1. Personal information

First and last name	Mariagrazia Uguccioni
Gender	Female
Place and date of birth	Pesaro, Italy - September 28, 1961
Nationality	Italian, Swiss
Institutional address	Institute for Research in Biomedicine (IRB) Via Vincenzo Vela 6 6500 Bellinzona, Switzerland. Tel. +41 91 8200316, fax:+41 91 8200305 mariagrazia.uguccioni@irb.usi.ch
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OrcID	0000-0002-9570-7011
Current position	Vice director, Institute for Research in Biomedicine Head of the "Chemokines in Immunity" laboratory

2. Education

1990	MD degree - University of Bologna, Italy
1990	State Exam – Bologna, Italy
1994	Specialization in Haematology - University of Bologna, Italy

3. Employment history

1990-1993	Research fellow, Immunology and Genetic, University of Bologna, Italy
1992	Visiting scientist, Guy's Hospital, Department of Rheumatology, London, UK
1993-2000	Research scientist, Theodor Kocher Institute, University of Bern, Switzerland
2000-present	Head of laboratory "Chemokines in Immunity", IRB, Bellinzona, Switzerland Bio-safety officer IRB
2010-present	Vice director, Institute for Research in Biomedicine
2016-present	Extraordinary Professor of Histology, Humanitas University, Rozzano (Milan), Italy

4. Institutional responsibilities

2000-present	Bio-safety officer, Institute for Research in Biomedicine.
2005-present	Coordinator Internal seminars, Institute for Research in Biomedicine.
2010-present	Vice-Director, Institute for Research in Biomedicine, and Coordinator for the New Headquarter.

5. Approved research projects

2000-2004	EU FP4 – DETEC, SIV/HIV vaccines – detecting efficacy and explaining inefficacy
2002-2005	EU FP5 – MUVADEN, Mucosal vaccines against human and simian immunodeficiency viruses based on dendritic cells
2004-2007	EU FP6 – MAIN, Targeting cell migration in chronic inflammation
2004-2006	OncoSwiss - Primary central nervous system lymphoma: from an improved biology knowledge of its peculiar molecular and biologic feature towards the optimization of treatment
2004-2007	SNSF – Impact of multiple chemokine expression in human disease
2005-2007	EU FP6 – TIP-VAC, Explaining and Improving Efficacy of targeted Immunodeficiency Virus-like Particle Vaccines against AIDS
2005-2008	San Salvatore Foundation - Molecular and biological mechanisms of non-Hodgkin's lymphomas growth at extranodal sites
2005-2009	EU FP6 – DEC-VAC, Development of a Dendritic cell-targeted vaccine against AIDS
2006-2009	SNSF/Cloetta to Daniel Venetz - Chemokines in extranodal Lymphomas (Supervisor)
2005-2010	EU FP6 – INNOCHEM, Innovative Chemokine-based Therapeutic Strategies for autoimmunity and Chronic Inflammation (Deputy Coordinator and Scientific Coordinator)
2008-2010	San Salvatore Foundation - Molecular and biological mechanisms of non-Hodgkin's lymphomas growth at extranodal sites
2008-2011	SNSF – Impact of multiple chemokine expression in human disease (follow on)
2009-2011	EU FP7 – IEF to Valentina Cecchinato – MD-THIV, Migration and Differentiation of Th17 Cells in HIV/SIV Infection (Supervisor)
2012-2013	Novartis Stiftung für Medizinisch-Biologische Forschung - Dampening Inflammation in Autoimmunity by Targeting Chemokine synergy-inducing molecules
2013	Jubilee Foundation Novartis to Lorenzo Raeli Dampening Inflammation by targeting chemokine synergy-inducing molecules (Supervisor)
2012-2014	SNSF – Analysis of molecular and cellular mechanisms in immune-mediated tissue damage of the skin: Hidradenitis suppurativa as a model disease (Co-investigator)
2013-2014	SNSF-HIV Cohort Studies – Migration and differentiation of TH17 cells in HIV infection
2012-2015	SNSF-ProDoc – Cell migration
2012-2016	EU FP7 – TIMER, TargetIng novel MEchanisms of Resolution in inflammation
2013-2016	SNSF - Impact of synergy-inducing molecules on chemokine activities

2013-2016	Gottfried und Julia Bangerter-Rhyner Stiftung - Dampening Inflammation in Autoimmunity by Targeting Chemokine Synergy-inducing Molecules
2011-2017	EU FP7 – ADITEC, Advanced Immunization Technologies
2018-2019	Foundation for research on viral diseases - The role of chemokines in tuning the inflammatory responses during Hepatitis C virus infection
2018-2020	San Salvatore Foundation – The role of chemokine synergy-inducing molecules in controlling the tumour microenvironment, cell migration and metastasis
2018-2020	Fondazione Ceschina - The role of chemokines in tuning the inflammatory responses in Ankylosing Spondylitis

6. Supervision of junior researchers at graduate and postgraduate level

MD students enrolled at the University of Bern, Medical School, 1994-1999: Davide Robbiani; Judith Scharer; Jan Braunwalder; Cornelia Hallenbarter-Betschart (all students from Switzerland).

