

BIOGRAPHICAL SKETCH

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NAME: **Maria Rescigno**

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

POSITION TITLE: **Vice rector and delegate for research Humanitas University, Milan, Italy**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Universita di Milano, IT	Masters	1990	Biology
Universty of Cambridge, UK, Visiting Scholar		1994	
Universita di Milano, IT	PhD	2000	Pharmacology and Toxicology
Universita di Milano, IT	Specialization	2001	Applied Biotechnology
Universita di Milano-Bicocca, IT	Post-Doc	2001	Mucosal Immunology

A. Personal Statement

Maria Rescigno has been pioneering the study of the interaction between host and microbes. She has deepened our knowledge on bacterial handling in the gut and what drives tolerance towards the microbiota. She has also deciphered important aspects of the gut-liver-brain axis by identifying a vascular axis with barriers and gates controlling what circulates between the gut and the rest of the body. She is using this knowledge to use bacteria-based treatment to fight cancer progression.

B. Positions, Scientific Appointments, and Honors

2024-present: Deputy scientific director Humanitas Research Hospital
 2024: Member and chair of the scientific advisory board of UK Leuven – Department Chrometa.
 2024-present: Member of the scientific advisory board of Oncolille, Lille, Fr
 2023-present: Chair EMBO council
 2023-present: Member of the scientific advisory board of I3B Porto.
 2018-present: Full Professor General Pathology Humanitas University, Milan
 2018- present: Group leader Mucosal Immunology and microbiota Unit, Humanitas Research Hospital
 2019-present: Vicerector of Humanitas University and delegate of Research
 2019-present: Member EMBO council
 2019_present: Member of the advisory Board L'Oreal-Unesco prize for women in science
 2019_present: Member of the advisory board Swiss National Science Foundation (SNSF)
 2022-present: Member of the scientific advisory board of the IRB (Switzerland)
 2024-present: Member of the scientific advisory board of AIRC (Italy)
 2023-present: Vice scientific Director Humanitas Research Hospital
 2014-2018: Director Immunotherapy program European Institute of Oncology, Milan

- 2001-2017: European Institute of Oncology, Milan: Director of Experimental Oncology Unit on Dendritic cell biology and Immunotherapy.
- 2014-2017: Associate Professor, Department of Health Science, University of Milan
- 2016-present: Founder and president of Postbiotica s.r.l. a spin-off of the University of Milan
- 2017-present: Member of the scientific and technical committee (CTS) of AIRC
- 2013: Abilitazione Nazionale I-Fascia settori disciplinari: 06/A2 (Patologia Generale Med04); 05/F1 (Biologia Applicata, Bio13)
- 2012-2016: Chair of the scientific and technical committee of Cogentech (a facility company established at IEO)
- 2012-2017: Member of the scientific and technical committee of the IEO Biobank
- 2008-2013: Visiting Professor University of Oslo; Subject: immunology
- 2000-2001: Università degli studi di Milano-Bicocca: Dipartimento Di Biotecnologie e Bioscienze. Postdoctoral Fellow
- 1995-1999: CNR, Consiglio Nazionale delle Ricerche: PhD in Pharmacology and Toxicology in the laboratory of Dr Paola Ricciardi-Castagnoli, Prof. of Immunology , Università di Milano, Italy.
- 1991-1994: University of Cambridge, U.K Fellow in the laboratory of Dr. Richard Perham, Prof. of Biochemistry, Department of Biochemistry, University of Cambridge, UK.

Honors

- 1995-1999: Winner of the MURST fellowship (Borsa Ministeriale) to attend the PhD in Pharmacology and Toxicology
- 1996: Winner of the Award from the “Fondazione Adriano Buzzati Traverso”
- 1998: 1998 *Cell Biology Roche Award* received in Viterbo during the XXVI Convegno Nazionale del Gruppo di cooperazione in Immunologia (GCI).
- 1999: Winner of the *Premio per le colture cellulari Mascia Brunelli*
- 2000-2001: Winner of the FIRC short term fellowship to set up a collaboration with Prof. R. Steinman at Rockefeller University NY
- 2006: Elected **EMBO Young Investigator**
- 2007: Associate Editor *Mucosal Immunology*
- 2007: Awarded an **ERC starting grant** (Dendroworld)
- 2008: Nominated member of the Henry Kunkel Society.
- 2008-2013: Visiting Professor University of Oslo
- 2008: Associate Editor *European Journal of Immunology, Beneficial Microbes, Immunology and Cell Biology*
- 2011: Winner of the Avon prize as the woman symbol of the city of Milan
- 2011: Elected **EMBO member**
- 2012: Awarded an **ERC Proof-of-concept grant** (7TRelmHo)
- 2013: Awarded an **ERC Consolidator grant** (HomeoGUT)
- 2017: Winner of **Bioupper** with Postbiotica S.r.l.
- 2017: Winner of **Mystart BCN** (Barcelona, Spain) with Postbiotica S.r.l.
- 2019: “Diseases specific universal vaccines as new combinatorial immunotherapy for metastatic melanoma sarcoma and osteosarcoma – UniCanVax” – AIRC 5x1000 program (Coordinator)
2022. **Honourable mention** conferred by the Belgian Embassy in Rome in collaboration with Galapagos biotech during the Biotech Bridge.
- 2022: **Premio Roma** per Economia, impresa e sociale (Rome award for economy, entrepreneurship and social activity)
- 2023: **Premio Fondazione De Sanctis for Social Health** (Salute Sociale)
- 2024: **The Pezcoller-Marina Larcher Fogazzaro-EACR Women in Cancer Research Award**
- 2024: Elected member of the **Accademia dei Lincei** (National Academy of Science)

