

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Alessia Cavazza

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Associate Professor in Molecular Biology at University of Modena and Reggio Emilia; Honorary Associate Professor in Gene Therapy at University College London

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Faculty of Life Sciences, University of Modena and Reggio Emilia, Italy	BSc	23/10/2006	Biotechnology
Faculty of Life Sciences, University of Modena and Reggio Emilia, Italy	MSc	23/10/2008	Medical Biotechnology
Faculty of Life Sciences, University of Modena and Reggio Emilia, Italy	PhD	28/03/2012	Molecular and Regenerative Medicine

A. Personal Statement

I am currently Associate Professor in Molecular Biology at the University of Modena and Reggio Emilia (UNIMORE, Italy) and Director of the Laboratory of Gene editing for Rare Diseases at the Center for Molecular Medicine and Rare Diseases. I am also a Group Leader at University College London (UCL) Institute of Child Health and Honorary Associate Professor in Gene Therapy at UCL (UK). I have over 15 years of professional experience in the design and implementation of strategies to treat human diseases, with a particular focus on stem cell biology, genetic diseases and the development of therapeutic platforms to tackle them.

As a PhD student in Prof. Mavilio's group at UNIMORE, I worked on projects aimed at investigating the molecular characteristics of human stem cells, by producing and integrating genome-wide epigenomic and transcriptomic data with a new retroviral scanning technology I developed to prospectively mark regulatory regions in epidermal stem cells, which lack a definitive set of markers for their isolation. In 2013, I moved to Prof Shivdasani's lab at Harvard Medical School (USA) as a Postdoctoral Fellow, and was later on awarded with a postdoctoral fellowship from the American-Italian Cancer Foundation, providing me with independent salary support. The project I proposed involved the discovery of transcriptional regulators of aggressive colorectal cancer and then converged into the study of the developing embryonic intestine and intestinal stem cells, with a combination of omics technologies and transgenic animal models. After 7 years spent in the field of stem cell biology and omics, I felt the urge to combine my acquired experience in basic biology with my interest in translational science, hence in 2016 I moved to one of the world-leading centers for pediatric diseases and gene therapy at UCL as a Senior Postdoc; one year later, I joined the UCL faculty with a tenured Assistant Professor position in Gene Therapy followed by promotion to Associate Professor in 2023. In 2024, I achieved tenure also at UNIMORE, where I moved my main research activities.

My interdisciplinary research combines the study of stem cell biology at different scales with the development of therapeutic platforms for genetic disorders. Throughout my career, I have operated in highly interdisciplinary environments, serving as an intellectual bridge between molecular biology, genomics, and translational application. My role has progressively evolved toward conceptual leadership, reflected by senior and corresponding authorship, responsibility for experimental design and data integration, and the training of junior scientists (7 postdocs, 4 PhD students, 2 Research Associates, >20 BSc/MSc students). Since establishing my independent group, I have earned international peer recognition, resulting in major outcomes such as:

- 12. >4M € in funding obtained as Principal Investigator (2.4M € in the UK and 1.9M € in Italy), including from United Kingdom Research and Innovation Medical Research Council (UKRI), LifeArc, GOSH Charity, Fondazione Telethon and Fondo Italiano per la Scienza (FIS);
- 12. leading role as a) chair of the European COST Action CA21113 Gene-HumDi, where I coordinate a network of 350 scientists from 28 different countries working on drug delivery and advanced therapies for human diseases (<https://www.cost.eu/actions/CA21113/>); b) Founding Partner and Executive Board member of the European Genomic Medicine Consortium (EGMEDC)
- 12. invitations to speak at >30 prominent conferences, including those of the EMBO, American Society of Haematology, European Bone Marrow Transplant Society, TEDx; selection of oral talks at >10 congresses;
- 12. establishment of a strong and international collaborative network;
- 12. filing of one patent, licensing of a therapeutic gene editing platform to Danaus Pharma and obtaining Orphan Drug Designation for the platform from EMA and FDA (see Contribution to science).

Taken together, my track record demonstrates sustained independence, methodological depth, sustained productivity across career stages, and a consistent ability to translate mechanistic insight into therapeutic innovation. The core scientific competencies I bring, barrier interrogation, genome-wide profiling, delivery biology, and quantitative analysis of gene editing, provide a robust and credible foundation for extending genome editing into new biological territories. I believe that this combination of methodological depth, conceptual continuity, and translational vision positions me well to pursue ambitious, high-risk questions at the interface of fundamental biology and therapeutic innovation.

