

Curriculum Vitae

Santo Landolfo, M.D., Ph.D.
Full Professor of Microbiology
Head Laboratory of Molecular Virology
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RESEARCH AND PROFESSIONAL EXPERIENCE

1974: Medical Degree, University of Turin, Italy

1978: Ph.D. in Microbiology

1975-1978: Visiting Fellow, National Cancer Institute, NIH, Bethesda, with a project addressed to study the role of a cytokines in the immunity against tumors induced by murine retroviruses (MSV, MLV).

1978-1980: Fellowship of the Italian National Research Council (CNR) to continue the project on the immunity against tumors induced by MSV.

1980-1982: Visiting Associate at the German National Research Institute, DKFZ, Heidelberg, with a research program addressed to explore the mechanisms of IFN-production by cells of the immune system and the mechanism responsible for IFN-antiproliferative activity.

1982-1985: Assistant Professor, Medical School, Turin. During this period the proponent defined the molecular structure of IFN- γ and demonstrate that IFN- γ is one of the main mediators of allograft rejection. Moreover, he clarified some aspects of the molecular mechanisms exploited by IFN-g to control replication of riboviruses.

1985-2004: Full Professor of Microbiology, Medical School of Turin. The main accomplishments achieved by its laboratory may be summarized as follows:

A) Human (HCMV) and mouse (MCMV) cytomegalovirus. To replicate in the infected cells HCMV and MCMV need to inhibit cell cycle progression and activate a set of cellular genes involved in the viral DNA synthesis. The results achieved have demonstrated that at the early phase of infection the two main proteins encoded by the Immediate Early (IE) genes, IE1-72 and IE2-86, behave as potent promiscuous transactivators inducing i) the expression of genes involved in the arrest of the cell cycle (p16INK4a) and the senescence process of the infected cells, and ii) activation of enzymes involved in the synthesis of the viral DNA (DHFR, TS, RNR). The outcome of this infection is the uncoupling of the cell cycle progression (cells arrested in late G1) from the process of the DNA synthesis.

B) Characterization of the mouse IFN-inducible *Ifi200* gene family. In particular the mechanisms responsible for *Ifi200* induction by IFNs have been clarified by demonstrating that *Ifi200* gene transcription depends on STAT1 activation and ISGF3 formation. Biochemical studies have shown that *Ifi204* undergoes phosphorylation and translocated into the nucleus upon IFN-treatment. Genetic studies using *Rb*^{-/-} mice demonstrated that the *Ifi204* exerts a significant antiproliferative activity towards normal or tumor cells by interacting with the *Rb* system. More recently these studies have been extended to the human *Ifi16* gene, the homologue of the *Ifi204* gene.

1997-2002: Director of the Immunogenetic and Experimental Oncology Center, CNR, Turin.

Awards :

1982: Premio “Baldi e Riberi”, Military Hospital, Turin, for his studies on antiviral activity mediated by Interferons.

2003: International Award of Virology “Lenghi-Magrassi”, Accademia Nazionale dei Lincei, Rome, for his studies on infections by Human Cytomegalovirus.

Societies:

American Society of Microbiology

International Society for Interferon and Cytokine Research

Italian Society for Medical Virology

Italian Society of Microbiology

Collaborations:

1985-1990 Hoffman-La Roche, Basel: project addressed to define the signal transduction pathway of IFN- γ .

20001-2004 Serono, Geneva: project addressed to clarify the nature and the mechanisms induced by HCMV to activate transcription factors (NF- κ B) involved in viral replication.

Seminars and Congress (2002-03)

-) “The Human Cytomegalovirus”, Accademia Nazionale di Medicina, Rome, Italy, April 2002.
-) “Cell Cycle Regulation by the Human Cytomegalovirus”, Dept. of Immunology and Microbiology, Stanford University, June 2002.
-) “Activation of IFN-inducible genes by the Human Papillomavirus”, DKFZ, Heidelberg, September 2002.
-) “International Congress on Cytokines”, President of the Organizing Committee, Turin, Italy, October 2002.
-) “Activation of the IFN-pathway by the HCMV”, XII International Congress on CMB, Maastricht, May 2003.
-) “HPV in the Head and Neck tumor development”, International Congress on HPV, ISS, Rome, June 2003.
-) “The Human Papillomavirus: from the laboratory to the clinics”, Residential Course, Accademia Nazionale di Medicina, Turin, October 2003.
-) “The HCMV as activator of cellular genes”, XXII Congress of the Italian Society of Microbiology, Rome, October 2003.

Financial Support (2002/04)

-) “Characterization of viral proteins as target in the anti-HCMV therapy”, V° AIDS Project, ISS, Rome, Italy.
-) “IFN-inducible genes as prognostic markers of Head and Neck SCC progression”, Associazione Italiana per la Ricerca sul Cancro, Milan, Italy.
-) “The NF- κ B complex as target for anti-HCMV therapy”, FIRB, MIUR, Rome, Italy.
-) “The IFN-inducible IFI16 gene in the control of angiogenesis”, Compagnia San Paolo, Turin, Italy.
-) “Activation of the NF- κ B complex by HCMV”, Project 40%, MIUR, Rome, Italy.

