

FABIO GRASSI

Curriculum Vitae

Personal Information

Name Fabio Grassi, M.D., Ph.D.
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Professional Information

Education

1985 M.D. University of Pavia
1993 Ph.D. University of Milano

Postdoctoral Training

1985-1988 Research Assistant, Department of Biology and Genetics, University of Milano, Italy.
1988 Anna Villa Rusconi Fellowship, The Unit for Applied Cell and Molecular Biology, University of Umeå, Sweden.
1989-1993 Post-doctoral fellow, Unité d'Immuno-chimie Analytique, Institut Pasteur, Paris, France.

Licensure and certification

1985 Approbation as General Practitioner

Fellowships

2001-2004 Special Fellow Award, The Leukemia & Lymphoma Society, New York.

Academic Appointments

1993-1994 Senior Investigator, Department of Biological and Technological Research at San Raffaele Scientific Institute, Milano, Italy.
1994-2000 Assistant Professor, Division of Immunology, Department of Biology and Genetics, University of Milano School of Medicine, Milano, Italy.
2000-2002 Instructor of Pathology, Harvard Medical School, Boston.
2002-present Associate Professor, Medical School, University of Milan, Italy

Teaching

Medical School, University of Milano, Italy
Biology courses for Medical School students
Medical Biotechnology School, University of Milano, Italy
Advanced courses for Master students

Supervisor of graduate students

Francesca Sutti	1994-1998	Differential gene expression during thymus development
Simona Porcellini	1995-2000	Thymus development in recombina-se-deficient mice
Maddalena Panigada	1996-2000	Analysis of pre-TCR regulated gene expression
Eleonora Maurizio	2003-2005	Role of calreticulin in T cell activation
Micol Ferro	2004-2006	Calcium ions homeostasis in the T cell
Denise Ferrera	2003-2008	Subcellular microdomains in T cell development
Anna Casati	2003-2008	Hematopoiesis during T cell mediated inflammation
Michela Frascoli	2008-2011	Purinergic signaling in T cell development
Fabia Filipello	2010-2013	Molecular and cellular mechanisms in astrocyte-T cell cross-talk
Caterina E. Faliti	2012-present	Purinergic control of T cell help in adaptive immune response
Andrea Romagnani	2012-present	Signal transduction by purinergic P2X7 receptor in murine T cells
Lisa Perruzza	2012-present	Purinergic antagonism to promote immunoregulation in T1 diabetes

Supervisor of post-docs

Ursula Schenk, Ph.D.	2004-2010	Purinergic control of T cell activation and immunopathology
Stefano Volpi, M.D.	2007-2008	Purinergic signaling in systemic lupus erythematosus
Michele Proietti, M.D.	2008-2013	Subcellular routing of P2 receptors in T cell activation

Report of Research

Major research interests

- Developmental biology of the thymus
- Signal transduction in the T cell
- Cell biology of T cell mediated inflammation

Description of main scientific achievements as principal investigator

Fabio Grassi has studied the developmental regulation of gene expression in the thymus upon pre-TCR signaling. Among the characterization of several aspects of cell and molecular regulation of thymus development he identified and characterized biochemically as well as functionally a new member of the immunoglobulin superfamily (EVA, Epithelial V-like Antigen) expressed in epithelia in a developmentally regulated fashion. In another set of experiments Fabio Grassi has studied signal transduction in pre-T cells. He described and characterized constitutive initiation of signaling as well as downregulation of the pre-TCR. More recently, he addressed the role of purinergic signalling in T cell development and peripheral control of T cell responses. He discovered that CD4 cells release ATP following TCR stimulation through pannexin-1 hemichannels and ATP acts as a crucial autocrine signal for productive T cell activation. In vivo inhibition of this co-stimulatory signalling pathway dramatically ameliorated the outcome of several T cell mediated inflammatory conditions. He found that the immunosuppressive activity of regulatory CD4 cells is regulated by P2X7 receptor activity. He described the relevance of autocrine purinergic signalling through P2X receptors in cell cycle control of hematopoietic stem cell and in $\gamma\delta$ T cell lineage development. Finally, he has contributed together with Dr. Anna Villa (CNR, Milan, Italy) to the development of the murine model of Omenn syndrome, a severe primary immunodeficiency in humans.

