

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Bonavida, Benjamin		POSITION TITLE Professor of Immunology	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of California, Los Angeles	B.A.	1964	Microbiology
University of California, Los Angeles	Ph.D.	1968	Immunochemistry
The Weizman Institute of Science	Postdoc	1969-1971	Immunochemistry

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

EMPLOYMENT

- 1969-1971 The Weizman Institute of Science, Postdoctoral Fellow (Immunochemistry of nucleic acids)
- 1971-1978 Assistant Professor, Department of Microbiology and Immunology, UCLA School of Medicine
- 1978-1983 Associate Professor, Department of Microbiology and Immunology, UCLA School of Medicine
- 1996-1997 Interim Chair, Department of Microbiology and Immunology, UCLA School of Medicine
- 1983-Present Professor, Department of Microbiology and Immunology, UCLA School of Medicine

HONORS

- 1979-1980 Member of the Ad Hoc Committee of Experimental Immunology Study Section
- 1980-1983 Member of the Advisory Committee "Clinical Investigation in Immunology & Immunotherapy - ACS"

EXPERIENCES

- Immunochemistry, Molecular Biology, Purification of Cytotoxic Factors, Cellular Immunology, Cancer Immunology, Immunochemistry, Molecular Immunology.
- Editorial Board: International Journal of Oncology, Biotherapy, Journal of Clinical Immunology, International Journal of Oral Biology, Cancer Biotherapy and Radiopharmaceuticals.

- 1984-1988 Member of the Study Section "Allergy and Immunology," NIH
- 1984-1992 Ad Hoc Member of NIH
- 1992-1995 Member of the Study Section NIAAA - NIH
- 1995-Present Ad Hoc Member of NIH and the DOD

B. Selected peer-reviewed publications (Selected from a list of 371)**RELEVANT PUBLICATIONS**

- Borsellino, N., Beldegrun, A., and Bonavida, B. Endogenous IL-6 is a resistance factor for CDDP and VP-16-mediated cytotoxicity of human prostate carcinoma cell lines. *Cancer Res.* 55:4633-4639, 1995.
- Jewett, A. and Bonavida, B. Target-induced inactivation and cell death by apoptosis in a subset of human NK cells. *J. Immunol.* 156:907-915, 1996.
- Mori, S., Murakami-Mori, K., Jewett, A., Nakamura, S., and Bonavida, B. Resistance of AIDS-associated Kaposi's sarcoma cells to Fas-mediated apoptosis. *Cancer Res.* 56:1874-1879, 1996.
- Uslu, R., Borsellino, N., Frost, P., Garban, H., Ng, C.P., Mizutani, Y., Beldegrun, A., and Bonavida, B. Chemosensitization of human prostate carcinoma cell lines to anti-Fas-mediated cytotoxicity and apoptosis. *Clin. Cancer Res.* 3:963-972, 1997.
- Jewett, A., Cavalcanti, M., and Bonavida, B. Pivotal role of endogenous TNF- α in the induction of functional inactivation and apoptosis in NK cells. *J. Immunol.* 159:4815-4822, 1997.

