Maria Chiara Bonini CV

Current Position

- Professor of Hematology, Università Vita-Salute San Raffaele, School of Medicine, Milan, Italy.
- Head of the Experimental Hematology Unit, IRCCS Ospedale San Raffaele (OSR) Milano, Italy.
- Member of the Stem Cell Programme, OSR.
- Member of the Division of Immunology, Transplantation and Infectiuous Diseases, OSR.

Education

1994- Medicine (summa cum laude)Università degli Studi, Medical School, Milan, Italy

1998 - Board in Hematology (summa cum laude), University of Pavia, Pavia, Italy

Positions

1991-1994	Undergraduate student, Experimental Hematology, OSR, Milano, Italy
1993	Undergraduate summer student, Bone Marrow Transplantation Unit, MSKCC, New York.
1995-1997	Medical fellow, Bone Marrow Transplant Unit, OSR.
1996-1998	Post-doctoral fellow, TIGET (Telethon Institute for Gene Therapy), DIBIT, OSR.
1998-2000	Post-doctoral fellow, Program in Immunology, FHCRC Seattle.
1998-2004	Hematologist, Bone Marrow Transplant Unit, OSR (leave of absence 1998-2000).
2000-2008	Group Leader, Experimental Hematology Unit, OSR.
Since 2008	Head of the Experimental Hematology Unit, OSR.
2014-2023	Deputy Director Division of Immunology, Transplantation and Infectious Diseases, OSR
Since 2015	Professor, Università Vita-Salute San Raffaele (UniSR), School of Medicine, Milan, Italy.

Selected honors

1999-2001	Cancer Research Institute Fellowship, NY, USA
2005	Young Investigator Award. American Society of Gene Therapy
2010	Team Science Recognition Award (iSBTC, now SITC)
2012 and 2016	Van Bekkum Award. European Society of Bone Marrow Transplantation (EBMT)
2012 and 2015	Van Rood Award. European Federation of Immunogenetics (EFI)
2013	Jon Van Rood Award. Immunobiology Working Party EBMT
2014 and 2017	Basic Science Award, EBMT.
2016	Melvin Jones Fellow for Humanitarian Services, Lions International.
2019-2026	Coordinator of the Research Program AIRC 5x1000, call on Metastases.
2020:	Excellence in Science Award. ASGCT
2023-	Member of the Editorial Board of Blood Cancer Discovery
2024-2026	TRTH Joint Oversight Subcommittee (EHA and ASH)
2024	Scientific committee of the 1st ASGCT Spotlight on Cancer Gene Therapy" Conference.

Professional and scientific activities

- Past member of the boards of the European (ESGCT) and American (ASGCT) societies of cell and gene therapy and the European bone marrow transplantation Society (EBMT), the Award Committee of the American Sociery of Hematology (ASH). Current member of the Board of European School of Hematology (ESH) and European Society of Hematology (EHA); Member of the Pezcoller Symposia Scientific Standing Committee.
- Since 2017, In charge of the class "Hematology", School of Medicine- International MD Program, UniSR, of the class "Cell and Gene Therapy", School of Biotechnology, UniSR, Secretary Specialty School of Hematology, UniSR. 2019-2023: Member of the Pedagogic Committee, School of Biotechnology, UniSR. Since 2021 Member of the Board of the PhD Program in Molecular Medicine, Gene Therapy branch, UniSR. Since 2022: In charge of the "Translational Track" School of Medicine- International MD Program, UniSR
- Her research team has been funded from the Italian Ministry of University and Research (MIUR, PRIN, and FIRB-ideas associated to ERC starting grant program), Telethon, the Italian Ministry of Health, The European Union (FP-IV, FP-V, FP-VI, FP-VII, H2020), the Italian Association for Cancer Research (AIRC), Fondazione Cariplo. In 2019 she received funding as a PI of an AIRC 5x1000 Program. She is a member of several EU funded projects aimed at fostering T cell therapy in Europe (ie: T2Evolve, Join4ATMP) and a founder of the GoCART Coalition, that brings together members of the EBMT and EHA Board of Directors, to foster and facilitate the access to engineered T cells by cancer patients.
- Member of expert Review Panels: French National Cancer Institute (INCA) Paris (2008…2023), Member of the Safety Board of the TRACE clinical Trial (since 2020), ASH global Awards (2019-2022); TRTH (2022-2023), ERC.

Scientific Production

The scientific production includes 176 papers in international scientific journals. Scopus "h" index: 60 and 9 international patents, largely already granted and licensed. ORCID N. 0000-0002-0772-1674. SCOPUS AUTHOR ID- 57211285047; Web of Science-REASERCHER ID: I-9202-2012. Invited speaker to more than 200 International Meetings, Workshops and Universities.