Master students enrolled at the Institute for Research in Biomedicine: Michelle Berni, Pharmacology, University of Basel; Francesco Mueller, University of Lausanne; Mara Ambrosini, Pharmacology, University of Basel; Francesco Bagnis, Medical School, University of Pavia (Italy); Enrico Fassi, Pharmacology, University of Milan (Italy).

PhD students enrolled at the Institute for Research in Biomedicine: Samantha Paoletti (Italy), Vibor Petkovic (Croatia), Katrin Kuscher (Germany), Daniel Venetz (Switzerland), Milena Schiraldi (Italy), Denise Bottinelli (Switzerland), Gianluca D'Agostino (Italy).

Post-docs enrolled at the Theodor Kocher Institute, University of Bern 1994-1999: Katherina Williman (Switzerland), PhD, Patricia Ogilvie (Germany), MD

Post-doc enrolled at the Institute for Research in Biomedicine: Patricia Ogilvie (Germany), MD; Ulf Panzer (Germany), MD; Silvia Sebastiani (Italy), PhD; Tamara Visekruna (Croatia), PhD; Luisa Stefano (Italy), PhD; Lorenzo Raeli (Italy), PhD; Michele Proietti (Italy), PhD, Valentina Cecchinato (Italy), PhD.

Visiting scientists at the laboratory of "Chemokines in Immunity" IRB: Several scientists over the years have visited the laboratory. They were working in different countries: Italy, Germany, Spain, United Kingdom, USA, Canada, Argentina, and Egypt.

7. Teaching activities

1999-2004	Adjunct Professor, School of Toxicology, Faculty of Pharmacology, University of Bologna, Italy
2006-2011	Adjunct Professor, School of Rheumatology, Faculty of Medicine, University of Bologna, Italy
2016-present	Professor at the Faculty of Medicine and Surgery, Humanitas University, Italy.

8. Memberships in panels, boards, and individual scientific activities

1998-2000	Chair 7th workshop on Human Leukocyte Differentiation Antigens (Cytokine-chemokine receptors)
2000-2004	Chair 8th workshop on Human Leukocyte Differentiation Antigens (Cytokine-chemokine receptors)
2005-2011	EU independent expert, panel evaluation Health-Innovation.
2009-2011	Member of the Commission for selection of candidates for the PhD programme in Molecular Medicine, San Raffaele University, Milan (Italy)
2009-2011	Member of Telethon Switzerland Scientific Committee.
2015, 2018	Member of the Commission for selection of candidates for the PhD programme in Molecular and Experimental Medicine at Humanitas University, University of Palermo and Italian National Council for Research (Italy).

Ad hoc reviewing for several scientific Journals, among which Science, Nature, Nature Immunology, Journal of Experimental Medicine. Reviewer for Swiss and European Funding Agencies, such as SNSF, Welcome Trust UK, MIUR IT, MRC UK.

9. Active membership in scientific societies

Swiss Society for Allergology and Immunology; British Society for Immunology; Italian Society for Immunology, Clinical Immunology and Allergy; International Society for Vaccines; International Society for Dendritic Cells and Vaccine Science.

10. Organization of international conferences

2010	Cytokines and Chemokines – Post transcriptional regulation – Saint Sorlin d'Arves (FR) – 22-24.03
2014	The chemokine system: molecules, mechanisms and functions – Borgo Santa Giulia (IT) – 25-27.09
2012-present	European Academy of Dermatology and Venereology "From the Bench to the Clinic" – yearly event
2017	Ankylosing Spondylitis: tales of molecules and patients – Lugano (CH) – 30.09/01.10

11. Prizes, awards, fellowships

2009 Nominated Member of the Academy of Science, Institute of Bologna
http://www.accademiascienzebologna.it/en/academy-of-sciences-of-bologna-institute

Fellowships: European Federation of Immunological Societies, 1990; Rizzoli Orthopaedic Institutes, Bologna, Italy, 1991; Italian National Institute of Health, Roma, 1992; Italian National Institute of Health, Roma, 1993.

12. Publications – h-index 49 - i10Index: 68

Publications in peer reviewed journals: 77.
Publications in peer reviewed journals on the 7th and 8th workshops on Human Leukocyte Differentiation Antigens: 11.
Book chapters: 8. https://scholar.google.ch/citations?hl=en&user=84f02BYAAAAJ&view_op=list_works&sortby=pubdate

MAJOR SCIENTIFIC ACHIEVEMENTS

The research activities performed in my group have been focused in the last twenty years on the modulation of cell migration in health and disease in humans. We have demonstrated over the years that we can identify and validate molecules able to block or enhance chemokine activities.

