

**Dott.ssa Barbara Frossi**  
**CV**

**GENERALITIES**

- Name and surname: BARBARA FROSSI
- Place and date of birth: Cividale del Friuli (UD) Italy, 29<sup>th</sup> September 1974
- 2 children

**POSITION**

Associated Professor in General Pathology (MED/04) at the Department of Medicine, University of Udine, Italy.

**EDUCATION AND TRAINING**

- 1993 High school Diploma "Liceo Scientifico "P. Diacono", (UD), Italy (score: 56/60).
- 1999 Doctor of Pharmaceutical Chemistry and Technologies (score: 110/110 magna cum laude and letter of encomium) at the University of Trieste (Italy) with a thesis in Biochemistry entitle: "Effect of structural and chemical-physical factors on the biological activity of antimicrobial peptides".
- 2001 Attainment of the qualification to practice as Pharmacist.
- 2004 PhD in Biomedical Sciences, Department of Medical and Biological Sciences - University of Udine, Italy. Dissertation: "Alternative signaling pathway for mast cell activation: mast cell as antenna of the microenvironment".
- National Academic Qualification as Associate Professor in General and Clinical Pathology, 06/A2 (from 09/04/2018 to 09/04/2024 art. 16, comma 1, Legge 240/10).
- National Academic Qualification as Full Professor in General and Clinical Pathology, 06/A2 (from 09/06/2023 to 09/06/2034 art. 16, comma 1, Legge 240/10).

**WORKING EXPERIENCE**

202-at today	Associated Professor, General Pathology, Department of Medicine, University of Udine, Udine, Italy
2019-2022	Assistant Professor, RTDb, General Pathology, Department of Medicine, University of Udine, Udine, Italy
2012-2019	Senior researcher in Immunology, Department of Medical and Biological Sciences, University of Udine, Udine, Italy
2007-2011	Senior researcher in Immunology, Department of Biomedical Sciences and Technologies, University of Udine, Udine, Italy
2004-2007	Postdoc, Department of Biomedical Sciences and Technologies, University of Udine, Udine, Italy
2003	Fellowship at Molecular Inflammation Section, Molecular Immunology and Inflammation Branch, NIAMS, National Health Institute, Bethesda, Maryland, USA
2000-2001	Fellowship at Department of Biomedical Sciences and Technologies, University of Udine, Udine, Italy

**SCIENTIFIC ACTIVITIES**

- Scientific Manager for the Research Activity "Screening of probiotic microorganisms for functional foods for celiac consumers" commissioned by Dr. Schar SPA and approved by Department of Medicine of University of Udine in the Decreto del Direttore n. 117 del 12.10.2020
- Member of the multi-interdisciplinary project of the University of Udine "Il tempo della mela" (member of the workpackage WP3) 2020-2021
- Member of interdepartmental project of the University of Udine "CibiAmo" (Coordinator of workpackage WP4) 2022-2025

- Participation in the research program PRIN 2015\_ protocol number 2015YYKPNN\_003
- Participation in the research program PRIN 2009\_ protocol number 2009WZHMW3\_006
- Member of the Italian Society of Immunology, Clinical Immunology and Allergology (SIICA)
- Member of the Friuli Venezia Giulia regional group of Immunology, Clinical Immunology and Allergology (GRIICA)
- Organizer of the EMBRN-COST International Mast Cell and Basophil Meeting 2013 Udine, 28-30 August 2013
- External Reviewer for the Czech Science Foundation, Repubblica Ceca
- External Reviewer for the Fondation pour la Recherche Médicale, Francia
- Ad hoc reviewer for Journal of Cellular Biochemistry, Molecular Immunology, British Journal of Dermatology, Free Radical Biology and Medicine, Results in Immunology, Scandinavian Journal of Immunology, European Journal of Immunology, Cytokines, Frontiers Immunology, IJMS.

