

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: Mazza, Massimiliano

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

POSITION TITLE: Principal Investigator and Coordinator of the Adoptive CAR T cell platform at IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" (IRST)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
University of Bologna	BSc	12/2001	Biotechnology
European Molecular Biology Laboratory (EMBL; Heidelberg) University of Milan Joint degree	PhD	12/2006	Genetics and Molecular Biology
European Institute of Oncology (Milan)	Postdoctoral	04/2017	Preclinical Experimental Oncology
IRCCS Istituto Romagnolo per lo Studio dei Tumori 'Dino Amadori' (IRST)	Principal Investigator	today	Translational Oncology, Molecular Immunology, Infectious Diseases

A. Personal Statement

I am a Principal Investigator at the IRCCS Istituto Romagnolo per lo Studio dei Tumori 'Dino Amadori' (IRST) located in Meldola (FC) and I coordinate a group of 11 researchers, 4 Postdocs and 7 PhD students affiliated with the University of Bologna.

I have a broad background on molecular biology, genetics and vector design that I have applied to disease models along my career to answer specific questions or improve disease models features. Currently, the subject my lab is mainly involved and interested in relates to molecular immunology that we explore from several perspectives. At first we are interested in investigating adaptive immunity in patients affected by cancer via B cell receptor and T cell receptor repertoire analysis by means of NGS technology from human matrices (i.e. blood, tissue). Second, we use molecular biology driven approaches like classical cloning to reconstruct those receptors and test their ability to target cancer cells as well as performing novel screenings by means of phage display technology.

We are interested in modulating the functions of human immune effector cells by genetic engineering and editing and we work to produce vectors with this purpose on primary human T and iPSCs. After COVID in 2020 we dedicated a lot of efforts also in trying to understand several aspects of the disease such as the role of sex hormones in defining disease severity and ACE2 receptor and TMPRSS2 expression in tissues, the analysis of T cell response specific to SARS-CoV-2 proteins and the definition of an anti-viral strategy called PACECOR to prevent mammalian cell infection by Coronaviridae targeting ACE2.

As PI or co-Investigator on university- and MoH-funded grants, I laid the groundwork for the proposed research by developing effective projects on rare tumors such as neuroendocrine tumors and

mesothelioma and performed immunological analyses for companies provided as a service or on a collaborative basis. In summary, I have the expertise, leadership, training, expertise, and motivation necessary to successfully carry out the proposed research project.

Ongoing and recently completed projects that I would like to highlight include:

E43C24000270007

Project Proof of Concept PNRR TOGGLER

Coordinator Dr. Bianchi, Role: co-investigator

01/01/2024-31/12/2026

E43C23000610005

Project Proof of Concept PNRR LIFEBELT

Coordinator Prof. Calabrò (PI), Role: co-investigator

01/09/2024-31/08/2026

E43C23000600005

Project Proof of Concept PNRR MIRAGE

Coordinator Prof. Zatelli (PI), Role: co-investigator

31/08/2024-31/08/2026

B49J23002010005

FIDIA project "Accordi per l'Innovazione"

Takis Biotechnology, Role: co-investigator

01/05/2022-30/04/2025

GreenVax project "Accordi per l'Innovazione"

Special SpA, Role: co-investigator

IRST funded project "PACECOR"

Dr. Mazza (PI)

01/01/2021-31/12/2024

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2020– Present	Leader of IRST Adoptive CAR T Cell Therapy platform at IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori" (SSD of Advanced Cellular Therapies and Rare Tumors)
2017 – 2020	Principal investigator at IRST IRCCS
2022	Invited speaker to SOHO Italy and ITCRC meeting
2021	Invited speaker to SOHO Italy, SOHO CAR T School and ITCRC meeting
2011	Cancer stem cells – hope for the future? Science in School Journal (2011) vol.21, pp.18-22 http://www.scienceinschool.org/sites/default/files/teaserPdf/issue21_cscs.pdf

2008	Invited speaker to ELLS (European Learning Labs) course EMBL Heidelberg
2007	Invited speaker to ELLS (European Learning Labs) course EMBL Monterotondo
2006	Lecture on “Life cycle and molecular biology in <i>S.cerevisiae</i> ” at the Università di Bologna (3rd year Biotech Class), Italy
2004	Set up of a yeast molecular biology course at EMBL Monterotondo, Italy