Publications

1. Peer-reviewed articles (original publications)

1. Cavallini A., Rezzonico Jost T., Ghoreishizadeh S., Olivo J., Op de Beeck M., Gorissen B., **Grassi F.**, De Micheli G., and Carrara S. A subcutaneous biochip for remote monitoring of human metabolism: development, packaging and biocompatibility assessment. *IEEE Sensors Journal*, in press.
2. Schena F., Volpi S., Faliti C.E., Penco F., Santi S., Proietti M., Schenk U., Damonte G., Salis A., Bellotti M., Fais F., Tenca C., Martini A., Gattorno M., Eibel H., Rizzi M., Warnatz K., Idzko M., Ayata K., Rakhmanov M., Galli T., Canossa M., **Grassi F.** and Traggiai E. Dependence of immunoglobulin class switch recombination in B cells on vesicular release of ATP and CD73 ectonucleotidase activity. *Cell Reports*, 3: 1824-1831 (2013).
3. Carrara S., Bolomey L., Boero C., Cavallini A., Meurville E., De Micheli G., Rezzonico Jost T., Proietti M. and **Grassi F.** Remote system for monitoring animal models with single-metabolite bio-nano-sensors. *IEEE Sensors Journal*, 13: 1018-1024 (2013)
4. Vergani A., Fotino C., D'Addio F., Tezza S., Podetta M., Gatti F., Chin M., Bassi R., Molano R.D., Corradi D., Gatti R., Ferrero M.E., Secchi A., **Grassi F.**, Ricordi C., Sayegh M.H., Maffi P., Pileggi A. and Fiorina P. Effect of the purinergic inhibitor oxidized-ATP in a model of islet allograft rejection. *Diabetes*, 62: 1665-1675 (2013)
5. Vergani A., Tezza S., D'Addio F., Fotino C., Liu K., Niewczas M., Bassi R., Molano R.D., Kleffel S., Petrelli A., Soleti A., Ammirati E., Frigerio M., Visner G., **Grassi F.**, Ferrero M.E., Corradi D., Abdi R., Ricordi C., Sayegh M.H., Pileggi A., Fiorina P. Long-term heart transplant survival by targeting the ionotropic purinergic receptor P2X7. *Circulation*, 127: 463-475 (2013)
6. Marrella V., Poliani P.L., Fontana E., Casati A., Maina V., Cassani B., Ficara F., Cominelli M., Schena F., Paulis M., Traggiai E., Vezzoni P., **Grassi F.*** and Villa A.* Anti-CD3 ϵ mAb improves thymic architecture and prevents autoimmune manifestations in a mouse model of Omenn syndrome: therapeutic implications. *Blood*, 120: 1005-1014 (2012) * equal contribution
7. Frascoli M., Marcandalli J., Schenk U. and **Grassi F.** Purinergic P2X7 receptor drives T cell lineage choice and shapes peripheral $\gamma\delta$ cells. *The Journal of Immunology*, 189: 174-180 (2012)
8. Frascoli M., Proietti M. and **Grassi F.** Phenotypic analysis and isolation of murine hematopoietic stem cells and lineage committed progenitors. *Journal of Visualized Experiments*, 65: e3736 (2012).
9. Pezzolato M., Maina E., Lonardi S., Bozzetta E., **Grassi F.**, Scanziani E. and Radaelli E. Development of tertiary lymphoid structures in the kidneys of pigs with chronic leptospiral nephritis. *Veterinary Immunology and Immunopathology*, 145: 546-550 (2012)
10. Ardisson V., Radaelli E., Zaratini P., Ardizzone M., Ladel C., Gattorno M., Martini A., **Grassi F.** and Traggiai E. Pharmacological purinergic P2X antagonism in the treatment of experimental collagen-induced arthritis. *Arthritis & Rheumatism*, 63: 3323-3332 (2011)