#### ACADEMIC APPOINTMENTS

- 2004-2009 Professor of Immunochemistry, Faculty of Medicine, School of Biomedical Technician, University of Udine, Italy
- 2009-2011 Professor of Physiopathology, Faculty of Medicine, School of Nursing, University of Udine,
- 2011-2012 Professor of Pathology and Physiopathology, Faculty of Medicine, School of Nursing, University of Udine, Italy.
- 2019-2022 Professor of Immunology, Faculty of Medicine, School of Nursing, University of Udine, Italy.
- 2019-2022 Professor of Immunology, Faculty of Medicine, School of Biomedical Technician, University of Udine, Italy.
- 2019-2020 Professor of General Pathology, Faculty of Medicine, School of Biomedical Technician, University of Udine, Italy
- 2020-2021 Professor of "Base Oncology", School of Biomedical Technician, University of Udine, Italy
- 2020-2021 Professor of "General Pathology", School of Tecnico della prevenzione sul posto di lavoro, University of Udine, Italy
- 2020-2022 Professor of General Pathology, Faculty of Medicine, University of Udine, Italy
- 2016-2019 Professor of the course of "Regulatory cell in inflammation", "Inflammation and Inflammatory diseases" International Master M2 Program, Paris-Diderot, Paris France.
- Member of the working group for the University Strategic Plan of the Department of Medicine, University of Udine 2022-2025
- Member of the PhD council in Biomedical Science and Biotechnology – 38th cycle, University of Udine
- Organizer of the course "Cell-cell communication", Journal club, PhD School Biomedical Sciences and Biotechnology, academic year 2021/2022
- Organizer and scientific director of the interdisciplinary course "Understanding personalized medicine in a gender perspective" for Department of Medicine and Azienda Sanitaria S. Maria della Misericordia of Udine (ECM course), academic year 2022/2023

#### PRIZE and HONORS

- Prize "Fondazione Crup" for best scientific publication in Medical Science of year 2009-2011 among young investigators of University of Udine.
- Prize "Donne Impresa" Confartigianato of Udine for Research
- National Academic Qualification as Associate Professor in General and Clinical Patology, 06/A2 (from 09/04/2018 to 09/04/2024 art. 16, comma 1, Legge 240/10).
- Prize "Paladini Italiani della Salute" Roma 2021

#### CONGRESS and SEMINAR (2019-2023)

- Speaker at the "Women Science day", San Vito al Tagliamento (UD) 11 February 2022
- Speaker of the seminar "Me & Mast cell", Seminars Journal Club, PhD School of Biomedical Science and Biotechnology 2021, University of Udine, 22 March 2021

- Speaker at the meeting "Vaccini: la scienza spiega", University of Udine, 18 May 2021
- Speaker of the seminar "Crosstalk between immune and epithelial cells in intestinal organoid development" within the course "Humans in a dish: the potential of organoids in modeling diseases" for the PhD course in Bioscience organized by the University of Padova, 8 June 2021
- Speaker at the Workshop of the multidisciplinary group on active aging of the University of Udine, Udine, 6 October 2019
- Speaker at Univax-Day, Udine, 21 February 2021
- Speaker at Univax-Day, Udine, 21 February 2020
- Speaker at Univax-Day, Udine, 19 April 2022
- Speaker at Univax-Day, Udine, 10 February 2023

## PUBBLICATION

### International and Peer reviewed publication (H index scopus)

*N. original manuscript: 43, 17 as first author, 7 as second author, 5 as last author, 4 as corresponding author. N. Citation: 2094 (Scopus 14/06/2023); H-index: 25 (Scopus 14/06/2023)*  
*ORCID: [orcid.org/0000-0001-9855-2396](https://orcid.org/0000-0001-9855-2396)*

De Zuani M, Dal Secco C, Tonon S, Arzese A, Pucillo CEM, Frossi B. LPS Guides Distinct Patterns of Training and Tolerance in Mast Cells. *Front. Immunol.* 2022 Feb 17;doi.org/10.3389/fimmu.2022.835348

Sulsenti R\*, Frossi B\*, Bongiovanni L, Cancila V, Ostano P, Fischetti I, Enriquez C, Guana F, Chiorino G, Tripodo C, Pucillo CE, Colombo MP, Jachetti E. Repurposing of the Antiepileptic Drug Levetiracetam to Restrain Neuroendocrine Prostate Cancer and Inhibit Mast Cell Support to Adenocarcinoma. *Front Immunol.* 2021 Mar 2;12:622001. doi: 10.3389/fimmu.2021.622001

Frossi B, De Carli M, Calabrò A. Coeliac Disease and Mast Cells. *Int J Mol Sci.* 2019 Jul 11;20(14).