Patents (Inventor):

PCT/EP2011/063440: **Method of antigen loading for immunotherapy**

WO2011/009848: **Therapeutic use of probiotics**

EP 13 162 326.6: **Thymic stromal lymphopoietin fragments and uses thereof**

EP n. 15194078.0: " **Method for obtaining tumor peptides and uses thereof**".

US 61/821,990: **Probiotics and methods of use**

PCT/EP2017/069681: **Postbiotic-based composition for treatment of ocular inflammation**

PCT/EP2019/052665: "Use of a postbiotic-based composition for the treatment of skin diseases" deposited in USA, Canada, EPO

PCT/EP2019/052669: "Postbiotic-based composition for the modulation of immune system activation and protection of mucosal barriers" deposited in USA, Canada, EPO

ET/151265A **Composizione a base di postbiotici per il trattamento di tumori**

WO2021013884 **CHI3L1 inhibitors and uses thereof**

WO2022008634 **Tumor-associated peptides and uses thereof**

C. Contributions to Science

1. Since finishing her PhD, Dr. Rescigno has devoted her research to mucosal and tumor immunology. In her early work with dendritic cells, she showed that dendritic cells extend protrusions across epithelial cells to directly sense the luminal content of the gut, including bacteria (Rescigno 2001) and food antigens (Mazzini 2014). She has also shown that the gut microenvironment dictates the phenotype of tolerogenic dendritic cells by conditioning them to release anti-inflammatory cytokines (such as IL-10) and promote the differentiation of T regulatory cells. Further, during the first days of life breastmilk can protect newborns from sepsis through the release of IgAs and these are drastically reduced when mice are treated with antibiotics, but could be restored through the administration of fermented formula.
 - a. **Rescigno M.**, Urbano M., Valzasina B, Francolini M., Bonasio R., Kraehenbuhl JP, Granucci F, Ricciardi-Castagnoli P. Dendritic cells express occludin, establish junctions with gut epithelial cells and sample bacteria preserving epithelial barrier integrity. (2001). *Nat Immunol.* 2:361-367
 - b. Mazzini E, Massimiliano L, Penna G, **Rescigno M.** Oral Tolerance Can Be Established via Gap Junction Transfer of Fed Antigens from CX3CR1+ Macrophages to CD103+ Dendritic Cells. *Immunity.* 2014 Jan 21. pii: S1074-7613(14)00003-X. doi: 10.1016/j.immuni.2013.12.012.
 - c. Rimoldi, M., Chieppa, M., Salucci, V., Sonzogni, A., Nespoli, A., Viale, G., Allavena, P., **Rescigno, M.** Intestinal immune homeostasis is regulated by the cross-talk between epithelial cells and dendritic cells. (2005) *Nat Immunol.* 6:507-14.
 - d. Iliev ID, Spadoni I, Mileti E, Matteoli G, Sonzogni A, Sampietro GM, Foschi D, Caprioli F, Viale G, **Rescigno M.** Human intestinal epithelial cells promote the differentiation of tolerogenic dendritic cells. *Gut.* 2009 Nov;58(11):1481-9. Doi: 10.1136/gut.2008.175166
 - e. Matteoli G, Mazzini E, Iliev ID, Mileti E, Fallarino F, Puccetti P, Chieppa M, **Rescigno M.** Gut CD103+ dendritic cells express indoleamine 2,3-dioxygenase which influences T regulatory/T effector cell balance and oral tolerance induction. *Gut.* 2010 May;59(5):595-604. Doi: 10.1136/gut.2009.185108
 - f. Roggero P, Liotto N, Pozzi C, Braga D, Troisi J, Menis C, Gianni ML, Berni Canani R, Paparo L, Nocerino R, Budelli A, Mosca F, **Rescigno M.** Analysis of immune, microbiota and metabolome maturation in infants in a clinical trial of *Lactobacillus paracasei* CBA L74-fermented formula. *Nat Commun.* 2020 Jun 1;11(1):2703. doi: 10.1038/s41467-020-16582-1.PMID: 32483147
 - g. C. Pietrasanta, C. Carlosama, M. Lizier, G. Fornasa, T. R. Jost, S. Carloni, .. **Rescigno M.** Prenatal antibiotics reduce breast milk IgA and induce dysbiosis in mouse offspring, increasing neonatal susceptibility to bacterial sepsis *Cell Host & Microbe* 2024 DOI: 10.1016/j.chom.2024.11.001

