NAME:Francesca Granucci

POSITION TITLE: Full Professor in Immunology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pisa, Italy	Master	02/1990	Molecular Biology
University of Milano, Italy	Ph.D.	10/1996	Immunology

A. Personal Statement

Since 2006, I lead a research group of about 10 people. I have a long record of achievements in the field of innate immunity and dendritic cell (DC) biology. I have pioneered systems biology approaches to study host-pathogen interactions and the role of DCs in inflammation. I have described some molecular events occurring during the interaction of DC with bacteria and molecularly characterized protective skin responses to fungal and bacterial infections. My research includes the study of the role of the NFATc pathway in the inflammatory process induced by microbial infections and the role NFATc pathway in innate immune cells in determining graft rejection. I have many national and international collaborators that allow me the access to knowledges and reagents (cell lines, antibodies, mutant mice) fundamental for the success of my research. My work has been successfully crowned by publications in outstanding scientific journals including Nature, Cell, Nat Immunology, Science Immunology and others (see below). As clearly evidenced in the section “Contribution to Science”, the current application builds up on my previous work.
As woman scientist and mother of two sons, I try to be an example for many young women that would like to follow the scientific career. As director of the Immunology program in the courses of Biology and Biotechnology, Erasmus coordinator at the University of Milano-Bicocca and Faculty of the DIMET PhD program, I encourage and motivate, by offering an intellectual and emotional support and by giving practical advices on family management, many undergraduate, graduate and PhD female students in biomedical sciences.

B. Positions and Honors

Current position
2016-present: Full Professor, Department of Biotechnology and Biosciences, University of Milano-Bicocca, Milan, Italy.

Previous positions
2006-2016: Associate Professor, Department of Biotechnology and Biosciences, University of Milano-Bicocca, Milan, Italy.
November 2014-present: PI of the Unit of Cell Signalling and Innate Immunity, Humanitas Clinical and Research Center, Rozzano, Milan, Italy
2001-2006: Researcher at the University of Milano-Bicocca (Milan). Member of the Dept. of Biotechnology and Biosciences
1997-2001: Post Doct at the National Research Council (CNR), Milan, Italy.
1996-1997: Research Fellow at the Dana Farber Cancer Institute, Harvard University, Boston, USA.

Fellowships and awards
2012: Ita Askonas prize from EFIS-EJI for best female group leader in immunology
2003: CIRE (Centro di Iniziative Regionale ed Europea) award, for important activities carried out in European projects.
1997: Harlan Nossal award for the best work on Experimental Immunology presented at the Italian Society of Immunology in 1997

1996-1997: Research fellowship of the Telethon Research Foundation for Muscular Dystrophy and Genetic Disorders
1995: FABT (Fondazione Adriano Buzzati-Traverso) award

Teaching activities
1998 at present: Basic and Advanced Immunology courses at the University of Milano-Bicocca, on average 160 hours per year.
Since 2001 at least three lectures per years to (inter)national courses or (inter)national institutes.

Institutional responsibilities
2001-today: Faculty member of the University of Milano-Bicocca, Milan, Italy
2003-today: Faculty of the International PhD School in Translational and Molecular Medicine (DIMET) of the University of Milano-Bicocca (www.DIMET.org)
2010-2012: Member of the Department Internal Board, Dep. of Biotechnology and Bioscience, University of Milano-Bicocca, Milan, Italy.
2014-today: Erasmus Plus program coordinator for the Dep. of Biotechnology and Bioscience, University of Milano-Bicocca, Milan, Italy
2014-today: Coordinator of the internationalization activities of the Dep. Of Biotechnology and Biosciences

Commission of trust
2014-today Member of the board of directors of SIICA (Società Italiana di Immunologia Clinica e Allergologia)
2016-today Immunology Councilor of IEIIS (International Endotoxin and Innate Immunity Society)
Editor in Chief of the section Molecular Innate Immunity of Frontiers in Immunology
Associate Editor of Molecular Immunology
Associate Editor of Mediators of Inflammation
Member of the Editorial Advisory Board of the Open Autoimmunity Journal
Member of the Editorial Board of the American Journal of Clinical and Experimental Immunology
Member of the Editorial Board AIMS Molecular Science