Jachetti E, D'Inca F, Danelli L, Magris R, Dal Secco C, Vit F, Cancila V, Tripodo C, Scapini P, Colombo MP, Pucillo C, Frossi B. Frontline Science: Mast cells regulate neutrophil homeostasis by influencing macrophage clearance activity. *J Leukoc Biol.* 2019 Apr;105(4):633-644

Frossi B, Antoniali G, Yu k, Akhatar N, Kaplan M, Kelly M, Tell G, Pucillo CE. Endonuclease and redox activities of human apurinic/aprimidinic endonuclease 1 have distinctive and essential functions in IgA class switch recombination. *J Biol Chem* 2019 294 (13):5198-5207

De Zuani M, Paolicelli G, Zelante T, Renga G, Romani L, Arzese A, Pucillo CEM, Frossi B. Mast Cells Respond to *Candida albicans* Infections and Modulate Macrophages Phagocytosis of the Fungus. *Front Immunol.* 2018 Nov 30;9:2829

De Zuani M, Dal Secco C, Frossi B. Mast cells at the crossroads of microbiota and IBD. *Eur J Immunol.* 2018 Dec;48(12):1929-1937. doi: 10.1002/eji.201847504

Cereser L, De Carli R, Girometti R, De Pellegrin A, Reccardini F, Frossi B, De Carli M. Efficacy of rituximab as a single-agent therapy for the treatment of Granulomatous and Lymphocytic Interstitial Lung Disease (GLILD) in patients with Common Variable Immunodeficiency (CVID). *J Allergy Clin Immunol Pract.* 2018 Nov 5. pii: S2213-2198(18)30712-8.

Jachetti E, Cancila V, Rigoni A, Bongiovanni L, Cappetti B, Belmonte B, Enriquez C, Casalini P, Ostano P, Frossi B, Sangaletti S, Chiodoni C, Chiorino G, Pucillo CE, Tripodo C, Colombo MP. Cross-Talk between Myeloid-Derived Suppressor Cells and Mast Cells Mediates Tumor-Specific Immunosuppression in Prostate Cancer. *Cancer Immunol Res.* 2018 May;6(5):552-565

Frossi B, Mion F, Sibilano R, Danelli L, Pucillo CEM. Is it time for a new classification of mast cells? What do we know about mast cell heterogeneity? *Immunol Rev.* 2018 Mar;282(1):35-46.

Mion F, Vetrano S, Tonon S, Valeri V, Piontini A, Burocchi A, Petti L, Frossi B, Gulino A, Tripodo C, Colombo MP, Pucillo CE. Reciprocal influence of B cells and tumor macro and microenvironments in the *ApcMin/+* model of colorectal cancer. *Oncoimmunology.* 2017 Jun 19;6(8):e1336593. doi: 10.1080/2162402X.2017.1336593

Frossi B, Mion F, Tripodo C, Colombo MP, Pucillo CE. Rheostatic Functions of Mast Cells in the Control of Innate and Adaptive Immune Responses. *Trends Immunol.* 2017 Apr 24. pii: S1471-4906(17)30060-1.

Cugno M, Tedeschi A, Frossi B, Bossi F, Marzano AV, Asero R. Detection of Low-Molecular-Weight Mast Cell-Activating Factors in Serum From Patients With Chronic Spontaneous Urticaria. *J Investig Allergol Clin Immunol*. 2016;26(5):310-313.

Frossi B, Tripodo C, Guarnotta C, Carroccio A, De Carli M, De Carli S, Marino M, Calabrò A, Pucillo CE. Mast cells are associated with the onset and progression of celiac disease. *J Allergy Clin Immunol*. 2017 Apr;139(4):1266-1274.e1.

Frossi B, Mion F, Pucillo C. Deciphering new mechanisms on T-cell costimulation by human mast cells. *Eur J Immunol*. 2016 May;46(5):1105-8.

Frossi B, De Carli S, Bossi F, Pucillo C, De Carli M. Co-Occurrence of Chronic Spontaneous Urticaria with Immunoglobulin A Deficiency and Autoimmune Diseases. *Int Arch Allergy Immunol*. 2016;169(2):130-4

Mekori YA, Hershko AY, Frossi B, Mion F, Pucillo CE. Integrating innate and adaptive immune cells: Mast cells as crossroads between regulatory and effector B and T cells. *Eur J Pharmacol*. 2016;778:84-9

Betto E, Usuelli V, Mandelli A, Badami E, Sorini C, Capolla S, Danelli L, Frossi B, Guarnotta C, Ingrao S, Tripodo C, Pucillo C, Gri G, Falcone M. Mast cells contribute to autoimmune diabetes by releasing interleukin-6 and failing to acquire a tolerogenic IL-10+ phenotype. *Clin Immunol*. 2015 Dec 27. pii: S1521-6616(15)30082-6. doi: 10.1016