11. Pallotta M.T., Orabona C., Volpi C., Vacca C., Belladonna M.L., Bianchi R., Servillo G., Brunacci C., Calvitti M., Biciato S., Mazza E.M.C., Boon L., **Grassi F.**, Fioretti M.C., Fallarino F., Puccetti P. and Grohmann U. Indoleamine 2,3-dioxygenase is a signaling protein in long-term tolerance by dendritic cells. *Nature Immunology*, 12: 870-878 (2011)
12. Schenk U., Frascoli M., Proietti M., Geffers R., Traggiai E., Buer J., Ricordi C., Westendorf A.M. and **Grassi F.** ATP inhibits the generation and function of regulatory T cells through the activation of purinergic P2X receptors. *Science Signaling*, 4: ra12 (2011)
13. Casati A., Frascoli M., Traggiai E., Proietti M., Schenk U. and **Grassi F.** Cell-autonomous regulation of hematopoietic stem cell cycling activity by ATP. *Cell Death & Differentiation*, 18: 396-404 (2011)
14. Traggiai E., Casati A., Frascoli M., Porcellini S., Ponzoni M., Sanvito F., Leng L., Bucala R., Moretta L. and **Grassi F.** Selective Preservation of Bone Marrow Mature Recirculating but Not Marginal Zone B Cells in Murine Models of Chronic Inflammation. *PLoS ONE* 5(6): e11262. doi:10.1371/journal.pone.0011262 (2010)
15. Cassani B., Poliani P.L., Marrella V., Schena F., Sauer A.V., Ravanini M., Strina D., Busse C.E., Regenass S., Wardemann H., Martini A., Facchetti F., van der Burg M., Rolink A.G., Vezzoni P., **Grassi F.**, Traggiai E. and Villa A. Homeostatic expansion of autoreactive immunoglobulin secreting cells in the *Rag2* mouse model of Omenn Syndrome. *The Journal of Experimental Medicine*, 207: 1525-1540 (2010)
16. Dolcetti L., Peranzoni E., Ugel S., Marigo I., Fernandez Gomez A., Mesa C., Geilich M., Winkels G., Traggiai E., Casati A., **Grassi F.** and Bronte V. Hierarchy of immunosuppressive strength among myeloid-derived suppressor cell subsets is determined by GM-CSF. *European Journal of Immunology*, 40: 22-35 (2010)
17. Schenk U., Westendorf A.M., Radaelli E., Casati A., Ferro M., Fumagalli M., Verderio C., Buer J., Scanziani E. and **Grassi F.** Purinergic control of T cell activation by ATP released through pannexin-1 hemichannels. *Science Signaling*, 1 (39), ra6 (2008)
18. Ferrera D., Panigada M., Porcellini S. and **Grassi F.** Recombinase-deficient T cell development by selective accumulation of CD3 into lipid rafts. *European Journal of Immunology*, 38:1148-1156 (2008)
19. Marrella V., Poliani P.L., Casati A., Rucci F., Frascoli L., Gougeon M-L., Lemerrier B., Bosticardo M., Ravanini M., Battaglia M., Roncarolo M.G., Cavazzana-Calvo M., Facchetti F., Notarangelo L.D., Vezzoni P., **Grassi F.** and Villa A. A hypomorphic R229Q *Rag2* mouse mutant recapitulates human Omenn syndrome. *The Journal of Clinical Investigation*, 117: 1260-1269 (2007)
20. Campese A.F., Garbe A.I., Zhang F., **Grassi F.**, Screpanti I. and von Boehmer H. Notch1-dependent lymphomagenesis is assisted by but does not essentially require pre-TCR signaling. *Blood*, 108: 305-310 (2006)
21. Porcellini S., Traggiai E., Schenk U., Ferrera D., Matteoli M., Lanzavecchia A., Michalak M. and **Grassi F.** Regulation of peripheral T cell activation by calreticulin. *The Journal of Experimental Medicine*, 203: 461-471 (2006)
22. Penkov D., Di Rosa P., Diaz L.F., Basso V., Ferretti E., **Grassi F.**, Mondino A. and Blasi F. Involvement of Prep1 in the $\alpha\beta$ TCR T-lymphocytic potential of hematopoietic precursors. *Molecular and Cellular Biology*, 25: 10768-10781 (2005)
23. Porcellini S., Vallanti G., Nozza S., Poli G., Lazzarin A., Tambussi G., Siccardi A.G. and **Grassi F.** Improved thymopoietic potential in aviremic HIV-infected individuals treated with HAART by intermittent IL-2 administration. *AIDS*, 17: 1621-1630 (2003)
24. Panigada M., Porcellini S., Barbier E., Hoeflinger S., Cazenave P-A., Gu H., Band H., von Boehmer H. and **Grassi F.** Constitutive endocytosis and degradation of the pre-T cell receptor. *The Journal of Experimental Medicine*, 195: 1585-1597 (2002)
25. Panigada M., Sturniolo T., Besozzi G., Bocchieri M.G., Sinigaglia F., Gialdroni Grassi G. and **Grassi F.** Identification of a promiscuous T-cell epitope in *Mycobacterium tuberculosis* mce proteins. *Infection and Immunity*, 70: 79-85 (2002)
26. Barbier E., Cazenave P.A. and **Grassi F.** A role for CD8 in limiting degeneracy of thymocyte selection. *Cellular and Molecular Biology*, 47: 129-133 (2001)
27. Saint-Ruf C., Panigada M., Azogui O., Debey P., von Boehmer H. and **Grassi F.** Different initiation of pre-TCR and $\gamma\delta$ TCR signalling. *Nature*, 406: 524-527 (2000)
28. Von Boehmer H., Aifantis I., Azogui O., Saint-Ruf C. and **Grassi F.** The impact of pre-T cell receptor signals on gene expression in developing T cells. In: *Signaling & Gene Expression in the Immune System*, Cold Spring Harbor Symposia on Quantitative Biology, Vol. LXIV: 283-289 (1999)
29. Calogero S., **Grassi F.**, Aguzzi A., Voigtlander T., Ferrier P. and Bianchi M.E. The lack of chromosomal protein HMG1 does not disrupt cell growth, but causes lethal hypoglycemia in newborn mice. *Nature Genetics*, 22: 276-280 (1999)
30. Porcellini S., Panigada M. and **Grassi F.** Molecular and cellular aspects of induced thymus development in recombinase-deficient mice. *European Journal of Immunology*, 29: 2476-2483 (1999)