2. Dr. Rescigno has analyzed the role the immune system plays in response to cancer treatments. In particular, she found that treatment with the monoclonal antibody cetuximab combined with chemotherapy fostered immunogenic cell death in patients with colorectal cancer, which was dependent on the mutational status of the EGFR signaling pathway and inhibition of the ER-stress response (as measured by inhibition of XBP1). Moreover, she found that response to treatment with mitomycin C in patients with non-muscle-invasive bladder cancer was also due to immunogenic cell death, which was however dependent on mitomycin c-driven metabolic reprogramming of tumor cells towards increased oxidative phosphorylation. Resistance to treatment was associated with mitochondrial dysfunction, and the identification of the mitochondria-mediated immunogenic cell death provides the opportunity to predict treatment efficacy. Dr Rescigno also analyzed the role of the microbiota in treatment efficacy and demonstrated that microbial metabolites can induce the upregulation of the HLA-class I locus, thus favoring antigen presentation
 - a. Pozzi C, Cuomo A, Spadoni I, Magni E, Silvola A, Conte A, Sigismund S, Ravenda PS, Bonaldi T, Zampino MG, Cancelliere C, Di Fiore PP, Bardelli A, Penna G, **Rescigno M.** [The EGFR-specific antibody cetuximab combined with chemotherapy triggers immunogenic cell death.](#) *Nat Med.* 2016 Jun;22(6):624-31. doi: 10.1038/nm.4078.
 - b. Mitochondrial metabolic reprogramming controls the induction of immunogenic cell death and efficacy of chemotherapy in bladder cancer. Oresta B, Pozzi C, Braga D, Hurle R, Lazzeri M, Colombo P, Frego N, Erreni M, Faccani C, Elefante G, Barcella M, Guazzoni G, **Rescigno M.** *Sci Transl Med.* 2021 Jan 6;13(575):eaba6110. doi: 10.1126/scitranslmed.aba6110.
 - c. Ferrari, V. Lo Cascio, A., Melacarne, A., Tanaskovic, N. Mozzarelli, A.M. Tiraboschi, L. Lizier, M., Salvi, M., Braga, D., Algieri, F., Penna, G., **Rescigno, M.**, Sensitizing cancer cells to immune checkpoint inhibitors by microbiota-mediated upregulation of HLA class I, 2023, **Cancer Cell** 2023 Oct 9;41(10):1717-1730.e4. doi: 10.1016/j.ccell.2023.08.014. Epub 2023 Sep 21.PMID: 37738976
3. Recently, Dr. Rescigno has identified a vascular barrier in the gut that resembles the blood brain barrier. This novel discovery also led to the identification of the GVB as a player in the development of diseases such as non-alcoholic steatohepatitis (NASH), whereby prevention of GVB damage also protects against the onset of the disease (Mouries). Moreover, the disruption of the GVB facilitates the translocation of intestinal bacteria to the liver, where they form a premetastatic niche, favoring the recruitment of metastatic cells (Bertocchi). Following her discovery of the GVB and its' control over bacterial dissemination from the intestine to the liver, Dr. Rescigno has uncovered a new vascular barrier in the choroid plexus, termed the PVB. The PVB is the major portal of entry of breast cancer cells during metastasis formation (manuscript in preparation).
 - c. Spadoni I, Zagato E, Bertocchi A, Paolinelli R, Hot E, Di Sabatino A, Caprioli F, Bottiglieri L, Oldani A, Viale G, Penna G, Dejana E, **Rescigno M.** A gut-vascular barrier controls the systemic dissemination of bacteria. *Science.* 2015 Nov 13;350(6262):830-4. doi: 10.1126/science.aad0135.
 - d. Spadoni L, Fornasa G, **Rescigno M.** Organ-specific protection mediated by cooperation between vascular and epithelial barriers. *Nature Reviews Immunology* 2017 Sep 4. doi: 10.1038/nri.2017.100.
 - e. Mouries J, Brescia P, Silvestri A, Spadoni I, Sorribas M, Wiest R, Miletì E, Galbiati M, Invernizzi P, Adorini L, Penna G, **Rescigno M.** Microbiota-driven gut vascular barrier disruption is a prerequisite for non-alcoholic steatohepatitis development. *J Hepatol.* 2019 Aug 13. pii: S0168-8278(19)30471-4. doi: 10.1016/j.jhep.2019.08.005.
 - f. Bertocchi A, Carloni S, Ravenda PS, Bertalot G, Spadoni I, Lo Cascio A, Gandini S, Lizier M, Braga D, Asnicar F, Segata N, Klaver C, Brescia P, Rossi E, Anselmo A, Guglietta S, Maroli A, Spaggiari P, Tarazona N, Cervantes A, Marsoni S, Lazzari L, Jodice MG, Luise C, Erreni M, Pece S, Di Fiore PP, Viale G, Spinelli A, Pozzi C, Penna G, **Rescigno M.** Gut vascular barrier impairment leads to intestinal bacteria dissemination and colorectal cancer metastasis to liver. *Cancer Cell.* 2021 May 10;39(5):708-724.e11. doi: 10.1016/j.ccell.2021.03.004.
 - g. Carloni S, Bertocchi A, Mancinelli S, Bellini M, Erreni M, Borreca A, Braga D, Giugliano S, Mozzarelli AM, Manganaro D, Fernandez Perez D, Colombo F, Di Sabatino A, Pasini D, Penna G, Matteoli M, Lodato S, **Rescigno M.** Identification of a choroid plexus vascular barrier closing during intestinal inflammation. *Science.* 2021 Oct 22;374(6566):439-448. doi: 10.1126/science.abc6108.