Membership of scientific societies
2002-today Member of SIICA (Società Italiana di Immunologia Clinica e Allergologia)
2012-today Member of EMDS (European Macrophage and Dendritic cell Society)
2012-today Member of ESCI (European Society of Clinical Investigation).
2013-2014 Member of SLB (Society of Leukocyte Biology)
2014-today Member of IEIIS (International Endotoxin and Innate Immunity Society)

C. Contributions to Science

My group has pioneered systems biology approaches to study complex dynamic processes of innate immunity, such as host-pathogen interactions and the process of DC maturation in response to different microbial stimuli. Using the GeneChip microarray technology we have described the molecular events occurring during bacterial-DC interactions, including cytoskeleton modifications (1). Moreover, we have discovered that DCs produce IL-2 early after microbial encounter (1). This DC property has been then identified by our and other research groups a as fundamental mechanism of T cell priming in humans and mice and NK cell activation (2, 3, 4). Our group has also uncovered an underlying mechanism of NK cell activation in studies, which demonstrate that dendritic cells (DC) serve as accessory cells to directly activate NK cells, rather than simply priming these cells as previously thought (3, 4).
The discovery of the DC capacity to produce IL-2 has motivated us to focus on deciphering new signaling pathways downstream of Pattern Recognition Receptors within cells of the mammalian innate immune system. Therefore, the research group has focused on the molecular mechanisms regulating selected aspects of the inflammatory process driven by LPS, a component of the outer membrane of Gram-negative bacteria. The research group has demonstrated that CD14, a molecule of the LPS receptor complex, is at the apex of all cellular responses to this bacterial stimulus, by controlling its recognition and TLR4 (the major component of LPS receptor complex) trafficking to the endosomal compartment with the consequent initiation of all the signaling pathways known to be activated in response to this microbial stimulus (5). Moreover, our group has

identified a new signaling pathway activated by LPS in dendritic cells completely controlled by CD14 and leading to the activation of NFAT transcription factor family members (6). The activation of the NFAT pathway in innate immune cells has then important consequences in the inflammatory process contributing to vasodilation and increase of vascular permeability in response to microbial stimuli (7). The activation of the NFATc signaling pathway in innate immunity is also fundamental for the elimination of microbial skin infection thanks to the induction of IFN-γ production (8). By studying the inflammatory process activated by microbes in the skin, we have been also able to identify TGF-β as a fundamental cytokine during the initial phases of the inflammatory response to avoid excessive microbial spreading in the tissue. Moreover, we have found IFN-γ, induced by NFATc pathway activation, contributes to microbial elimination not only by the induction of type 1 macrophages and neutrophils, but also via the activation of the fibrinolytic system (8). More recently, we have contributed to the characterization of the role of IFN-λ in neutrophils during the inflammatory process. IFN-λ specifically activates a signaling pathway that diminishes the production of reactive oxygen species and degranulation in neutrophils, thus contributing to limit tissue damage (9).