Research Activity

The main research focus of my lab is the development, preclinical and clinical validation of T-cell based gene therapy approaches to treat cancer. I had the privilege to initiate the preclinical and clinical use of suicide gene therapy applied to allogeneic stem cell transplantation (allo-HSCT). This approach aims at benefitting from the ability of the donor immune system to recognize cancer cells (graft-versus-leukemia), while selectively controlling the graft-versus-host disease) its major complication. Pioneered in OSR in the '90s (Bonini et al., Science 1997), optimized and tested in different academic and, since 2000, industry-sponsored clinical trials, (Bonini et al., Nat Med 2003; Ciceri et al., Blood 2007; Ciceri, Bonini et al, Lancet Oncology 2009; Vago et al., Blood 2012; Oliveira et al.. Science Translational Medicine 2015), the suicide gene therapy approach has obtained approval from EMA in 2016, thus representing the first cell based gene therapy product approved for cancer patients in Europe. I have been involved in every step of this long and exciting scientific path, thus learning important lessons on the many hurdles that need to be faced to foster cellular therapy from the pioneering phase to the stage of real life. I then exploited this experience in projects designed to redirect T cell specificity against tumor antigens.

My lab is currently focused on cancer immunotherapy (Meric-Bernstam et al, The Lancet 2020), genetic manipulation of T cells, including TCR/CAR gene transfer (Norelli et al, Nat Med 2018; Greco B., STM 2023, Manfredi et al, Front Immunol 2020, Bonini HGT, 2023). A major achievement is represented by the TCR gene editing platform (Provasi, Genovese et al., Nature Medicine 2012; Mastaglio et al., Blood 2017; Ruggiero et al., STM 2022, Potenza, Balestrieri et al., GUT 2023). This approach aims at redirecting T cell specificity against tumor antigens through genome editing. We initially exploited zinc finger nucleases (ZFN), and more recently CRISPR/Cas9, to efficiently disrupt the endogeneous TRAC and TRBC genes, thus allowing to completely redirect T cell specificity through the gene transfer of a tumor specific TCR in mature T cells. TCR edited T cells proved more effective and specific than T cells modified by TCR gene transfer in vitro and in vivo. The project has been validated with TCRs specific for WT1 and NY-ESO-1 derived peptides. We are currently exploiting TCRs specific for additional tumor antigens, recently isolated in the lab. With this project we learned to edit the genome of T cells in conditions that do not perturb their homeostasis, and that allow to preserve an early functional differentiation phenotype.

In recent years the experience gained in the context of T cell therapy for hematological malignancies has been translated to face the challenge of solid tumors. Through an Institutional effort, involving 18 clinical and preclinical research teams in the Institute, and through dedicated funding from AIRC 5x1000, we set up a pipeline of new ATMPs designed to be active in patients with liver metastases from CRC and PDAC (ie: Potenza, Balestrieri et al., GUT 2023, Caronni et al., Nature 2023, https://research.hsr.it/en/divisions/immunology-transplantation-and-infectious-diseases/airc-5x1000-advanced-therapies-for-liver-metastases.html).

An additional relevant activity of the lab is represented by the Immunomonitoring sub-Unit. This section of the lab is dedicated to the analyses of immunological correlates with clinical outcome in the context of hematopoietic stem cell transplantation (ie: Cieri et al., Blood 2015; Peccatori et al., Leukemia 2015; Greco BBMT 2016, Tassi et al., Haematologica 2023; Noviello et al., Blood Adv 2023), cellular therapy (ie: Noviello, Mol. Ther. 2014; Cossu, EMBO Mol. Med. 2015;) and Gene Therapy (ie: Mavilio, et al., Nat. Med. 2006; Biasco et a., STM 2015). In recent years we investigated the role of central memory (T_{CM}) and memory stem T cells (T_{SCM}) in allo-HSCT and in gene therapy clinical trials. These T cell subsets proved endowed with high expansion and persistence ability, and innovative protocols for their in vitro expansion, genetic engineering and multiple genome editing have been developed in the lab (Kaneko et al., Blood 2009, Bondanza et al., Blood 2011, Cieri et al., Blood 2013, Cieri et al., Blood 2015, Oliveira, STM 2015; rev in Gattinoni et al., Nat Med 2017; Cianciotti et al, Arthritis Rheumatol 2020;72:565-575, Ruggiero et al., STM 2023).

During my mandate as Chair of the Cellular Therapy and Immunobiology Working Party of EBMT I worked at a European Cellular Therapy Registry, to collect clinical information on patients receiving cell and gene therapy products in Europe. The Registry has recently received a regulatory qualification from EMA as a proper registry to support novel CAR T-cell and other gene therapies (https://www.ebmt.org/ebmt/news/ebmt-receives-regulatory-qualification-european-medicine-agency-ema-use-its-patient, 2019). As a member of the EHA board of Director, I am actually involved in the GoCART Coalition (https://thegocartcoalition.com), that brings together members of the EBMT and EHA Board of Directors, to foster and facilitate the access to engineered T cells by cancer patients.

My major aim today, is to actively participate to the exciting transition of cellular therapy from the investigational phase to the phase of real life by developing and validating at preclinical and clinical level innovative cellular therapy products for cancer and autoimmune diseases.