4. In 2016, Dr. Rescigno founded a biotech start-up called Postbiotica s.r.l. (www.postbiotica.com). Postbiotica is a biopharmaceutical company engaged in the development of Postbiotics as innovative, natural compounds for new applications in different sectors. Postbiotics are compounds released by the microbiota during the fermentation process and can regulate the interaction between the host and microbes, leading to a beneficial effect on our health. Many pathologies are associated with a dysregulation of the microbiota and a subsequent disequilibrium of its' associated metabolites. Thus, postbiotics can be used to re-establish host-microbe interactions in cases where this equilibrium is lost. Postbiotics with their intrinsic low toxicity, immunomodulatory properties represent the solution for a number of medical and industrial applications. They also showed that postbiotic can protect from the leaky gut and could be used for the prevention of several pathologies associated to the leaky gut. Dr. Rescigno has had already secured two rounds of funding and been awarded two prizes (Bioupper, Rome, 2017) and Mysterstart BCN (Barcelona, Spain, 2017) for this work.
 - h. Tsilingiri K, Barbosa T, Penna G, Caprioli F, Sonzogni A, Viale G, Rescigno M. Probiotic and postbiotic activity in health and disease: comparison on a novel polarised ex-vivo organ culture model. **Gut**. 2012 Feb 1. Doi: 10.1136/gutjnl-2011-300971.
 - i. Algieri F, Tanaskovic N, Rincon CC, Notario E, Braga D, Pesole G, Rusconi R, Penna G, **Rescigno M**. *Lactobacillus paracasei* CNCM I-5220-derived postbiotic protects from the leaky-gut. **Front Microbiol**. 2023 Mar 20;14:1157164. doi: 10.3389/fmicb.2023.1157164.

5. In addition to her work on how the microbiota can shape tumor development and immune responses, Dr. Rescigno found that bacteria can promote the transfer of antigens from tumor cells to dendritic cells through gap junctions. This work led to the discovery of a novel class of immunogenic peptides derived by a *Salmonella*-induced exacerbation of the ER-stress response in cancer cells, for which she has recently been awarded a 20M grant from the Italian Association for Cancer Research (AIRC) to pursue the development of a universal cancer vaccine for patients with melanoma and sarcoma. This new approach has proven to be very effective in the treatment of osteosarcoma and hemangiosarcoma in dog patients.
 - j. Saccheri F, Pozzi C, Avogadri F, Barozzi S, Faretta M, Fusi P, **Rescigno M**. Bacteria-induced gap junctions in tumors favor antigen cross-presentation and antitumor immunity. **Sci Transl Med**. 2010 Aug 11;2(44):44ra57.
 - k. Melacarne A, Ferrari V, Tiraboschi L, Mishto M, Liepe J, Aralla M, Marconato L, Lizier M, Pozzi C, Zeira O, Penna G, **Rescigno M**. Identification of a class of non-conventional ER-stress-response-derived immunogenic peptides. **Cell Rep**. 2021 Jul 6;36(1):109312. doi: 10.1016/j.celrep.2021.109312.