

BRIEF CURRICULUM VITAE

NAME Alberto MANTOVANI
GENDER Male
DATE OF BIRTH October 29, 1948, Milan, Italy
CITIZENSHIP Italian
MARITAL STATUS Married, four children
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EDUCATION

1973: M.D., University of Milan, Italy
1976: Specialist in Oncology, University of Pavia, Italy

HONORS

1973: Graduate summa cum laude
1973: Fellow of the Italian Association Against Leukemias
1974: Fellow of the Anna Villa Rusconi Foundation
1975: Fellowship from the British Council
1978: Yamagiwa - Yoshida International Study grant from UICC, Geneva, Switzerland
1979: Awarded a NATO fellowship
1987: Eleanor Roosevelt UICC fellow
1998: Biotec Award
2000: Marie T. Bonazinga Award, Boston, USA
2003: Otto Hertz Lecturer, Tel Aviv
2004: Guido Venosta Award for Cancer Research by the President of the Republic of Italy
2004: Walter Cottman Lecturer, Monash University, Melbourne, Australia
2006: "Onorificenza al Merito della Repubblica Italiana" (Commendatore) for scientific contribution by the President of the Republic of Italy
2006: European Federation of Immunological Societies – Schering Plough, 1st European Immunology Prize, Paris, France
2006: XIV Premio per la Ricerca Finalizzata alla Lotta Contro i Tumori, Cassa di Risparmio di Asti
2007: Galileo Galilei Prize for Research in Biomedical Sciences (International Jury composed by Ronald B Herberman, Stuart A Aaronson, Klas Karre, Reinhold E Schmidt)
2007: Premio PISO (international Jury composed by past awardees: Luc Montagnier, Anthony Fauci, Lorenzo Moretta, P. Mannuccio Mannucci)
2009: William Harvey Award, Outstanding Scientist 2009, London, UK.
2010: Paul Kallos Lecturer, Collegium Internationale Allergologicum
2011: IMID Award for Excellence in Immunology
2012: Hans J. Müller-Eberhard Lecturer, Complement Workshop, Crete

MEMBERSHIPS AND BOARDS

1995-1998: President, Italian Federation of Immunological Societies
1998-2001: President, Italian Society of Immunology
2000 to date: European Molecular Biology Organization (EMBO) Member
2002: Member, The Henry Kunkel Society
2007-2010: Board Member of the Global Alliance for Vaccines and Immunization (GAVI Alliance)
2008: Member, Faculty of 1000 Biology
2009-2010: President, International Cytokine Society
2011-to date: Board Member, International Union of Immunological Societies (IUIS)

RESEARCH EXPERIENCE

- 1973-1975:** Research assistant Department of Tumor Immunobiology and Chemotherapy Istituto "Mario Negri", Milan, Italy.
- 1975-1976:** Visiting fellow at the Department of Tumor Immunology Chester Beatty Research Institute, Belmont, Sutton, Surrey, England.
- 1978:** Visiting fellow at the Laboratory of Immunodiagnosis, NIH Bethesda, MD., USA, supported by a NATO Grant.
- 1979-1981:** Senior investigator, Department of Tumor Immunology and Chemotherapy Istituto "Mario Negri", Milan, Italy.
- 1981:** Chief, Laboratory of Immunology, Istituto "Mario Negri", Milan, Italy.
- 1987:** Eleanor Roosevelt UICC Scholar, Laboratory of Molecular Immunoregulation, NIH Frederick, MD., USA.
- 1994 to 2001:** Full Professor of General Pathology, School of Medicine University of Brescia, Italy.
- 1996 to 2005:** Head, Department of Immunology and Cell Biology Istituto "Mario Negri", Milan, Italy.
- 2001 to date:** Full Professor of General Pathology, School of Medicine, State University of Milan, Italy
- Sept. 2005 to date:** Scientific Director, Istituto Clinico Humanitas and President Fondazione Humanitas per la Ricerca.

Main contributions

Tumor biology: Demonstration of the protumor function of tumor-associated macrophages (TAM) linking inflammation and cancer (reviewed in Balkwill and Mantovani, Lancet, 2001); TAM as a prototypic M2 population (Mantovani et al., Nature 2008; Balkwill et al., Cancer Cell 2005); first molecular linking of a genetic event (RET/PTC rearrangement) sufficient to cause cancer in humans to the construction of an inflammatory microenvironment (Borrello et al., PNAS 2005). Alberto Mantovani is generally recognized as a founding father of the renaissance of the inflammation-cancer connection.