31. **Grassi F.**, Barbier E., Porcellini S., Von Boehmer H. and Cazenave P.A. Surface expression and functional competence of CD3-independent TCR ζ chains in immature thymocytes. *The Journal of Immunology*, 162: 2589-2596 (1999)
32. Panigada M., Porcellini S., Sutti F., Doneda L., Pozzoli O., Consalez G.G., Guttinger M. and **Grassi F.** GKLF in thymus epithelium as a developmentally regulated element of thymocyte-stroma cross-talk. *Mechanisms of Development*, 81: 115-125 (1999)
33. Teesalu T., **Grassi F.** and Guttinger M. Expression pattern of the epithelial V-like antigen (EVA) transcript suggests a possible role in placental morphogenesis. *Developmental Genetics*, 23: 317-323 (1998)
34. Guttinger M., Sutti F., Panigada M., Porcellini S., Merati B., Mariani M., Teesalu T., Consalez G.G. and **Grassi F.** EVA, a novel member of the immunoglobulin superfamily expressed in embryonic epithelia with a potential role as homotypic adhesion molecule in thymus histogenesis. *The Journal of Cell Biology*, 141: 1061-1071 (1998)
35. **Grassi F.**, Liberman I., Cazenave P.A. and Rueff-Juy D. Intrathymic development of mouse ab and gd lymphocytes. *Bulletin de l'Institut Pasteur*, 92:197-211 (1994).
36. **Grassi F.**, Barbier E. and Cazenave P.A. Early degenerate selection of thymocytes by class I major histocompatibility complex. *European Journal of Immunology*, 24:627-634 (1994).
37. Lopalco L., De Santis C., Meneveri R., Longhi R., Ginelli E., **Grassi F.**, Siccardi A.G. and Beretta A. Human immunodeficiency virus type 1 gp120 C5 region mimics the HLA class I a1 peptide binding domain. *European Journal of Immunology*, 23: 2016-2021 (1993).
38. **Grassi F.**, Meneveri R., Gullberg M., Lopalco L., Rossi G.B., Lanza P., De Santis C., Brattsand G., Buttò S., Ginelli E., Beretta A. and Siccardi A.G.. Human immunodeficiency virus type I gp120 mimics a hidden monomorphic epitope borne by class I major histocompatibility complex heavy chains. *The Journal of Experimental Medicine*, 174: 53-62 (1991).
39. **Grassi F.**, Lopalco L., Lanza P., Ciccomascolo F., Cazzola F., Di Martino A., Kirshner G., Callegaro L., Chieco-Bianchi L. and Siccardi A.G.. Chemical residues of gangliosides molecules involved in interactions with lymphocyte surface targets leading to CD4 masking and inhibition of mitogenic proliferation. *European Journal of Immunology*, 20:145-150 (1990).

2. Reviews

1. Borowski C., Martin C., Gounari F., Haughn L., Aifantis I., **Grassi F.** and von Boehmer H. On the brink of becoming a T cell. *Current Opinion in Immunology*, 14: 200-206 (2002)
2. Von Boehmer H., Aifantis I., Gounari F., Azogui O., Haughn L., Apostolou I., Jaeckel E., **Grassi F.** and Klein L. Thymic selection revisited : how essential is it ? *Immunological Reviews*, 191 : 62-78 (2003)
3. Marrella V., Poliani P.L., Sobacchi C., Grassi F. and Villa A. Of Omenn and mice. *Trends in Immunology*, 29: 133-140 (2008)
4. Grassi F. Purinergic control of neutrophil activation. *Journal of Molecular Cell Biology*, 2:176-177 (2010)

3. Educationally Relevant Publications

1. Chapter : « Anticorpi Monoclonali » in « Enciclopedia Medica Italiana »
2. Nonprint Materials : Scenography of the film strip « Lymphocyte Development » commissioned by Enciclopedia Italiana Treccani for the electronic version of the Enciclopedia Italiana.