Danelli L, Frossi B, Pucillo CE. Mast cell/MDSC a liaison immunosuppressive for tumor microenvironment. *Oncoimmunology* 2015Mar 24:4(4), e1001232

Danelli L, Frossi B, Gri G, Mion F, Guarnotta C, Bongiovanni L, Tripodo C, Mariuzzi L, Marzinotto S, Rigoni A, Blank U, Colombo MP, Pucillo CE. Mast cells boost myeloid-derived suppressor cell activity and contribute to the development of tumor-favoring microenvironment. *Cancer Immunol Res*. 2015 Jan;3(1):85-95

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Sibilano R, Frossi B, Pucillo CE. Mast cell activation: a complex interplay of positive and negative signaling pathways. *Eur J Immunol*. 2014 Sep;44(9):2558-66

Sibilano R, Pucillo C, Frossi B. Modulation of FcεRI-dependent mast cell response by OX40L. *Methods Mol Biol*. 2014;1155:23-30

Franco G, Guarnotta C, Frossi B, Piccaluga PP, Boveri E, Gulino A, Fuligni F, Rigoni A, Porcasi R, Buffa S, Betto E, Florena AM, Franco V, Iannitto E, Arcaini L, Pileri SA, Pucillo C, Colombo MP, Sangaletti S, Tripodo C. Bone marrow stroma CD40 expression correlates with inflammatory mast cell infiltration and disease progression in splenic marginal zone lymphoma. *Blood*. 2014 Mar 20;123(12):1836-4

Pignatti P, Frossi B, Pala G, Negri S, Oman H, Perfetti L, Pucillo C, Imbriani M, Moscato G. Oxidative Activity of Ammonium Persulfate Salt on Mast Cells and Basophils: Implication in Hairdressers' Asthma. *Int Arch Allergy Immunol*. 2012 Nov 23;160(4):409-419

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Sibilano R, Frossi B, Calvaruso M, Danelli L, Betto E, Dall'agnese A, Tripodo C, Colombo MP, Pucillo CE, Gri G. The aryl hydrocarbon receptor modulates acute and late mast cell responses. *J Immunol*. 2012 Jul 1;189(1):120-7.

Sibilano R, Frossi B, Suzuki R, D'Inca F, Gri G, Piconese S, Colombo M, Rivera J, Pucillo C. Modulation of FcεRI-dependent mast cell response by OX40L via Fyn, PI3K and RhoA. *J Allergy Clin Immunol*. 2012 Sep;130(3):751-760.e2

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Frossi B, D'Inca F, Crivellato E, Sibilano R, Gri G, Mongillo M, Danelli L, Maggi L, Pucillo CE. Single-cell dynamics of mast cell-CD4+ CD25+ regulatory T cell interactions. *Eur J Immunol*. 2011 Jul;41(7):1872-82.

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Frossi B, Gri G, Tripodo C, Pucillo C. Exploring a regulatory role for mast cells: 'MCregs'? *Trends Immunol.* 2010 Mar;31(3):97-102.

Merluzzi S\*, Frossi B\*, Gri G, Parusso S, Tripodo C, Pucillo C. Mast cells enhance proliferation of B lymphocytes and drive their differentiation toward IgA-secreting plasma cells. *Blood.* 2010 Apr 8;115(14):2810-7.

Bossi F, Fischetti F, Regoli D, Durigutto P, Frossi B, Gobeil F Jr, Ghebrehiwet B, Peerschke EI, Cicardi M, Tedesco F. Novel pathogenic mechanism and therapeutic approaches to angioedema associated with C1 inhibitor deficiency. *J Allergy Clin Immunol.* 2009 Dec;124(6):1303-10.e4

Piconese S, Gri G, Tripodo C, Musio S, Gorzanelli A, Frossi B, Pedotti R, Pucillo CE, Colombo MP. Mast cells counteract regulatory T-cell suppression through interleukin-6 and OX40/OX40L axis toward Th17-cell differentiation. *Blood.* 2009 Sep 24;114(13):2639-48.

Gri G, Piconese S, Frossi B, Manfroi V, Merluzzi S, Tripodo C, Viola A, Odom S, Rivera J, Colombo MP, Pucillo CE. CD4+CD25+ regulatory T cells suppress mast cell degranulation and allergic responses through OX40-OX40L interaction. *Immunity.* 2008 Nov 14;29(5):771-81.