Chemokines: original description of Monocyte Chemoattractant Protein-1 as tumor-derived chemotactic factor (Bottazzi et al, Science 1983); characterization of chemokines and role in pathophysiology, including dendritic cell and polarized T cell migration. Induction of chemokine production by IL-6 in endothelial cells via trans-signaling (Romano et al, Immunity 1997). Characterization of D6 as a decoy receptor for CC chemokines (Mantovani et al, Nature Rev. Immunol 2006).

IL-1/Toll-like receptors (TLR): endothelial cell activation by IL-1 and cytokines (Rossi et al., Science 1985; Bussolino et al, Nature 1989; Romano et al, Immunity 1997); identification of the type II receptor as a decoy anti-IL-1 molecule (Colotta et al, Science 1993; decoy receptors are now recognized as a general strategy to tune cytokines, chemokines and growth factors); cloning of an intracellular isoform of IL-1ra (Muzio et al., J. Exp. Med. 1995); first demonstration of MyD88 as the adaptor of TLR and downstream transducers (Muzio et al., J. Exp. Med. 1998); cloning and characterization of TIR8/SIGIRR, a negative regulator of IL-1 receptor and TLR signalling (Garlanda et al., Trends Immunol. 2009).

Humoral innate immunity: cloning (cDNA and genomic, mouse and human), structural and functional characterization of the first long pentraxin PTX3 (Basile et al, J. Biol. Chem. 1997; Garlanda et al, Nature 2002; Jeannin et al, Immunity 2005; Deban et al, Nature Immunol. 2010); structural immunobiology; role as a paradigm for humoral innate immunity; diagnostic and therapeutic translation (ongoing).

Impact

For several years now, bibliometric analyses have indicated that he is one of the, or the, most quoted Italian scientist(s). As of spring 2012 he has had over 41.000 citations. A recent ranking indicates that he is the most quoted Italian scientist working in Italy (http://www.topitalianscientists.org/Top_italian_scientists_VIA-Academy.aspx;) and one of the 10 most quoted immunologists (H-index ISI 108; http://www.tisreports.com/products/19-Top_scientists_in_the_world_the_Via_academy_compilation.aspx).

Selected publications

Originals

Deban L, Castro Russo R, Sironi M, Moalli F, Scanziani M, Zambelli V, Cuccovillo I, Bastone A, Gobbi M, Valentino S, Doni A, Garlanda C, Danese S, Salvatori G, Sassano M, Evangelista V, Rossi B, Zenaro E, Constantin G, Laudanna C, Bottazzi B, Mantovani A. Binding to P-selectin and regulation of leukocyte recruitment by the long pentraxin PTX3, a key component of humoral innate immunity. *Nature Immunol*, 11: 328-334, 2010.

Di Liberto D, Locati M, Caccamo N, Vecchi A, Meraviglia S, Salerno A, Sireci G, Nebuloni M, Cardona P-J, Dieli F, Mantovani A. Role of the chemokine decoy receptor D6 in balancing inflammation, immune activation and antimicrobial resistance in *Mycobacterium tuberculosis* infection. *J. Exp. Med.* 205: 2075-2084, 2008

Lech M, Kulkarni OP, Pfeiffer S, Savarese E, Krug A, Garlanda C, Mantovani A, Anders H-J. Tir8/Sigirr prevents murine lupus by suppressing the immunostimulatory effects of lupus autoantigens. *J. Exp. Med.* 205: 1879-1888, 2008.

Jaillon S, Peri G, Delneste Y, Frèmaux I, Doni A, Moalli F, Garlanda C, Romani L, Gascan H, Bellocchio S, Bozza S, Cassatella MA, Jeannin P, Mantovani A. The humoral pattern recognition receptor PTX3 is stored in neutrophil granules and localized in extracellular traps. *J. Exp. Med.*, 204, 793-804, 2007.

Martinez de la Torre Y, Buracchi C, Borroni EM, Dupor J, Bonecchi R, Nebuloni M, Pasqualini F, Doni A, Lauri E et al. Protection against inflammation- and autoantibody- caused fetal loss by the chemokine decoy receptor D6. *PNAS* 104:2319-2324, 2007.