Most relevant publications from 1999 to 2004 (Santo Landolfo)

1. De Petrini M, Rittà M, Schena M, Chiusa L, Campisi P, Giordano C, Landolfo V, Pegorari G, Landolfo S. Head and neck squamous cell carcinoma: role of the human papillomavirus in tumor progression.
New Microbiol. (2006), 29:25-33.
2. Zannetti C, Mondini M, De Andrea M, Caposio P, Hara E, Peterson G, Gribaudo G, Gariglio M, Landolfo S. The expression of p6INK4a tumor suppressor is upregulated by human cytomegalovirus infection and required for optimal viral replication.
Virology (2006), 349:79-86.
3. Drosera M, Facchetti F, Landolfo S, Mondini M, Nyberg F, Parodi A, Santoro A, Zampieri S, Doria A. Role of soluble and cell surface molecules in the pathogenesis of autoimmune skin diseases.
Clin Exp Rheumatol. (2006), 24:S7-13. Review
4. Lembo D, Donalisio M, De Andrea M, Cornaglia M, Scutera S, Musso T, Landolfo S. A cell-based high-throughput assay for screening inhibitors of human papillomavirus-16 long control region activity.
FASEB J. (2006), 20:148-150.
5. Azzimonti B, Mondini M, De Andrea M, Gioia D, Dianzai U, Mesturini R, Leigh G, Tiberio R, Landolfo S, Gariglio M. CD8+ T –cell lymphocytopenia and lack of EVER mutation in a patient with clinically and virologically typical epidermodysplasia verruciformis.
Arch. Dermatol. (2005), 141:1323-1325.
6. Gugliesi F, Mondini M, Ravera R, Robotti A, De Andrea M, Gribaudo G, Gariglio M, Landolfo S. Up-regulation of the interferon IFI16 gene by oxidative stress triggers p53 transcriptional activity in endothelial cells.
J Leukoc. Biol. (2005), 77:820-829.
7. Lembo D., Donalisio M., Hofer A., Cornaglia M., Brune W., Koszinowski U., Thelander L., and Landolfo S. The ribonucleotide reductase R1 homolog of murine cytomegalovirus is not a functional enzyme subunit but is required for pathogenesis.
J. Virol. (2004), 78:4278-4288.
8. Caposio P., Dreano M., Garotta G., Gribaudo G., and Landolfo S. Human cytomegalovirus stimulates IKK2 activity and requires the enzyme for productive replication.
J. Virol. (2004), 78:3190-3195.
9. Gribaudo G., Riera L, Caposio P., Maley F., and Landolfo S. Human cytomegalovirus requires cellular deoxycytidylate deaminase for replication in quiescent cells.
J. Gen. Virol. (2003), 84 1437-41.
10. Landolfo S., Gariglio M., Gribaudo G., and Lembo D. The human cytomegalovirus.
Pharmacol. Therap. (2003) 98: 269-297.

11. Gribaudo G., Riera L., Rudge T.L., Caposio P., Johnson L.F., and Landolfo S. Human cytomegalovirus infection induces cellular thymidylate synthase gene Expression in quiescent fibroblasts. **J. Gen. Virol.** (2002), 83:2983-2993.
12. Noris E., Zannetti C., Demurtas A., Sinclair J., De Andrea M., Gariglio M., and Landolfo S. Cell Cycle Arrest by Human Cytomegalovirus 86-kDa IE2 Protein Resembles Premature Senescence. **J. Virol.** (2002), 76: 12135-12148.
13. De Andrea M., Zannetti C., Noris E., Gariglio M., Azzimonti B., and Landolfo S. The mouse Interferon-Inducible gene IFI 204 product interacts with the Tpr protein, a component of the nuclear pore complex **J. INF. Cytok. Res.** (2002), 22: 1113-1121.
14. Gariglio M., Azzimonti B., Pagano M., Palestro G., De Andrea M., Valente G., Voglino G., Navino L., and Landolfo S. Immunohistochemical Expression Analysis of the Human Interferon-Inducible Gene IFI 16, a Member of the HIN200 Family, Not Restricted to Hematopoietic Cells. **J. INF. Cytok. Res.** (2002), 22:815-821.
15. De Andrea M., Ravotto M., Noris E., Ying GG., Gioia D., Azzimonti B., Gariglio M., Landolfo S. The interferon-inducible gene, Ifi204, acquires malignant transformation capability upon mutation at the Rb-binding sites. **FEBS Letters** (2002) 515: 51-57.
16. Cavallo R, Lembo D, Gribaudo G, Landolfo S. Murine cytomegalovirus infection induces cellular folypolyglutamate synthetase activity in quiescent cells. **Intervirology** (2001), 44: 224-6.
17. Riera L, Gariglio M, Pagano M, Gaiola O, Simon MM, Landolfo S. Control of murine cytomegalovirus replication in salivary glands during acute infection is independent of the Fas ligand/Fas system. **New Microbiol.** (2001), 24: 231-8.
18. Santoro P., De Andrea M., Migliaretti G., Trapani C., Landolfo S., and Gariglio M. High prevalence of autoantibodies against the nuclear high mobility group (HMG) protein SSRP1 in sera from patients with Systemic Lupus Erythematosus, but not other rheumatic diseases. **J. Rheumatol.** (2001), 28, 60-64.
19. Cavallo R., Lembo D., Gribaudo G., Landolfo S. Murine cytomegalovirus induces folypolyglutamate synthetase activity in quiescent cells. **Intervirology** (2001), 44, 224-227.
20. Rolle S., De Andrea M., Gioia D., Lembo D., Hertel L., Landolfo S., and Gariglio M. The interferon-inducible 204 gene is transcriptionally activated by mouse cytomegalovirus and is required for its replication. **Virology** (2001) 286, 249-255.