B. Positions, Scientific Appointments, and Honors

Positions

- 2024 - Present **Associate Professor in Molecular Biology and Group Leader**
School of Medicine, University of Modena and Reggio Emilia, Modena, Italy
- 2024 - Present **Honorary Associate Professor in Gene Therapy and Group Leader**
Faculty of Population Health Sciences, University College London, UK
- 2023 – 2024 **Associate Professor in Gene Therapy and Group Leader**
Faculty of Population Health Sciences, University College London, UK
- 2017 – 2023 **Lecturer in Gene Therapy and Group Leader**
Great Ormond Street Institute of Child Health, University College London, London, UK
- 2016 – 2017 **Senior Research Associate** (Supervisor: Prof Adrian J Thrasher)
Ormond Street Institute of Child Health, University College London, London, UK
- 2013 – 2016 **Postdoctoral Fellow** (Supervisor: Prof Ramesh Shivdasani)
Dana Farber Cancer Institute, Harvard Medical School, Boston, USA
- 2012 – 2013 **Postdoctoral Fellow** (Supervisor: Prof Fulvio Mavilio)
Centre for Regenerative Medicine, University of Modena and Reggio Emilia, Italy

Scientific Appointments

- 2025 – Founding Partner and Executive Board member, European Genomic Medicine Consortium
- 2023 – Scientific Committee member, CRISPR Medicine
- 2022 – Co-chair, EU Horizon 2020 COST Action CA21113

2022 – 2022 Member, Scientific Advisory Board, Resolution Therapeutics
2019 – 2021 Scientific Consultant, Orchard Therapeutics

Honors

2014 – 2016 **Research For Life Postdoctoral Fellowship**, American Italian Cancer Foundation, USA
(host institution: Dana Farber Cancer Institute, Harvard Medical School, USA)
2014 – 2016 **PhD Scholarship**, Italian Ministry of Education, Italy
2007 – 2007 **Scholarship**, 6th Framework Programme of the European Commission (host institution: University College London, UK)

C. Contributions to Science

Manuscripts: 30 (+ 3 submitted/in preparation); Citations: 936; H index: 16.
(7 as first author, 12 as corresponding author (*))

1. Defining stem cell identity through integrative functional genomics

My early work established integrative strategies to define the molecular identity of human stem cells lacking definitive surface markers. By combining genome-wide epigenomic and transcriptomic profiling with a novel retroviral scanning approach, I prospectively marked regulatory elements controlling epidermal and hematopoietic stem cell function. This work provided mechanistic insight into stem cell heterogeneity and self-renewal and introduced tools to functionally interrogate regulatory landscapes in rare cell populations.

Representative outputs:

1. **Cavazza, A.**, Miccio, A., Romano, O., Petiti, L., Malagoli Tagliazucchi, G., Peano, C., ...Mavilio F. (2016). Dynamic Transcriptional and Epigenetic Regulation of Human Epidermal Keratinocyte Differentiation. STEM CELL REPORTS (CELL PRESS), 6 (4), 618-632. doi:10.1016/j.stemcr.2016.03.003
2. Romano, O., Peano, C., Tagliazucchi, G.M., Petiti, L., Poletti, V., Cocchiarella, F., Rizzi E., Severgnini M., **Cavazza A.** ...Miccio A. (2016). Transcriptional, epigenetic and retroviral signatures identify regulatory regions involved in hematopoietic lineage commitment. SCIENTIFIC REPORTS, 6 doi:10.1038/srep24724

2. Revealing chromatin-encoded plasticity in adult stem cell systems

During my postdoctoral training at Harvard Medical School, I helped redefine how lineage commitment is regulated in self-renewing tissues. By integrating single-cell transcriptomics, epigenomics, and in vivo functional models, I contributed to the discovery of multilineage transcriptional priming and reversible intermediate states in adult stem cells. These studies established a conceptual framework in which biological barriers to cell fate are regulatory and plastic rather than fixed, with broad implications for regeneration and disease.

Representative outputs:

3. Cejas, P., **Cavazza, A.**, Yandava, C., Moreno, V., Horst, D., Moreno-Rubio, J., ...Shivdasani R.A. (2016). Transcriptional regulator CNOT3 defines an aggressive colorectal cancer subtype.. CANCER RESEARCH, doi:10.1158/0008-5472.CAN-16-1346
4. Jadhav, U., **Cavazza, A.**, Banerjee, K.K., Xie, H., O'Neill, N.K., Saenz-Vash, V., ...Shivdasani R.A. (2019). Extensive Recovery of Embryonic Enhancer and Gene Memory Stored in Hypomethylated Enhancer DNA. MOLECULAR CELL, 74 (3), 542-554. doi:10.1016/j.molcel.2019.02.024
5. Murata, K., Jadhav, U., Madha, S., van Es, J., Dean, J., **Cavazza, A.**, ...Shivdasani, R.A*. (2020). Ascl2-Dependent Cell Dedifferentiation Drives Regeneration of Ablated Intestinal Stem Cells. CELL STEM CELL, 26 (3), 377-+. doi:10.1016/j.stem.2019.12.011

3. Enabling safe and effective therapeutic genome editing in human stem cells

As an independent investigator, I established a translational research program focused on overcoming fundamental barriers to therapeutic genome editing, from ex vivo manipulation of human hematopoietic

stem cells to systemic in vivo delivery across biological barriers. My team developed optimized culture and editing strategies that preserve stemness while enabling efficient and durable genome modification, enabling the first CRISPR-based correction strategy for Wiskott–Aldrich syndrome to advance from proof-of-concept to advanced preclinical validation, licensing to Danaus Pharma, and Orphan Drug Designation from the EMA. In parallel, I pioneered receptor-targeted virus-like particle platforms for systemic and in utero delivery of genome and base editors, including first-in-field studies targeting the brain and hematopoietic system in Krabbe disease.