Honors

2020	Collaborator of the AIFA project “Retreatment” together with Fondazione Tettamanti Monza, ASST Papa Giovanni XXIII Bergamo
2019	ACT4COVID international multicentric project awarded by CellNex
2019	National CAR T project from the Ministry of Health under the aegis of Alleanza Contro il Cancro
2019	Multicentric mesothelioma project promoted by AFeVA
2019	Post-doctoral fellowship awarded by FUV to Dr. Nicolini
2018	Post-doctoral fellowship awarded by FUV to Dr. Nicolini
2017	Post-doctoral fellowship awarded by FUV (Fondazione Umberto Veronesi)
2014-2015	18 months Research Enhancement Package grant awarded by CEN (Centro Europeo di Nanomedicina)
2013-14	Research fellowship awarded by FUV (Fondazione Umberto Veronesi)
2013	Funding for projects on children disease awarded by Vogue
2009-2011	Long term fellowship awarded by FIRC (Fondazione Italiana Ricerca sul Cancro)

C. Contributions to Science

2019 – Present	PhD tutor (XXXIX-XXXVIII-XXXIV cycle at the DIBINEM department of the University of Bologna)
2011	Cancer stem cells – hope for the future? Science in School Journal (2011) vol.21, pp.18-22 http://www.scienceinschool.org/sites/default/files/teaserPdf/issue_21_cscs.pdf
2009-2011	BSc thesis supervisor of 3 students enrolled at the Università degli Studi di Milano diploma thesis performed at the Experimental Oncology Department (IEO)

Complete List of Published Work:

- Mazzotti, L., Gaimari, A., Bravaccini, S., Maltoni, R., Cerchione, C., Juan, M., Navarro, E.A.-G., Pasetto, A., Nascimento Silva, D., Ancarani, V., Sambri, V., Calabrò, L., Martinelli, G., **Mazza, M.** T-Cell Receptor Repertoire Sequencing and Its Applications: Focus on Infectious Diseases and Cancer (2022) *International Journal of Molecular Sciences*, 23 (15), art. no. 8590, DOI: 10.3390/ijms23158590
- Egri, N., Olivé, V., Hernández-Rodríguez, J., Castro, P., De Guzman, C., Heredia, L., Segura, A.C., Fernandez, M., de Moner, N., Torradeflot, M., Ballús, J., Martinez, R., Vazquez, M., Costa, M.V., Dobaño, C., **Mazza, M.**, Mazzotti, L., Pascal, M., Juan, M., González-Navarro, E.A., Calderón, H. CoVITEST: A Fast and Reliable Method to Monitor Anti-SARS-CoV-2 Specific T Cells From Whole Blood (2022) *Frontiers in Immunology*, 13, art. no. 848586, DOI: 10.3389/fimmu.2022.848586
- Silva, D.N., Chrobok, M., Rovesti, G., Healy, K., Wagner, A.K., Maravelia, P., Gatto, F., **Mazza, M.**, Mazzotti, L., Lohmann, V., Sällberg Chen, M., Sällberg, M., Buggert, M., Pasetto, A. Process Development for Adoptive Cell Therapy in Academia: A Pipeline for Clinical-Scale Manufacturing of Multiple TCR-T Cell Products (2022) *Frontiers in Immunology*, 13, art. no. 896242 DOI: 10.3389/fimmu.2022.896242
- Bravaccini, S., Nicolini, F., Zanoni, M., Gaimari, A., Cerchione, C., Maltoni, R., Pirini, F., Mazzotti, L., Cortesi, M., Ravaioli, S., Tumedei, M.M., **Mazza, M.** Why the complications of COVID-19 patients differ in elderly and young cancer patients (2022) *Translational Oncology*, 26, art. no. 101541, DOI: 10.1016/j.tranon.2022.101541
- Martino, M., Naso, V., Loteta, B., Canale, F.A., Pugliese, M., Alati, C., Musuraca, G., Nappi, D., Gaimari, A., Nicolini, F., **Mazza, M.**, Bravaccini, S., Derudas, D., Martinelli, G., Cerchione, C. Chimeric Antigen Receptor T-Cell Therapy: What We Expect Soon (2022) *International Journal of Molecular Sciences*, 23 (21), art. no. 13332, DOI: 10.3390/ijms232113332
- Maltoni R, Ravaioli S, Bronte G, **Mazza M.**, ... Bravaccini S. Chronological age or biological age: What drives the choice of adjuvant treatment in elderly breast cancer patients? *Transl Oncol.* (2022);15(1):101300. doi: 10.1016/j.tranon.2021.101300.
- Tettamanti S. et al. **Mazza M.** Bertilaccio MTS. Lenalidomide enhances CD23.CAR T cell therapy in chronic lymphocytic leukemia, *Leuk&Lymphoma* (2022) 63(7), 1566–1579. <https://doi.org/10.1080/10428194.2022.2043299>
- Martino M.,...**Mazza M.**, Cerchione C. CART-Cell Therapy: Recent Advances and New Evidence in Multiple Myeloma. *Cancers* (Basel). (2021) May 27;13(11):2639. doi: 10.3390/cancers13112639.
- Bravaccini S, ... **Mazza M.*** Estrogen and Androgen Receptor Inhibitors: Unexpected Allies in the Fight Against COVID-19. *Cell Transplant.* (2021) Jan-Dec;30:963689721991477. doi: 10.1177/0963689721991477. (*corresponding and last author)
- Bravaccini S, ... **Mazza M.*** Tamoxifen protects breast cancer patients from COVID-19: first evidence from real world data *Res Sq. Preprint.* (2021). doi: 10.21203/rs.3.rs-598293/v1 (*corresponding and last author)