Biswas SK, Gangi L, Paul S, Schioppa T, Saccani A, Sironi M, Bottazzi B, Doni A, Vincenzo B, Pasqualini F, Vago L, Nebuloni M, Mantovani A*, Sica A. (* corresponding author). A distinct and unique transcriptional program expressed by tumor-associated macrophages (defective NF-kappaB and enhanced IRF-3/STAT1 activation). *Blood* 107:2112-2122, 2006.

Borrello MG, Alberti L, Fischer A, Degl'Innocenti D, Ferrario C, Gariboldi M, Marchesi F, Allavena P, Greco A, Collini P, Pilotti S, Cassinelli G, Bressan P, Fugazzola L, Mantovani A*, Pierotti M* (*corresponding authors). Induction of a proinflammatory programme in normal human thyrocytes by the RET/PTC1 oncogene. *PNAS*, 102: 14825-14830, 2005.

Jeannin P., Bottazzi B., Sironi M., Doni A., Rusnati M., Presta M., Maina V., Magistrelli G., Haeuw J.F., Hoeffel G., Thieblemont N., Corvaia N., Garlanda C., Delneste Y., Mantovani A. Complexity and complementarity of outer membrane protein-A recognition by cellular and humoral innate immunity receptors. *Immunity* 22: 551-560, 2005.

Bertini R, Allegretti M, Bizzarri C, Moriconi A, Locati M, Zampella G, Cervellera M N, Di Cioccio V, Cesta M C, Galliera E, Martinez F O, Di Bitondo R, Troiani G, Sabbatini V, Anacardio R, Cutrin J C, Cavalieri B, Mainiero F, Strippoli R, Villa P, Di Girolamo M, Martin F, Gentile M, Santoni A, Corda D, Ghezzi P, Poli Giuseppe, Mantovani A, Colotta F. A new class of non-competitive allosteric inhibitors of the inflammatory chemokine receptors CXCR1 and CXCR2: Prevention of reperfusion injury. *Proc Natl Acad Sci USA* 101: 11791-11796, 2004.

Garlanda C, Riva F, Polentarutti N, Buracchi C, Sironi M, De Bortoli M., Muzio M, Bergottini R, Scanziani E, Vecchi A, Hirsch E, Mantovani A. Intestinal inflammation in mice deficient in TIR8, an inhibitory member of the IL-1 receptor family. *Proc Natl Acad Sci USA* 101: 3522-3526, 2004.

Schioppa T., Uranchimeg B., Saccani A., Biswas S., Doni A., Rapisarda A., Bernasconi S., Saccani S., Nebuloni M., Vago L., Mantovani A., Melillo G., Sica A. Regulation of the chemokine receptor CXCR4 by hypoxia. *J. Exp. Med.* 198: 1391-1402, 2003.

Wittamer V, Franssen J D, Vulcano M, Mirjolet J F, Le Poul E, Migeotte I, Brezillon S, Tyldesley R, Blanpain C, Detheux M, Mantovani A, Sozzani S, Vassart G, Parmentier M, Communi D. Specific recruitment of antigen-presenting cells by Chemerin, a novel processed ligand from human inflammatory fluids. *J Exp Med* 198: 977-985, 2003.

Garlanda C., Hirsch E., Bozza S., Salustri A., De Acetis M., Nota R., Maccagno A., Riva F., Bottazzi B., Peri G., Doni A., Vago L., Botto M., De Santis R., Carminati P., Siracusa G., Altruda A., Vecchi A., Romani L., Mantovani A. Non-redundant role of the long pentraxin PTX3 in anti-fungal innate immune response. *Nature* 420: 182-186, 2002.

Fratice P, Sironi M, Bianchi G, D'Ambrosio D, Albanesi C, Stoppacciaro A, Chieppa M, Allavena P, Ruco L, Girolomoni G, Sinigaglia F, Vecchi A, Mantovani A Fractalkine (CX3CL1) as an amplification circuit of polarized Th1 responses. *J Clin Invest.* 107: 1173-1181, 2001

D'Amico G, Frascaroli G, Bianchi G, Doni A, Transidico P, Vecchi A, Sozzani S, Allavena P, Mantovani A. Uncoupling of inflammatory chemokine receptors by interleukin 10: Generation of functional decoys. *Nature Immunol.* 1: 387-391, 2000.

Hirsch E, Katanaev V L, Garlanda C, Azzolino O, Silengo L, Sozzani S, Mantovani A, Altruda F, Wymann M P. Central role for G protein-coupled phosphoinositide 3-kinase γ in inflammation. *Science* 287: 1049-1053, 2000.