1. Granucci F, Vizzardelli C, Pavelka N, Feau S, Persico M, Virzi E, Rescigno M, Moro G, Ricciardi-Castagnoli P. Inducible IL-2 production by dendritic cells revealed by global gene expression analysis. **Nat Immunol**. 2001 Sep;2(9):882-8.
2. Granucci F, Zanoni I, Pavelka N, Van Dommelen SL, Andoniou CE, Belardelli F, Degli Esposti MA, Ricciardi-Castagnoli P. A contribution of mouse dendritic cell-derived IL-2 for NK cell activation. **J Exp Med**. 2004 Aug 2;200(3):287-95.
3. Zanoni I, Spreafico R, Bodio C, Di Gioia M, Cigni C, Broggi A, Gorletta T, Caccia M, Chirico G, Sironi L, Collini M, Colombo MP, Garbi N, Granucci F. IL-15 cis presentation is required for optimal NK cell activation in lipopolysaccharide-mediated inflammatory conditions. **Cell Report**. 2013 Sep 26;4(6):1235-49. doi: 10.1016/j.celrep.2013.08.021. Epub 2013 Sep 19.
4. Mingozzi F, Spreafico R, Gorletta T, Cigni C, Di Gioia M, Caccia M, Sironi L, Collini M, Soncini M, Rusconi M, von Andrian UH, Chirico G, Zanoni I, Granucci F. Prolonged contact with dendritic cells turns lymph node-resident NK cells into anti-tumor effectors. **EMBO Mol Med**. 2016 Sep 1;8(9):1039-51.
5. Zanoni I, Ostuni R, Marek LR, Barresi S, Barbalat R, Barton GM, Granucci F*, Kagan JC*. CD14 controls the LPS-induced endocytosis of Toll-like receptor 4. **Cell.** 2011 Nov 11;147(4):868-80.
   *equal contribution, co-corresponding
6. Zanoni I, Ostuni R, Capuano G, Collini M, Caccia M, Ronchi AE, Rocchetti M, Mingozzi F, Foti M, Chirico G, Costa B, Zaza A, Ricciardi-Castagnoli P, Granucci F. CD14 regulates the dendritic cell life cycle after LPS exposure through NFAT activation. **Nature.** 2009 Jul 9;460(7252):264-8.
7. Zanoni I, Ostuni R, Barresi S, Di Gioia M, Broggi A, Costa B, Marzi R and Granucci F. Mechanism of lipopolysaccharide-induced skin edema formation in the mouse. **J Clin Invest**. 2012 May;122(5):1747-57. doi: 10.1172/JCI60688.
8. Santus W, Barresi S, Mingozzi F, Broggi A, Orlandi I, Stamerra G, Vai M, Martorana A, Polissi M, Köhler JR, Liu N, Zanoni I, Granucci F. Skin infections are eliminated by cooperation of the fibrinolytic and innate immune systems. **Science Immunology**, in press.
9. Broggi A, Tan Y, Granucci F*, Zanoni I*. IFN-λ suppresses intestinal inflammation by non-translational regulation of neutrophil function. **Nat Immunol**. 2017 Aug 28. doi: 10.1038/ni.3821.
   *equal contribution, co-corresponding

Complete List of Published Work: https://www.ncbi.nlm.nih.gov/pubmed/?term=granucci+f

International and National Funding

Title	Source	Role	Duration	Amount
DC THERA Network of Excellence: Dendritic cells for novel immunotherapies	EC FP6	PI	2005-2009	120.000
MUGEN Network of Excellence: Integrated functional genomics in mutant mouse models as tools to investigate the complexity of human immunological disease	EC FP6	co-investigator	2005-2009	160.000

Molecular mechanisms of dendritic cell-induced activation of anti-tumor innate immunity	Cariplo Foundation	PI	2005-2007	180000
Mechanisms of tolerance induction in autoreactive T cells involved in Herpes Stromal Keratitis	Cariplo Foundation	PI	2007-2009	180000
Molecular mechanisms of dendritic cell-induced activation of anti-tumor innate immunity	AIRC	PI	2005-2007	120000
Key regulators of DC-primed anti-tumor NK cell functions	AIRC	PI	2007-2010	180000
Cellular and molecular mechanisms of dendritic cell-induced activation of anti-tumor NK cell functions	PRIN 2007 Italian Ministry of Research	PI	2007-2009	100000
Normalisation of immune reactivity in old age – from basic mechanisms to clinical .application Tolerage	EC FP7	PI	2007-2012	565.000
European Network for Cell Imaging and Tracking Expertise ENCITE	EC FP7	PI	2007-2012	593.000
Role of IL-2 and probiotics in modulating cancer immunosurveillance: identification of new therapeutic strategies	Cariplo Foundation	Co-investigator	2011-2014	180.000
Induction and maintenance of cancer innate immunosurveillance by selected commensal Gram-positive bacteria	AIRC	PI	2010-2013	190000
Lombardy immunology network LIIN	Regione Lombardia	PI	2010-2012	60000
Modulation of natural killer cell-mediated tumor immunosurveillance.	PRIN 2009 Italian Ministry of Research	PI	2011-2013	50000
Naiter, EARLY SYSTEM NANOTECHNOLOGY	Fondazione per la Ricerca Biomedica	Co-PI	2012-2017	1000000
The Type I INF-IL-15 axis in the induction of anti-tumor activities of NK cells	AIRC	PI	2014-2016	230000
Activation state and functionality of dendritic cells from peripheral blood of ALS patients	ARISLA (Italian foundation against SLA)	PI	2015-2016	50.000
Role of the NFAT signalling pathway in determining inflammation during aging and neurodegeneration	Cariplo Foundation	PI	2015-2018	320.000
Study of the capacity of the NFAT transcription factors to favor cancer progression by immunoevasion and chemoresistance.	AIRC	PI	2016-2019	290000