11. Nolan S, Vignali M, ... **Mazza M**, Robins H.S. A large-scale database of T-cell receptor beta (TCR β) sequences and binding associations from natural and synthetic exposure to SARS-CoV-2 Res Sq. Preprint. (2020) doi: 10.21203/rs.3.rs-51964/v1
12. Snyder T. M., **Mazza M**, Robins H.S. Magnitude and Dynamics of the T-Cell Response to SARS-CoV-2 Infection at Both Individual and Population Levels (2020) medRxiv. Preprint. (2020) doi: 10.1101/2020.07.31.20165647
13. Nicolini F, **Mazza M*** Fully Human Antibodies for Malignant Pleural Mesothelioma Targeting. Cancers. (2020), 12(4) <http://doi.org/10.3390/cancers12040915> (*corresponding and last author)
14. Bocchini M., Nicolini F, Severi S., Bongiovanni A., Ibrahim T., Simonetti G., Grassi I., **Mazza M***. Biomarkers for Pancreatic Neuroendocrine Neoplasms (PanNENs) management – an updated review. Frontiers in Oncology. (2020) 10:831 doi: 10.3389/fonc.2020.00831 (*corresponding and last author)
15. Ravaoli, S., Tebaldi, M., Fonzi, E., **Mazza M**, Martinelli, G., Bravaccini, S. ACE2 and TMPRSS2 Potential Involvement in Genetic Susceptibility to SARS-COV-2 in Cancer Patients Cell transplantation. (2020), 29: 0963689720968749 doi: 10.1177/0963689720968749
16. Nicolini F, Bravaccini S, **Mazza M***, Gruszka A.M, ..., Martinelli G, Cerchione C CAR T cells targeting options in the fight against multiple myeloma Panminerva medica. (2020), Sep 21, DOI: 10.23736/S0031-0808.20.04146-4 (*corresponding author)
17. De Conti G., Gruszka AM ... **Mazza M*** PG Pelicci. Generation of t(15;17) and t(8;21) murine leukemia models to assess the role of essential genes in AML. Cancers. (2020), 12(12):3768. (*corresponding author)
18. Nicolini F, **Mazza M*** Malignant Pleural Mesothelioma: State-of-the-Art on Current Therapies and Promises for the Future., Frontiers in Oncology. (2019), 9, 1519. <http://doi.org/10.3389/fonc.2019.01519> (*corresponding and last author)
19. Carelli S, Giallongo T, Gombalova Z, Rey E, Gorio MCF, **Mazza M**, Di Giulio AM. Counteracting neuroinflammation in experimental Parkinson's disease favors recovery of function: effects of Er-NPCs administration. Journal of neuroinflammation. (2018), Nov 30;15(1):333. doi: 10.1186/s12974-018-1375-2
20. Carelli S*, Giallongo T*, Viaggi C, Latorre E, Gombalova Z, **Mazza M**, Vaglini F, Di Giulio AM, and Gorio A. Recovery from experimental parkinsonism by intrastriatal application of erythropoietin or EPO-Releasing neural precursors. Neuropharmacology. (2017), Mar 31. pii: S0028-3908(17)30127-2 doi: 10.1016/j.neuropharm.2017.03.035
21. Saia, M., Termanini, A., Rizzi, N., **Mazza, M.**, et al. AML1/ETO accelerates cell migration and impairs cell-to-cell adhesion and homing of hematopoietic stem/progenitor cells. Scientific Reports. (2016), 6, 34957
22. Carelli, S., Giallongo, T., Viaggi, C., Gombalova, Z., Latorre, E., **Mazza, M.**, et al. Grafted Neural Precursors Integrate Into Mouse Striatum, Differentiate and Promote Recovery of Function Through Release of Erythropoietin in MPTP-Treated Mice. ASN. Neuro. (2016), 8(5) doi: 10.1177/1759091416676147.
23. **Mazza M**, Pelicci PG Is PML a Tumor Suppressor? Front Oncol. (2013), Jul 9;3:174 doi: 10.3389/fonc.2013.00174
24. Maier P, Rathfelder N, ... **Mazza M**, ... Michael Knop Cytokinesis in yeast meiosis depends on the regulated removal of Ssp1p from the prospore membrane EMBO J. (2007), Apr 4; 26(7): 1843–1852. doi: 10.1038/sj.emboj.7601621