Muzio M, Natoli G, Sacconi S, Levrero M, Mantovani A.. The human Toll signaling pathway: Divergence of nuclear factor κ B and JNK/SAPK activation upstream of tumor necrosis factor receptor-associated factor 6 (TRAF6). *J. Exp. Med.* 187: 2097-2101, 1998.

Sozzani S, Allavena P, D'Amico G, Luini W, Bianchi G, Kataura M, Imai T, Yoshie O, Bonecchi R, Mantovani A.. Differential regulation of chemokine receptors during dendritic cell maturation: A model for their trafficking properties. *J. Immunol.* 161: 1083-1086, 1998.

Sozzani, S., S. Ghezzi, G. Iannolo, W. Luini, A. Borsatti, N. Polentarutti, A. Sica, M. Locati, C. Mackay, T. N. C. Wells, P. Biswas, E. Vicenzi, G. Poli, and A. Mantovani.. Interleukin-10 increases CCR5 expression and HIV infection in human monocytes. *J. Exp. Med.* 187:439-444, 1998.

Bonecchi R, Bianchi G, Panina Bordignon P, D'Ambrosio D, Lang R, Borsatti A, Sozzani S, Allavena P, Gray P A, Mantovani A, Sinigaglia F. Differential expression of chemokine receptors and chemotactic responsiveness of type 1 T helper cells (Th1s) and Th2s. *J. Exp. Med.* 187: 129-134, 1998.

Romano M, Sironi M, Toniatti C, Polentarutti N, Fruscella P, Ghezzi P, Faggioni R, Luini W, Van Hinsberg V, Sozzani S, Bussolino F, Poli V, Ciliberto G, Mantovani A. Role of IL-6 and its soluble receptor in induction of chemokines and leukocyte recruitment. *Immunity* 6: 315-325, 1997.

Godiska R, Chantry D, Raport C J, Sozzani S, Allavena P, Leviten D, Mantovani A, Gray P W. Human macrophage-derived chemokine (MDC), a novel chemoattractant for monocytes, monocyte-derived dendritic cells, and natural killer cells. *J. Exp. Med.* 185: 1595-1604, 1997.

Sica, A., A. Sacconi, A. Borsatti, C. A. Power, T. N. C. Wells, W. Luini, N. Polentarutti, S. Sozzani, and A. Mantovani.. Bacterial lipopolysaccharide rapidly inhibits expression of C-C chemokine receptors in human monocytes. *J. Exp. Med.* 185:969-974, 1997.

Re, F., M. Sironi, M. Muzio, C. Matteucci, M. Introna, S. Orlando, G. Penton-Rol, S. K. Dower, J. E. Sims, F. Colotta, and A. Mantovani. Inhibition of interleukin-1 responsiveness by type II receptor gene transfer: a surface "receptor" with anti-interleukin-1 function. *J. Exp. Med.* 183: 1841-1850, 1996.

Sozzani S, Sallusto F, Luini W, Zhou D, Piemonti L, Allavena P, Van Damme J, Valitutti S, Lanzavecchia A, Mantovani A. Migration of dendritic cells in response to formyl peptides, C5a, and a distinct set of chemokines. *J. Immunol.* 155: 3292-3295, 1995.

Colotta, F., S. Orlando, E. J. Fadlon, S. Sozzani, C. Matteucci, and A. Mantovani. Chemoattractants induce rapid release of the interleukin 1 type II decoy receptor in human polymorphonuclear cells. *J. Exp. Med.* 181:2181-2188, 1995.

Muzio, M., N. Polentarutti, M. Sironi, G. Poli, L. De Gioia, M. Introna, A. Mantovani, and F. Colotta. Cloning and characterization of a new isoform of the interleukin-1 receptor antagonist. *J. Exp. Med.* 182:623-628, 1995.

Colotta, F., F. Re, M. Muzio, R. Bertini, N. Polentarutti, M. Sironi, J. G. Giri, S. K. Dower, J. E. Sims, and A. Mantovani. Interleukin-1 type II receptor: a decoy target for IL-1 that is regulated by IL-4. *Science* 261: 472-475, 1993.

Bussolino, F., J. M. Wang, P. Defilippi, F. Turrini, F. Sanavio, C. J. Edgell, M. Aglietta, P. Arese, and A. Mantovani. Granulocyte- and granulocyte-macrophage-colony stimulating factors induce human endothelial cells to migrate and proliferate. *Nature* 337: 471-473. 1989.