Bibliometric indexes:
HI: 44, total publications 113, total citations 10470

Publications (Last 10 years, selected)

1. Grasselli C, Ferrari D, Zalfa C, Soncini M, Mazzoccoli G, Facchini FA, Marongiu L, Granucci F, Copetti M, Vescovi AL, Peri F, De Filippis L. Toll-like receptor 4 modulation influences human neural stem cell proliferation and differentiation. Cell Death Dis. 2018 Feb 15;9(3):280.
2. Granucci F. The family of LPS signal transducers increases. The arrival of chanzymes. Immunity, 2018 Jan 16;48(1):4-6.
3. Zanoni I, Granucci F, Broggi A. Interferon (IFN)-λ Takes the Helm: Immunomodulatory Roles of Type III IFNs. Front Immunol. 2017 Nov 28;8:1661. doi: 10.3389/fimmu.2017.01661. eCollection 2017. Review.
4. Granucci F, Prosperi D. Nanoparticles: "magic bullets" for targeting the immune system. Semin Immunol. 2017 Dec;34:1-2. doi: 10.1016/j.smim.2017.10.002. No abstract available.
5. Santus W, Barresi S, Mingozzi F, Broggi A, Orlandi I, Stamerra G, Vai M, Martorana AM, Polissi A, Köhler JR, Liu N, Zanoni I, Granucci F. Skin infections are eliminated by cooperation of the fibrinolytic and innate immune systems. Sci Immunol. 2017 Sep 22;2(15). pii: eaan2725. doi: 10.1126/sciimmunol.aan2725.
6. Prosperi D, Colombo M, Zanoni I, Granucci F. Drug nanocarriers to treat autoimmunity and chronic inflammatory diseases. Semin Immunol. 2017 Dec;34:61-67. doi: 10.1016/j.smim.2017.08.010. Epub 2017 Aug 30. Review.

