Gian Carlo Avanzi

Curriculum vitae

PERSONAL DATA

Born in Turin on July 13, 1954
Resident in Novara, via Magistrini 15
Tel 0321-3733848 Office

BIO AND EDUCATION

In 1984 he obtained the MD degree at the University of Turin, then he spent an internship at the Laboratory of Experimental Hematology directed by Prof. Luigi Pegoraro, University of Turin,
In 1986 he obtained a scholarship of '' Italian Association for Cancer Research "with a research project entitled" chromosomal alterations and leukemogenesis "; in the same year he was visiting scientist at the Wistar Institute in Philadelphia, USA, where he studied the purification of hematopoietic growth factors, in the same year spent a period as visiting scientist at the Department of Clinical Genetics of the 'University of Lund, Sweden, where he studied for chromosome aberrations in leukemias.
In 1987, he gained the specialization in General Hematology (Clinical and Laboratory) at the University of Modena.
In 1988 he was visiting scientist at the Department of Pathology, School of Medicine, Temple University, Philadelphia, USA, where he studied the expression of some genes of the cell cycle.
In 1989 he obtained a scholarship of "Gigi Ghirotti Committee", research entitled: "Environmental damage and chromosomal abnormalities"
In 1990 he rwas again visiting scientist at the Department of Pathology, School of Medicine, Temple University, Philadelphia, USA, where he learned methods of molecular biology and gene cloning.
In 2003 he obtained the responsibility of 'Learning –Clinical Unit (UDA) in Emergency Medicine at the Hospital Maggiore of Charity of Novara.
In 2005 he got the responsibility of the Allergy and Clinical Immunology ward at the University Hospital Maggiore of Charity of Novara.
In 2010 he got Responsibility of the Emergency Room, at the University Hospital Maggiore of Charity of Novara.

UNIVERSITY CAREER

2006-2009	Full Professor of Internal Medicine, Eastern Piedmont University, School of Medicine at Novara
2000-2006	Associate Professor of Internal medicine Eastern Piedmont University, School of Medicine at Novara
1994-2000	Assistant Professor of Internal Medicine University of Turin II School of Medicine at Novara

UNIVERSITY POSITIONS

2015-	Director of Traslational Medicine Department
2009-	Member of Peer Commission Piedmont Region-University

2009-	Director of Residency in Emergency Medicine
2007-	Director of Nurse Master in Critical and Emergency Medicine
2006-	President of Master degree in Nursing and Midwifery sciences
2005-2012	President of Bachelor degree in Nursing

SCIENTIFIC POSITIONS

2008-	Member of Academy of Emergency Medicine and Care (AcEMC)
2008-	Member of Global Research in Acute Condition Team (GREAT)
2008-	Member of italian Society of Emergency medicine (SIMEU)
2007-	Member of American College of Emergency Medicine (ACEP)
2001-	Member of Italian Society of Internal Medicine (SIMI)

MAIN FIELDS OF INTEREST

1. Cytogenetics oncoematologica

2. hematopoietic growth factors and their receptors

3. inflammation

4. tyrosine kinase receptors

5. sepsis

6. autoimmune diseases

CURRENT ISSUES OF RESEARCH

Role of GAS6 in modulating the immune response

we evaluated the effect on cytokine secretion by monocytes/macrophages and the molecular pathways involved. GAS6 inhibits TNF-α and IL-6 secretion by LPS-stimulated U937 cells and monocytes/machrophages. We evidenced that among GAS6 receptors, only Mer (but not Axl or Tyro3) is expressed on differentiated U937 cells, and its activation is responsible for the reduction of cytokine expression. In immunoblot analysis, Mer was activated after GAS6 stimulation, giving rise to an increased phosphorylation of Akt. We also observed GSK3 phosphorylation and consequent inhibition of NF-**κ**B nuclear translocation. Therefore, GAS6 modulates macrophage cytokine secretion, triggering an “anti-inflammatory pathway” involving PI3K/Akt/GSK3 and NF-**κ**B

Mer/Gas6 and TPO/Mpl axis in severe sepsis and septic shock.