Rossi, V., F. Breviario, P. Ghezzi, E. Dejana, and A. Mantovani. Prostacyclin synthesis induced in vascular cells by interleukin-1. *Science* 229: 174-176, 1985.

Bottazzi, B., N. Polentarutti, R. Acero, A. Balsari, D. Boraschi, P. Ghezzi, M. Salmona, and A. Mantovani. Regulation of the macrophage content of neoplasms by chemoattractants. *Science* 220:210-212, 1983.

Reviews

Sica A, Mantovani A. Macrophage plasticity and polarization: in vivo veritas. *J Clin Invest.* 122: 787-795, 2012.

Biswas S.K. and Mantovani A. Orchestration of metabolism by macrophages. *Cell Metab.* 15: 432-437, 2012.

Mantovani A, Cassatella MA, Costantini C, Jaillon S. Neutrophils in the activation and regulation of innate and adaptive immunity. *Nat Rev Immunol.* 11: 519-531, 2011.

Biswas S.K. and Mantovani A. Macrophage plasticity and interaction with lymphocyte subsets: cancer as paradigm. *Nat Immunol* 11: 889-896, 2010.

Bottazzi B, Doni A, Garlanda C, Mantovani A. An Integrated View of Humoral Innate Immunity: Pentraxins as a Paradigm. *Annu Rev Immunol.* 28:157-183, 2010.

Garlanda C, Anders HJ, Mantovani A. TIR8/SIGIRR: an IL-1R/TLR family member with regulatory functions in inflammation and T cell polarization. *Trends Immunol.* 30: 439-446, 2009.

Mantovani A. Cancer: Inflaming metastasis. *Nature* 45: 36-37, 2009.

Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-Related Inflammation. *Nature* 454: 436-444, 2008.

Mantovani, A., Romero, P., Paluka, AK., Marincola, FM. Tumor immunity: effector response to tumor and the influence of the microenvironment. *Lancet* 371:771-783, 2008.

Mantovani A, Bonecchi R, Locati M. Tuning inflammation and immunity by chemokine sequestration: decoys and more. *Nature Rev. Immunol.* 6: 907-918, 2006.

Balkwill F, Charles KA, Mantovani A. Smouldering and polarized inflammation in the initiation and promotion of malignant disease. *Cancer Cell* 7: 211-217, 2005.

- Garlanda C., Bottazzi B., Bastone A., Mantovani A., Pentraxins at the crossroads between innate immunity, inflammation, matrix deposition, and female fertility *Annu. Rev. Immunol.*, 23: 337-366, 2005.
- Mantovani A., Sica A., Sozzani S., Allavena P., Vecchi A., Locati M. The chemokine system in diverse forms of macrophage activation and polarization. *Trends Immunol.* 25: 677-686, 2004.
- Mantovani A., Sozzani S., Locati M., Allavena P., Sica A. Macrophage polarization: tumor-associated macrophages as a paradigm for polarized M2 mononuclear phagocytes. *Trends Immunol.* 23: 549-555, 2002.
- Mantovani A., Locati M., Vecchi A., Sozzani S., Allavena P. Decoy receptors as a strategy to regulate inflammatory cytokines and chemokines. *Trends Immunol.* 22: 328-336, 2001.
- Balkwill F. and Mantovani A. Inflammation and cancer: back to Virchow? *Lancet* 357: 539-545, 2001.
- Mantovani A. The chemokine system: redundancy for robust outputs. *Immunol. Today* 20: 254-257, 1999.
- Mantovani, A., F. Bussolino, and M. Introna. Cytokine regulation of endothelial cell function: from molecular level to the bed side. *Immunol. Today.* 18:231-239, 1997.
- Colotta, F., S. K. Dower, J. E. Sims, and A. Mantovani. The type II 'decoy' receptor: novel regulatory pathway for interleukin-1. *Immunol. Today.* 15:562-566, 1994.
- Mantovani, A., F. Bussolino, and E. Dejana. Cytokine regulation of endothelial cell function. *FASEB. J.* 6:2591-2599, 1992.
- Mantovani, A., B. Bottazzi, F. Colotta, S. Sozzani, and L. Ruco. The origin and function of tumor-associated macrophages. *Immunol. Today.* 13:265-270, 1992.
- Mantovani, A. and E. Dejana. Cytokines as communication signals between leukocytes and endothelial cells. *Immunol. Today.* 10:370-375, 1989.