Arcidiacono D, Odom S, Frossi B, Rivera J, Paccani SR, Baldari CT, Pucillo C, Montecucco C, de Bernard M. The *Vibrio cholerae* cytolysin promotes activation of mast cell (T helper 2) cytokine production. *Cell Microbiol.* 2008 Apr;10(4):899-907.

Frossi B, De Carli M, Piemonte M, Pucillo C. Oxidative microenvironment exerts an opposite regulatory effect on cytokine production by Th1 and Th2 cells. *Mol Immunol.* 2008 Jan;45(1):58-64.

Frossi B, Rivera J, Hirsch E, Pucillo C. Selective activation of Fyn/PI3K and p38 MAPK regulates IL-4 production in BMMC under nontoxic stress condition. *J Immunol.* 2007 Feb 15;178(4):2549-55.

Frossi B, De Carli M, Pucillo C. The mast cell: an antenna of the microenvironment that directs the immune response. *J Leukoc Biol.* 2004 Apr;75(4):579-85.

Frossi B, De Carli M, Daniel KC, Rivera J, Pucillo C. Oxidative stress stimulates IL-4 and IL-6 production in mast cells by an APE/Ref-1-dependent pathway. *Eur J Immunol.* 2003 Aug;33(8):2168-77.

Frossi B, Tell G, Spessotto P, Colombatti A, Vitale G, Pucillo C. H(2)O(2) induces translocation of APE/Ref-1 to mitochondria in the Raji B-cell line. *J Cell Physiol.* 2002 Nov;193(2):180-6.

\*First co-authors

### Book Chapters

Tonon S, Martinis E, Dal Secco C, Tosoni L, Tomadini G, Vitale G, Pucillo C, Frossi B. Use of organoids in cancer: a new therapeutic and research approach. *Handbook in Cancer and Immunology 2022 paper in press*

Frossi B, M De Carli. La celiachia: cause e meccanismi patogenetici di una malattia complessa. *Notiziario Allergologico (2018) Anno 37-volume 36, n.1 ISSN 2038-2553*

Frossi B, De Carli R, De Carli M. Chronic Spontaneous Urticaria in Patients with Common Variable Immunodeficiency. *European Medical Journal 2018;3(4):95-102*

Frossi B, Mion F, Pucillo C. Il mastocita: il nuovo Giano bifronte della risposta immunitaria. *Notiziario Allergologico (2017) Anno 36-volume 35, n.1 ISSN 2038-2553*

Francesconi A, Paparella G, Frossi B, Del Terra E, Ambesi Impiombato F, Curcio F. C-kit positive cells from failing human hearts: role of culturing media on cardiomyogenic potentials. *J Cardiovasc Med Cardiol* 2015;2(1):005-012 doi: 10.17352/2455-2976.000013

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INTEREST and CONTRIBUTION TO SCIENCE

The research activity of Dr. Frossi has focused on the study of the contribution of innate immunity and in particular of the mast cells in the regulation of the immune response in multiple inflammatory contexts. Pupil of Prof. Rivera, pioneer of mast cell biology, Dr. Frossi studied the ability of the mast cell to react specifically in response to diverse stimuli coming from the microenvironment and the ability of mast cell to interact with tissue cells and other cells of the immune system in multiple inflammatory contexts. The studies conducted by Dr. Frossi during her doctorate at the Department of Biomedical Sciences and Technologies of the University of Udine have helped to understand the heterogeneity and multifunctionality of mast cells not only in allergic manifestations, but also in the maintaining of tolerance to self through bidirectional interaction with regulatory immune cells (regulatory T and B lymphocytes, suppressive myeloid cells), and with cellular partners present in the microenvironment (macrophages, neutrophils, stromal cells). Her studies have helped to identify the crucial role in these interactions of membrane molecules constitutively expressed by mast cells, such as CD40L and OX40, which are responsible for regulating the immune response in autoimmune settings, chronic inflammation and cancer. Moreover, Dr. Frossi has extended her in vitro studies to various human pathological contexts, from autoimmune urticaria to celiac disease and cancer. She is currently studying the interaction of mast cells with the cells of the intestinal microenvironment, including the commensal microbiota, in contexts of homeostasis, chronic inflammation and neoplastic disease.

Cividale del Friuli, 14<sup>th</sup> June 2023

Barbara Frossi

Autorizzo il trattamento dei dati personali contenuti nel mio curriculum vitae in base all'art. 13 del D. Lgs. 196/2003.