Representative outputs:

6. Rai, R., Romito, M., Rivers, E., Turchiano, G., Blattner, G., Vetharoy, W., ... **Cavazza, A***. Targeted gene correction of human hematopoietic stem cells for the treatment of Wiskott - Aldrich Syndrome. NATURE COMMUNICATIONS, 2020, 11 (1), doi:10.1038/s41467-020-17626-2
7. Rai R, Vetharoy W, Naseem A, Steinberg Z, Thrasher AJ, Santilli G, **Cavazza A***. Optimized cell culture conditions promote ex-vivo manipulation and expansion of primitive hematopoietic stem cells for therapeutic gene editing. MOLECULAR THERAPY – METHODS AND CLINICAL DEVELOPMENT (CELL PRESS). 2023 Feb 28;29:58-69. doi: 10.1016/j.omtm.2023.02.014
8. Rai R, Steinberg Z, Romito M, Zinghirino F, Hu Y, White N, Naseem A, Thrasher AJ, Turchiano G, **Cavazza A***. CRISPR/Cas9-Based Disease Modeling and Functional Correction of Interleukin 7 Receptor Alpha Severe Combined Immunodeficiency in T-Lymphocytes and Hematopoietic Stem Cells. HUMAN GENE THERAPY. 2024 Apr;35(7-8):269-283.
9. Bahal S, Zinicola M, Moula SE, Whittaker TE, Schejtman A, Naseem A, Blanco E, Vetharoy W, Hu YT, Rai R, Gomez-Castaneda E, Cunha-Santos C, Burns SO, Morris EC, Booth C, Turchiano G, **Cavazza A**, Thrasher AJ, Santilli G. Hematopoietic stem cell gene editing rescues B-cell development in X-linked agammaglobulinemia. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY. 2024 Jul;154(1):195-208.e8.
10. Whittaker TE, Moula SE, Bahal S, Bakri FG, Hayajneh WA, Daoud AK, Naseem A, **Cavazza A**, Thrasher AJ, Santilli G. Multidimensional Response Surface Methodology for the Development of a Gene Editing Protocol for p67^{phox}-Deficient Chronic Granulomatous Disease. HUMAN GENE THERAPY. 2024 Apr;35(7-8):298-312.
11. Naseem A, Vetharoy W, Whittaker TE, Zinghirino F, Ghosh R, Gomez Castaneda E, Ali H, Cipriani C, Montini E, Thrasher AJ, Santilli G, Cesana D, Turchiano G, **Cavazza A.*** In-Depth Characterization of Stem Cell Potency and Genotoxicity for Clinical-Scale Ex Vivo CRISPR/Cas9 Gene Editing. Accepted in MOLECULAR THERAPY ADVANCES, 2026; Bioarchive link: <https://doi.org/10.64898/2026.01.08.698401>

4. Establishing quantitative frameworks for genome-editing safety and genotoxicity

To address a critical translational gap, I co-developed CLEAR-Time, a quantitative framework for assessing genome-editing genotoxicity across clinically relevant cell types. By integrating single-cell editing assays, deep sequencing, and computational modeling, this work provided unprecedented mechanistic insight into how genome editors engage endogenous DNA repair pathways in human stem cells, setting new standards for preclinical safety assessment. In earlier works, I developed and applied a high-throughput pipeline based on LM-PCR to map and dissect retroviral vector integration and genotoxicity in the genome of human stem cells.

Representative outputs:

12. White N, Chalk JA, Hu YT, Pins SM, Joseph CR, Antoniou P, Wimberger S, Svensson S, Caetano-Silva SP, Mudde ACA, Rai R, Selvaraj S, Feist WN, Romito M, Sienski G, Nitsch R, Booth C, Santilli G, **Cavazza A**, Porteus MH, Maresca M, Thrasher AJ, Turchiano G. Unveiling the cut-and-repair cycle of designer nucleases in human stem and T cells via CLEAR-time dPCR. NATURE COMMUNICATIONS, 2025;16(1):9571.
13. White N, Hu Y, Chalk J.A, Kurgan G, Schmaljohn E, Sturgeon M, **Cavazza A**, Thrasher A.J, Turchiano G. DNA-PKcs inhibitor AZD7648 reveals 1 gRNA cross-contaminants and enhanced sensitivity of genome engineering off-target activity in HSPCs. Accepted in Nucleic Acid Research
14. **Cavazza, A.**, Cocchiarella, F., Bartholomae, C., Schmidt, M., Pincelli, C., Larcher, F., Mavilio, F. (2013). Self-inactivating MLV vectors have a reduced genotoxic profile in human epidermal keratinocytes. GENE THERAPY, 20 (9), 949-957. doi:10.1038/gt.2013.18

15. International Patent "Multipurpose editing genotoxicity assessment (MEGA): ddPCR for safety monitoring in gene therapy". Inventors (in order of contribution): Giandomenico Turchiano, Alessia Cavazza, Adrian Thrasher, Nathan White (WO2023079285).

Complete List of Published Work:

<https://unimore.unifind.cineca.it/get/person/091526>