25. **Mazza M***, Riedel C.G.*, et al. Differential requirement for phospholipase D/SPO14 and its novel interactor SMA1 for regulation of exocytotic vesicle fusion in yeast meiosis. J Biol Chem. (2005), Nov 11; 280(45): 37846–52 doi: 10.1074/jbc.M504244200 (*co-first)
26. Knop M, ... **Mazza M**, ... Jäntti J Molecular Interactions Position Mso1p, a Novel PTB Domain Homologue, in the Interface of the Exocyst Complex and the Exocytic SNARE Machinery in Yeast Mol Biol Cell. (2005), Oct; 16(10): 4543–4556. doi: 10.1091/mbc.E05-03-0243
27. Bravaccini S., **Mazza M.**, Maltoni R. No more disparities among regions in Italy: recent approval of genomic test reimbursability for early breast cancer patients in the country (2023). Breast Cancer Research and Treatment. 201 (1), DOI: 10.1007/s10549-023-07000-3
28. Canale F.A., Martino M., Porto G., Verduci C., Console G., Irrera G., Loteta B., Naso V., Pugliese M., Moscato T., Ferreri A., Nappi D., Nicolini F., **Mazza M.**, Martinelli G., Cerchione C. The power of telemedicine to improve CAR-T cell therapy programs: lessons learned from COVID-19 pandemic (2023) Supportive Care in Cancer. 31 (6), DOI: 10.1007/s00520-023-07811-6
29. Rey F, Maghraby E., Messa L., Esposito L., Barzaghini B., Pandini C., Bordoni M., Gagliardi S., Diamanti L., Raimondi M.T., **Mazza M.**, Zuccotti G., Carelli S., Cereda C. Identification of a novel pathway in sporadic Amyotrophic Lateral Sclerosis mediated by the long non-coding RNA ZEB1-AS1 (2023) Neurobiology of Disease. 178, DOI: 10.1016/j.nbd.2023.106030
30. Bocchini M., Tazzari M., Ravaoli S., Piccinini F., Foca F., Tebaldi M., Nicolini F., Grassi I., Severi S., Calogero R.A., Arigoni M., Schrader J., **Mazza M***, Paganelli G. Circulating hsa-miR-5096 predicts 18F-FDG PET/CT positivity and modulates somatostatin receptor 2 expression: a novel miR-based assay for pancreatic neuroendocrine tumors (2023), Frontiers in Oncology. 13, DOI: 10.3389/fonc.2023.1136331 (*corr author)
31. Calabrò L, Bronte G, Grosso F, Cerbone L, Delmonte A, Nicolini F, **Mazza M**, Di Giacomo AM, Covre A, Lofiego MF, Crinò L, Maio M. Immunotherapy of mesothelioma: the evolving change of a long-standing therapeutic dream. Front Immunol. 2024 Jan 8;14:1333661. DOI: 10.3389/fimmu.2023.1333661.
32. Maltoni R, Roncadori A, Balzi W, **Mazza M**, Nicolini F, Palleschi M, Ulivi P, Bravaccini S. An Italian Real-World Study Highlights the Importance of Some Clinicopathological Characteristics Useful in Identifying Metastatic Breast Cancer Patients Resistant to CDK4/6 Inhibitors and Hormone Therapy. Biomedicines. 2024 Feb 22;12(3):498. doi: 10.3390/biomedicines12030498.
33. Irene Gagliardi, Federica Campolo, Patricia Borges de Souza, Lucrezia Rossi, Manuela Albertelli, Federica Grillo, Luigi Caputi, **Massimiliano Mazza**, Antongiulio Faggiano, Maria Chiara Zatelli. Comparative targeted genome profiling between solid and liquid biopsies in gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs): a proof-of-concept pilot study. Neuroendocrinology. 2024 Oct 24;1-20. doi: 10.1159/000541346.
34. Gaimari, A.; De Lucia, A.; Nicolini, F.; Mazzotti, L.; Maltoni, R.; Rughi, G.; Zurlo, M.; Marchesini, M.; Juan, M.; Parras, D.; et al. Mazza M. Significant Advancements and Evolutions in Chimeric Antigen Receptor Design. Int. J. Mol. Sci. 2024, 25, 12201. <https://doi.org/10.3390/ijms252212201>