

Active grants

- ***2025-2026*** *AFM-Telethon (ID 2940) Hematopoietic Stem Cell Gene Therapy (HSC GT) for GM2 Gangliosidosis: Advancing Therapeutic Efficacy and Translational Potential (HStemGT-GM2).* **Role: P.I.**
- ***2025-2027*** *Fondazione Italiana Sclerosi Multipla (FISM) – progetto speciale.* **H**ematopoietic stem cells engineered to release therapeutic **ex**t**ra**cell**ul**ar v**es**icles in the central nervous system: a novel treatment platform for multiple sclerosis (HERCULES). **Role P.I.**
- ***2022-2026*** *Fondazione Telethon TTAGD0222TT.* Exploiting novel gene therapy platforms and human-based pre-clinical models to understand biology and advance the treatment of genetic neurodegenerative and demyelinating diseases. **Role: P.I.**
- ***2022-2026*** *Bespoke Gene Therapy Consortium (BGTC) FNIH RFP NUMBER: 2022-BGTC003*. Investigating Innate Sensing and Antiviral Restriction of AAV vectors in the Human Central Nervous System. **Role: Co-P.I**. (P.I: A. Kajaste-Rudnitski)

Completed grants

- ***2023-2025*** *European Leukodystrophy Association (ELA) ELA 2022-009C2.* Development of editing technologies to treat Alexander's disease. **Role: P.I.**
- ***2023-2025*** *European Leukodystrophy Association (ELA) ELA 2022-006C2.* Liver-directed gene therapy with enhanced-bioavailability transgenes to treat nervous system pathology in globoid cell leukodystrophy. **Role: co-PI** (P.I. A. Cantore).
- ***2024-2025*** *National Tay-Sachs and Allied Disease Association (NTSAD). ENHANCING THE THERAPEUTIC POTENTIAL OF HEMATOPOIETIC STEM CELL GENE THERAPY TO TREAT GM2 GANGLIOSIDOSES. PILOT PROJECT* **Role: P.I.**
- ***2020-2023*** *European Joint Programme on Rare Diseases (EJP RD).* Exploring neuron-glia interactions in leukodystrophies using human iPSC-based models: implication for therapy (NG4Leuko). **Role: Responsible of Research Unit**
- ***2022-2023*** *Vaincre les Maladies Lysosomales (VML).* Dissecting the post-translational modifications of Arylsulfatase A (ARSA) in human myeloid cells: relevance for hematopoietic stem cell GT in Metachromatic Leukodystrophy. **Role: P.I.**
- ***2020-2022*** *European Leukodystrophy Association (ELA) ELA 2019-015I2.* Development of chimeric lysosomal enzymes with improved bioavailability to advance gene therapy strategies for globoid cell leukodystrophy. **Role: P.I.**
- ***2021-2022*** *European Leukodystrophy Association (ELA) ELA 2020-011I2.* Evaluating the mechanisms of macrophage/microglia-mediated enzymatic cross-correction of human MLD neurons and glial cells in vitro. **Role: P.I.**
- ***2018-2021*** *(extended to 2023) Italian Ministry of Health RF-2016-02362404.* Exploiting targeted epigenetic editing to increase efficiency and safety of oligodendroglial progenitor cell generation from human iPSC: implications for cell therapy of leukodystrophies. **Role: P.I.**
- ***2016-2021*** *Fondazione Telethon TGT16D02.* Lysosomal Storage Disorders: Modelling the disease complexity to refine gene/cell therapy treatment strategies. **Role: P.I.**

Members of A. Gritti's lab have been awarded fellowships/grants from:

- Fondazione U. Veronesi Post-doctoral Fellowships 2016 (A. Ricca)
- Fondazione Centro San Raffaele Post-doctoral Fellowship 2018 (E. Mangiameli) and 2019 (F. Cascino)
- Italian Ministry of Health (GR-2019-12368930 to V. Meneghini; GR-2019-12369357 to A. Ricca)
- Marie Skłodowska-Curie Actions (2020-2022 H2020-MSCA-IF-2019 to V. Meneghini)
- US Department of Defence (FY21 MS Research Program Early Investigator Research Award 2021 to M. Luciani).

Milano, 26.03.2026