The sepsis syndrome is a disease entity of universal impact. The incidence of severe sepsis, although mortality is decreasing, remains unacceptably high. The sepsis syndrome exists along a

disease continuum that includes severe sepsis and septic shock, based on the occurrence of sepsis-related organ dysfunction. Multiple organ dysfunction syndrome is the leading cause of morbidity and mortality. Infection process is highly regulated by a mixture of pro-inflammatory and anti-inflammatory mediators secreted by macrophages, which have been triggered and activated by the invasion of tissue by bacteria. In sepsis the pro-inflammatory milieu spreads in blood where leads to the recruitment of PMNs and macrophages due to the presence of several circulating cytokines and mediators that activate endothelial cells and platelets. Despite a clear understanding of the inflammatory and coagulation mechanisms triggered during the early stage of severe sepsis, not much is known about the mechanisms that lead to organ dysfunction and death. Two relatively new mediator/effector systems that we have been shown preliminarily to be involved in sepsis, Gas6/Mer and TPO/Mpl , are here proposed for investigation in animal model and in humans. Aims of our study are: a) to prove if the activation of the Gas6/Mer and/or the inhibition of TPO/MpL systems, in an experimental animal model of severe sepsis/septic shock, can, in vivo, control the severity of the disease, including death, and can reduce derangements of different target organs. In the same models we will evaluate the reduction of the expression of inflammatory cytokines and of the activation of innate immunity cells, through the repression of the intracellular inflammation signaling; b) to obtain Gas6, sMer and TPO plasma concentrations in defined cohorts of patients, and to assess their potential use as positive predictors, severity prognostic predictors and as unique or combined markers for the patient risk stratification in severe sepsis and septic shock. The results of the present project will provide further advances in pathophysiology, molecular and cellular immunology and clinical aspects of sepsis/septic shock. The expected biomedical outcomes will essentially be: disclosure of clinical effects of the modulation of two inflammation control mechanisms in a mouse model - that can lead to identification of new potential targets for inflammation control - and identifying new potential biomarkers in humans.

PROGETTI FINANZIATI IN CORSO

LE CINQUE PUBBLICAZIONI PIÙ SIGNIFICATIVE DELLA CARRIERA

1. Avanzi G.C., Brizzi M.F., Giannotti J., Ciarletta A., Yang Y.C., Pegoraro L., Clark S.C., The M-07e human leukemic factor dependent cell line provides a rapid and sensitive bioassay for the human cytokines GM-CSF and IL-3., **J. Cell. Phisiol**. 145: 458-464, 1990.
2. Avanzi G.C., Porcu P., Brizzi M.F., Ghigo D., Bosia A., Pegoraro L., Interleukin 3-dependent proliferation of the human M-07e cell line is supported by discrete activation of late G-1 genes. **Cancer Research** 51: 1741-1743, 1991
3. Manfioletti G., Brancolini C., Avanzi G.C., Schneider C. The protein encoded by a growth-arrest specific gene (GAS 6) is a new member of the vitamin-K dependent proteins related to protein-S, a negative coregulator in the blood coagulation cascade. **Mol. Cell. Biol**. 13: 4976-4985, 1993.
4. Sainaghi PP, Castello L, Bergamasco L, Galletti M, Bellosta P, Avanzi GC. GAS6 induces proliferation in prostate carcinoma cell lines expressing the axl receptor **J. Cell. Physiol.** 2005; 204:36-44
5. Alciato F, Sainaghi PP, Sola D, Castello L, Avanzi GC TNF-alpha, IL-6 and IL-1 expression is inhibited by GAS6 in monocytes/macrophages. **Journal of Leukocyte Biology**, 2010, 87: 869-875.

PREMI E RICONOSCIMENTI

ULTERIORI INFORMAZIONI