7. Broggi A, Tan Y, Granucci F*, Zanoni I*. IFN-λ suppresses intestinal inflammation by non-translational regulation of neutrophil function. Nat Immunol. 2017 Oct;18(10):1084-1093. doi: 10.1038/ni.3821. Epub 2017 Aug 28. . *equal contribution, co-corresponding
8. Rusconi M, Gerardi F, Santus W, Lizio A, Sansone VA, Lunetta C, Zanoni I, Granucci F. Inflammatory role of dendritic cells in Amyotrophic Lateral Sclerosis revealed by an analysis of patients' peripheral blood. Sci Rep. 2017 Aug 10;7(1):7853. doi: 10.1038/s41598-017-08233-1.
9. Diani M, Galasso M, Cozzi C, Sgambelluri F, Altomare A, Cigni C, Frigerio E, Drago L, Volinia S, Granucci F, Altomare G, Reali E Blood to skin recirculation of CD4+ memory T cells associates with cutaneous and systemic manifestations of psoriatic disease. Clin Immunol. 2017 Jul;180:84-94. doi: 10.1016/j.clim.2017.04.001. Epub 2017 Apr 6.
10. Mingozzi F, Spreafico R, Gorletta T, Soncini MC, Cigni C, Di Gioia M, Caccia M, Sironi L, Collini M, Rusconi M, Chirico G, Zanoni I and **Granucci F** Lymph node-resident NK cells become anti-tumor effectors upon prolonged contact with dendritic cells. EMBO Mol Med 2016 Sep 1;8(9):1039-51
11. Sgambelluri F, Diani M, Frigerio E, Drago L, **Granucci F**, Banfi G, Altomare G, Reali E. A role for CCR5+CD4 T cells in cutaneous psoriasis and for CD103+ CCR4+ CD8 Teff cells in the associated systemic inflammation. J. of Autoimmunity 2016 Jun;70:80-9
12. Broggi A, **Granucci F**. Microbe- and danger-induced inflammation. Mol Immunol. 2015 Feb;63(2):127-33. doi: 10.1016/j.molimm.2014.06.037
13. **Granucci F**, Lutz MB, Zanoni I The nature of activatory and tolerogenic dendritic cell-derived signal 2. Front Immunol. 2014 Feb 6;5:42. doi: 10.3389/fimmu.2014.00042. eCollection 2014.
14. Zanoni I, Spreafico R, Bodio C, Di Gioia M, Cigni C, Broggi A, Gorletta T, Caccia M, Chirico G, Sironi L, Collini M, Colombo MP, Garbi N, **Granucci F**. IL-15 cis presentation is required for optimal NK cell activation in lipopolysaccharide-mediated inflammatory conditions. Cell Report. 2013 Sep 26;4(6):1235-49. doi: 10.1016/j.celrep.2013.08.021. Epub 2013 Sep 19.
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16. Broggi A, Zanoni I, **Granucci F**. Migratory conventional dendritic cells in the induction of peripheral T cell tolerance. J Leukoc Biol. 2013 Nov;94(5):903-11. doi: 10.1189/jlb.0413222. Epub 2013 Jul 29.
17. **Granucci F**, Lutz MB, Zanoni I. The nature of activatory and tolerogenic dendritic cell-derived signal 2. Front Immunol. 2013 Jul 16;4:198. doi: 10.3389/fimmu.2013.00198. eCollection 2013..
18. Vitali C, Mingozzi F, Broggi A, Barresi S, Zolezzi F, Bayry J, Raimondi G, Zanoni I, **Granucci F**. Migratory, and not lymphoid-resident, dendritic cells maintain peripheral self-tolerance and prevent autoimmunity via induction of iTreg cells. Blood. 2012 Aug 9;120(6):1237-45.
19. Zanoni I, **Granucci F**. Regulation and dysregulation of innate immunity by NFAT signaling downstream of pattern recognition receptors (PRRs). Eur J Immunol. 2012 Aug;42(8):1924-31.
20. Zanoni I, Ostuni R, Barresi S, Di Gioia M, Broggi A, Costa B, Marzi R and **Granucci F.** Mechanism of lipopolysaccharide-induced skin edema formation in the mouse. J Clinical Investigation 2012 May;122(5):1747-57. doi: 10.1172/JCI60688
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22. Ostuni R, Zanoni I, **Granucci F**. Deciphering the complexity of Toll-like receptor signaling. Cell Mol Life Sci. 2010 Dec;67(24):4109-34. Epub 2010 Jul 31.
23. Zanoni I, **Granucci F**. The regulatory role of dendritic cells in the induction and maintenance of T-cell tolerance. Autoimmunity. 2011 Feb;44(1):23-32. Epub 2010 Jul 29.
24. Zanoni I, **Granucci F**. Regulation of antigen uptake, migration, and lifespan of dendritic cell by Toll-like receptors. J Mol Med (Berl). 2010 Sep;88(9):873-80. Epub 2010 Jun 18
25. **Granucci F**, Zanoni I. The dendritic cell life cycle. Cell Cycle. 2009 Dec;8(23):3816-21. Epub 2009 Dec 4.
26. Zanoni I, Ostuni R, Capuano G, Collini M, Caccia M, Ronchi AE, Rocchetti M, Mingozzi F, Foti M, Chirico G, Costa B, Zaza A, Ricciardi-Castagnoli P, **Granucci F**. CD14 regulates the dendritic cell life cycle after LPS exposure through NFAT activation. Nature. 2009 Jul 9;460(7252):264-8.
27. **Granucci F**, Zanoni I. Role of Toll like receptor-activated dendritic cells in the development of autoimmunity. Front Biosci. 2008 May 1;13:4817-26.
28. **Granucci F**, Zanoni I, Ricciardi-Castagnoli P. Central role of dendritic cells in the regulation and deregulation of immune responses. Cell Mol Life Sci. 2008