- .21. Gribaudo G, Riera L, Lembo D, De Andrea M, Johnson LF, Landolfo S. Related Articles The anticytomegaloviral activity of raltitrexed is abrogated in quiescent mouse fibroblasts that overexpress thymidylate synthase. **Virus Res.** (2001), 73:57-65.
22. Lembo D, Gribaudo G, Hofer A, Riera L, Cornaglia M, Mondo A, Angeretti A, Gariglio M, Thelander L, Landolfo S. Expression of an altered ribonucleotide reductase activity associated with the replication of murine cytomegalovirus in quiescent fibroblasts. **J Virol.** (2000), 74:11557-65.
23. Lembo D, Gribaudo G, Riera L, Mondo A, Cavallo R, Angeretti A, Landolfo S. The thymidylate synthase inhibitor ZD1694 potently inhibits murine and human cytomegalovirus replication in quiescent fibroblasts. **Antiviral Res.** (2000), 47 :111-20.
24. Hertel L, Rolle S, De Andrea M, Azzimonti B, Osello R, Gribaudo G, Gariglio M, Landolfo S. Related Articles The retinoblastoma protein is an essential mediator that links the interferon-inducible 204 gene to cell-cycle regulation. **Oncogene.** (2000), 27 :3598-608.
25. Riera L, Gariglio M, Valente G, Mullbacher A, Museteanu C, Landolfo S, Simon MM. Related Articles Murine cytomegalovirus replication in salivary glands is controlled by both perforin and granzymes during acute infection. **Eur J Immunol.** (2000), 30:1350-5.
26. Gribaudo G, Riera L, Lembo D, De Andrea M, Gariglio M, Rudge TL, Johnson LF, Landolfo S. Murine cytomegalovirus stimulates cellular thymidylate synthase gene expression in quiescent cells and requires the enzyme for replication. **J Virol.** (2000), 74:4979-87.
27. Hertel L, De Andrea M, Azzimonti B, Rolle A, Gariglio M, Landolfo S. Related Articles The interferon-inducible 204 gene, a member of the Irf 200 family, is not involved in the antiviral state induction by IFN-alpha, but is required by the mouse cytomegalovirus for its replication. **Virology.** (1999), 262 :1-8.
28. Lembo D, Cavallo R, Cornaglia M, Mondo A, Hertel L, Angeretti A, Landolfo S. Related Articles Overexpression of cellular dihydrofolate reductase abolishes the anticytomegaloviral activity of methotrexate. **Arch Virol.** (1999), 144:1397-403.
29. Gribaudo G, Riera L, De Andrea M, Landolfo S. Related Articles The antiproliferative activity of the murine interferon-inducible Irf 200 proteins depends on the presence of two 200 amino acid domains. **FEBS Lett.** (1999), 456 :31-6.

30. Azzimonti B, Hertel L, Aluffi P, Pia F, Monga G, Zocchi M, Landolfo S, Gariglio M. Related Articles Demonstration of multiple HPV types in laryngeal premalignant lesions using polymerase chain reaction and immunohistochemistry. ***J Med Virol.*** (1999), 59:110-6.
31. Hertel L, De Andrea M, Bellomo G, Santoro P, Landolfo S, Gariglio M. Related Articles The HMG protein T160 colocalizes with DNA replication foci and is down-regulated during cell differentiation. ***Exp Cell Res.*** (1999), 250 :313-28.
32. Lembo D, Gribaudo G, Cavallo R, Riera L, Angeretti A, Hertel L, Landolfo S. Related Articles Human cytomegalovirus stimulates cellular dihydrofolate reductase activity in quiescent cells. ***Intervirology.*** (1999), 42:30-6.