Old achievements

In the late nineties, we have characterized the activity of novel chemokines, the expression of chemokine receptors in leukocyte subpopulations, such as basophils, Th1 and Th2 lymphocytes, and the ***in situ*** **expression of several chemokines**, both in secondary lymphoid organs and in tissues from patients with different pathological conditions. Over the years, we have published several articles on this topic also in collaboration with other groups. Among those: Journal of Clinical Investigation (DOI: 10.1172/JCI119624); Nature (DOI: 10.1038/34812); Current Biology (doi: 10.1016/S0960-9822(00)00380-8); Journal of Clinical Investigation (DOI: 10.1172/JCI7830); European Journal of Immunology (DOI: 10.1002/eji.200425830).

The observation that several chemokines are concomitantly expressed in inflammatory conditions and tumours, led us to start exploring whether the microenvironment milieu could regulate the activity of chemokine receptors. These studies allowed us to discover the first **natural chemokine antagonist** as published in Blood in 2001 (PMID 11264152) and to identify additional natural antagonists in 2003 and 2004. An example of these studies is the characterization of two chemokines, CCL11 and CCL6, as antagonists for CCR1, CCR2, and CCR5. These natural antagonists would counteract the effect of all "classical" inflammatory CC chemokines on any cell type expressing CCR1, CCR2 or CCR5, but lacking CCR3, skewing the balance between a Th1 or Th2 type response towards the Th2 branch.

These results encouraged us to further investigate the effects of the microenvironment on chemokine activities. The "**Synergism between chemokines**" was identified in 2004 and published in Blood (DOI: 10.1182/blood-2004-04-1648).

At this point, the chemokine community was not truly prepared to accept this additional feature of chemokines, and it took us time, several papers, and the concomitant discoveres performed by the groups of Jo Van Damme in Belgium and of Christian Weber in Germany, to convince that this activity is indeed relevant for modulating cell migration.

The controversy on the relevance of GAGs and chemokine heterocomplexes acting for enhancing chemokine responses, was discussed in a reconciliatory review that Amanda Proudfoot and I decided to write together in **2016**, and that have been published in Frontiers in Immunology (DOI: 10.3389/fimmu.2016.00183**)**.

Recent Achievements

The analysis of the microenvironment in human inflammatory conditions led us to evaluate also molecules different from chemokines, such as the alarmin HMGB1, in modulating cell migration. HMGB1 was reported to be a chemoattractant, but the receptor responsible for this activity was unknown. In **2012**, we have been able to show in two different papers published in Journal of Experimental Medicine (DOI: 10.1084/jem.20111739 and 10.1084/jem.20120189), that **CXCL12 can form a heterocomplex with HMGB1**, and that the effect on cell migration reported for HMGB1 is indeed due to the triggering of CXCR4 in the presence of CXCL12. Thus, HMGB1 works as an enhancer of CXCL12, as the synergy-inducing chemokines we described previously. We summarized

the activities of the different forms of HMGB1 on different receptors in a review published in Molecular Immunology the year after (DOI: 10.1016/j.molimm.2012.10.037).

The studies on the basic mechanisms governing the modulation of chemokine activities, was never separated by the analyses of chemokine expression in human pathological conditions, and by the assessment of how the disease can affect chemokine responses.

In recent years, we have disclosed two different aspect governing chemokine responses in inflammation.

In a study published in the Journal of Immunology in 2017 (DOI: 10.4049/jimmunol.1600568) we have shown that **persistent immune activation, occurring in HIV infection, causes impairment of lymphocytes to respond to chemotactic stimuli**, despite the fact that the expression of chemokine receptors on T cell surface remains unaltered compared to healthy individuals. This prevents T cell trafficking from the blood stream to peripheral organs. The defect is in the inability of these cells to rearrange the cytoskeleton upon chemokine stimulation. As a proof of principle, the use of a compound able to promote, both *in vitro* and *in vivo,* the remodelling of the cytoskeleton indicates that there is room for further pharmacological approaches in these patients, to overcome the failure in repopulating the gut immune system with the present therapy.

In a study published this year in Frontiers in Immunology (DOI: 10.3389/fimmu.2018.02118) on the **activity of the CXCL12/HMGB1 heterocomplex in Rheumatoid Arthritis**, we have demonstrated the presence of the heterocomplex in a human pathological condition. Moreover, we have shown how in an unbalanced inflammatory microenvironment, the activation of mechanisms counteracting the oxidative stress is essential for preserving HMGB1 in the reduced form. This form is required for the formation and the activity of the CXCL12/HMGB1 heterocomplex, which contributes to fuel the influx of inflammatory cells.

Our last published study, demonstrates that **lidocaine, at clinical concentrations, inhibits the activity of CXCR4** (DOI: 10.1016/j.bja.2018.07.015), and the migration of a **breast cancer** cell line. This study tells us how intricate can be the correlation between the microenvironment and therapeutic strategies.

In collaboration with University of La Laguna (Tenerife, Spain), we have hosted for several month a PhD student, which have conducted a study on B cells **in Rheumatoid Arthritis**. The results have been published in Arthritis Research and Therapy this year, and suggest that **CXCL13 and CCL20** might play major roles in RA pathogenesis by **acting** singly on their selective receptors and **synergistically in the accumulation of B cells** within the inflamed synovium. This is another example on how we identify modulating molecules, starting from the analysis of human pathological conditions.