- Mizutani, Y., Yoshida, O., and Bonavida, B. Prognostic significance of soluble Fas in the serum of patients with bladder cancer. *J. Urol.* 160:571-576, 1998.
- Mori, S., Murakami-Mori, K., and Bonavida, B. Dexamethasone enhances expression of membrane and soluble interleukin-6 receptors by prostate carcinoma cell lines. *Anticancer Res.* 18:4403-4408, 1998.
- Borsellino, N., Bonavida, B., Ciliberto, G., Toniatti, C., Travali, S., and D'Alessandro, N. Blocking signaling through the gp130 receptor chain by interleukin-6 and oncostatin M inhibits PC-3 cell growth and sensitizes the tumor cells to VP-16 and CDDP-mediated cytotoxicity. *Cancer* 85:134-144, 1999.
- Mori, S., Murakami-Mori, K., Nakamura, S., Ashkenazi, A., and Bonavida, B. Sensitization of AIDS-Kaposi's sarcoma cells to Apo-2 ligand (Apo-2L)-induced apoptosis by actinomycin D. *J. Immunol.* 162:5616-5623, 1999.
- Frost, P., Beldegrun, A., and Bonavida, B. Sensitization of immunoresistant prostate carcinoma cell lines to Fas/Fas ligand-mediated killing by cytotoxic lymphocytes: Independence of *de novo* protein synthesis. *Prostate* 41:20-30, 1999.
- Mizutani, Y., Yoshida, O., Miki, T., and Bonavida, B. Synergistic cytotoxicity and apoptosis by Apo-2L ligand and adriamycin against bladder cancer cells. *Clin. Cancer Res.* 5: 2605-2612, 1999.
- Mizutani, Y., Nakao, M., Ogawa, O., Yoshida, O., Bonavida, B., and Miki, T. Enhanced Sensitivity of Bladder Cancer Cells to Tumor Necrosis Factor Related Apoptosis Inducing Ligand (TRAIL) Mediated Apoptosis by Cisplatin and Carboplatin. *J. Urol.* 165:263-270, 2001.
- Frost, P., Butterfield, L., Dissette, V., Economou, J., and Bonavida, B. Immunosenitization of Melanoma Tumor Cells to Non-MHC Fas-Mediated Killing by MART-1 specific CTL cultures. *J. Immunol.* 166:3564-3573, 2001.
- Garban, H. and Bonavida, B. Nitric Oxide disrupts H₂O₂-dependent activation of NF- κ B: Role in Sensitization of human tumor cells to TNF- α -induced cytotoxicity. *J. Biol. Chem.* 276(12):8918-8923, 2001.
- Garban, H. and Bonavida, B. Nitric Oxide Inhibits the Transcription Receptor Yin-Yang 1 Binding Activity at the Silencer Region of the Fas Promoter: A Pivotal Role for Nitric Oxide in the Upregulation of Fas Gene expression in Human Tumor Cells. *J. Immunol.* 167:75-81, 2001.
- Alas, S. and Bonavida, B. Rituximab Inactivates Signal Transducer and Activation of Transcription 3 (STAT3) Activity in B-Non-Hodgkin's Lymphoma through Inhibition of the Interleukin 10 Autocrine/Paracrine Loop and Results in Down-Regulation of Bcl-2 and Sensitization to Cytotoxic Drugs. *Cancer Res.* 61:5137-5144, 2001.
- Zisman, A., Ng, C-P., Pantuck, A.J., Bonavida, B., and Beldegrun, A.S. Actinomycin D and gemcitabine synergistically sensitize androgen-independent prostate cancer cells to Apo2L/TRAIL-mediated apoptosis. *J. Immunother.* 24:459-471, 2001.
- Jazirehi, A.R., Ng, C-P., Schiller, G. and Bonavida, B. Adriamycin Sensitizes the Adriamycin-resistant 8226/Dox40 Human Multiple Myeloma Cells to Apo2L/TRAIL-mediated Apoptosis. *Clin. Cancer Res.* 7:3874-3883, 2001.
- Ng, C-P. and Bonavida, B. A new challenge to immunotherapy by tumors that are resistant to apoptosis: Two complementary signals to overcome cross-resistance. *Adv. In Cancer Res.* 85:145-174, 2002.
- Ng, C-P., Zisman, A., and Bonavida, B. Synergy is achieved by complementation with Apo2L/TRAIL and Actinomycin D in Apo2L/TRAIL-mediated apoptosis of prostate cancer cells: Role of XIAP in resistance. *Prostate.* 53(4):286-99, 2002.
- Ng, C-P. and Bonavida, B. X-linked Inhibitor of apoptosis (XIAP) blocks Apo2 Ligand/Tumor necrosis factor-related apoptosis-inducing ligand-mediated apoptosis of prostate cancer cells in the presence of mitochondrial activation: sensitization by overexpression of second mitochondria-derived activator of caspase/direct IAP-binding protein with low pl (Smac/DIABLO). *Molecular Cancer Therapeutics* 1:1051-1058, 2002.
- Huerta S, Vega M, Garban H, and Bonavida B. TNF- α controls the expression and activity of the transcriptional repressor Yin-Yang 1 (YY1) via NF- κ B. *Oncogene* (under revision).
- Huerta S, Vega M, Garban H, and Bonavida, B. Nitric oxide sensitizes prostate carcinoma cell lines to TRAIL-mediated apoptosis via inactivation of NF- κ B and inhibition of Bcl-xL expression. (To be submitted)
- Seligson D, Shi T, Horvath S, Roberts A, Hanna S, Huerta-Yepes S, Garban H, Chia D, Goodglick L, and Bonavida B. Nuclear Expression of transcription factor YY1 in prostate cancer. (To be submitted)

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

Ongoing Research Support

5 P50 AT00151-03 (PI: Heber)

9/30/99-7/31/04

NIH/NCCAM

Proposal Title: UCLA Center for Dietary Supplement Research: Botanicals

Project Title: Immunological Effects of Fractions of Echinacea

The major goal of this project is to examine the immunomodulatory activities of Echinacea and fractions.

Role: Sub Project PI

#DAMD17-02-10023 (PI: deKernion)

12/15/01-1/14/05

DOD/US Army Prostate Cancer Research Program

Regulation of TRAIL-Mediated Apoptosis in Prostate Cancer by Overexpression of XIAP

The long term goal of this project is to determine the effect of anti-apoptotic gene product regulation in prostate cancer cells and their response to immunotherapy.

Role: Pilot Feasibility Study (PI)

UCLA SPORE in Prostate Cancer (PI: Bonavida)

1/1/03-12/31/03

Clinical significance of YY1 expression in prostate cancer: target for immunotherapeutic intervention

The major goal of this project is to understand the role of the transcription repressor YY1 in human prostatic malignancies and its potential clinical implications as a diagnostic/prognostic marker for this disease and as a therapeutic target.

Role: PI

Completed Research Support

Norman Cousins Center for Psychoneuroimmunology

10/1/00-9/30/01

Neuropsychiatric Institute UCLA

Mechanism of norpinephrine-mediated regulation of TNF- α secretion and survival of human NK cells: Involvement of NF κ B and iNOS

This grant examines the role of catecholamines on the induction of NF κ B and INOS in the regulation of cytokines secretion.

Role: PI

H870219 (PI: Bonavida)

9/1/96-8/31/02

Boiron Research Foundation

Immunological and Molecular Research With Ultra High Dilutions: Molecular Signaling & Synergistic Immuno-Stimulating Activities

This grant examines the effect of subphysiological concentrations of cytokines and drugs on the immune response by peripheral blood.

Role: PI(PI: Benjamin Bonavida, Ph.D.)

Dannon

2/1/00-2/15/01

Effect of Consumption of ACTIMEL on Immunological Markers II

This proposal examines the effect of consumption of the French yogurt Actimel in humans on the modification of immunological parameters examined *ex vivo*. Circulating cytokines and immunoglobulin are assessed by ELISA.

Role: PI

