CURRICULUM VITAE

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Education and Training

1973–1977	**University of California, Santa Barbara** B.A.: Cellular and Organismal Biology B.A.: Psychology
1978–1985	**Rush University** M.D., Ph.D.: Pharmacology
1985–1987	**University of California, Irvine** Internal Medicine Residency
1987–1992	**National Cancer Institute,** Bethesda, MD Clinical Oncology Program Medical Staff Fellow Research Officers Group, Commissioned Corps, PHS Biotechnology Fellow

Professional Positions

1993–2000 2003–2013	Assistant Clinical Professor, U.C. Irvine Associate Professor of Clinical Medicine, Biological Chemistry, Pharmaceutical Sciences and Biomedical Engineering
July 2014-present	Professor of Clinical Medicine, Biological Chemistry, Pharmaceutical Sciences and Biomedical Engineering
2004-present	Director, Clinical Pharmacology and Developmental Therapeutics Chao Family Comprehensive Cancer Research Center University of California, Irvine

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Work Experience
Oncotech, Inc.

1992-1998	Vice President and Medical Director
1998-2002	Senior Vice President and Medical Director
2002-2004	Chief Scientific Officer

Licensure	**Year**
California CA G58826	1986
Maryland D006157	1987

Certifications

American Board of Internal Medicine, Medical Oncology #124351, Recertified 2011

Memberships and Societies

American Association for Cancer Research	1988–Present
American Society of Clinical Oncology	1996–Present
SWOG, Melanoma Committee	1998–Present

Awards and Honors

Consumers Research Council of America Award for **Top** Oncologist	2007
OCMA Physician of Excellence	2010, 2014, 2016
U.S. News Top Doctor	2011
Teacher of the Year UCI Oncology Fellows	2011

Research Experience

1993-present UC Irvine

My group has focused on mechanisms of drug action and resistance with the goal of developing predictive tests that improve therapeutic outcomes for cancer patients. Active areas in my laboratory at UC Irvine include the role of glutathione and redox mechanisms in drug resistance, development of vascular endothelial cell models to predict response to antiangiogenesis agents, and the examination of differential gene expression that can distinguish between drug resistant and drug sensitive tumors. More recently we have focused on translating our bench work to the bedside through the development of clinical trials that include correlative laboratory studies.

Discovery of agents that inhibit formation of tumor blood vessels continues to be an active area of therapeutic development. Insights into the immunomodulatory activity of antiangiogenesis agents has led to their effective combination with check point inhibitors (UCI 16-63). However, resistance to antiangiogenesis agents as a deterrent to the success of this approach has been overlooked. In order to define the role of angiogenesis in tumor progression, and to develop models that might predict treatment response, my group developed an angiogenesis index based on mutant p53, the angiogenesis suppressor thrombospondin-1 (TSP1), and intratumor

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microvessel counts (US Patent # 5,840,507). We applied this marker set to ovarian cancer patients receiving bevacizumab on a GOG clinical trial, finding that TSP1 expression was significantly associated with durability of response to Avastin (Gynecol Oncol 119:484-90, 2010).

Our group has also explored the relationship between tumor class, drug response and differential gene and protein expression (Clinical Cancer Res 5 (Suppl), #476, 1999). One significant deficiency in current molecular approaches to cancer genomics is specimen purity. The complex mixture of cells within a tumor makes it difficult to delineate which mRNA species are cancer cell specific. We therefore developed flow-cytometry methods to selectively separate malignant cells and tumor derived vascular endothelial cells (VEC) from their stromal background tissue. Transcript levels were determined for the purified cancer cell and VEC cell populations using Affymetrix U133 A and B gene arrays containing 30,000 distinct genes and EST's. Differential gene expression patterns that classify endothelial cells into drug resistance categories have been identified (Proc Am Assoc Cancer Res 43: #4502, 2002; Breast Cancer Res and Treat 76: #562, 2002; Proc Am Assoc Cancer Res 2003, #3998 (Minisymposium Podium Presentation).

My current position as Director of Clinical Pharmacology and Developmental Therapeutics in the Chao Family Comprehensive Cancer Center at UC Irvine allows me to take a translational approach to predictive oncology and to apply bioprofiling to patients on clinical trials. The tremendous complexity of aberrant pathways in cancer has been a major deterrent in the development of targeted therapeutics. With the advent of gene arrays and advanced mass spectrometry methods, this complexity may finally be captured. The capability to bioprofile the unique proteogenomic characteristics of an individual patient's tumor is at hand. Co-development of proteogenomic "theragnostic" tests in conjunction with clinical trials of targeted agents are helping to define patient subsets most likely to benefit, while excluding patients with inappropriate biomarker profiles from potentially toxic treatment. The convergence of biotechnology, molecular biology and clinical pharmacology with bioinformatics should enable a rational approach to target cancer related pathways and improve outcomes for patients with cancer.

Research Background

1987-1993 National Cancer Institute, NIH, Clin Pharm Branch
Examined the mechanisms of cross resistance between chemotherapy and tumor necrosis factor in breast cancer and prostate cancer cell lines.

1978-1985 Rush University, Department of Pharmacology
Determined a novel mechanism of action of BCNU to inhibit DNA synthesis via glutathione depletion in conjunction with inhibition of glutathione recycling. (PhD Thesis)

1975-1977 University of California, Santa Barbara, Dpt. Of Chemistry
Worked on the isolation of the red blood cell glucose transporter using 3-deoxy-3-fluoro-glucose.

Active Research Grant and Contract Support

Current Peer Reviewed Awards

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01/31/19–01/31/24 NIH/NCI P30, CA-62203-14
UCI Cancer Center Support Grant. Center Grant to support UCI Cancer Center.
Role: Chair, Data Safety Monitoring Board

Company Sponsored Laboratory Research Awards
1/18-12/14/21 Astellas
Topotecan Reversal of Enzalutamide Resistance in 22Rv1 Cells via Blockade of AR-V7 Nuclear Translocation
Role: PI
$172,154.00

Recently Completed Peer Reviewed Support
01/01/11–12/31/16 NIH/NCI R21, CA156032-02
Novel biologic markers of treatment resistance in locally advanced cervical carcinoma.
Role: C0-PI
$150,000 (T)

6/13-5/18 NIH/NCI RO1
PAK Kinases Regulate Melanoma Chemoresistance and Metastasis
Role: Co-I (PI Anand Ganesan)
$1,210,649 (T)

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Current Clinical Trials Funding

Industry Sponsored Trial/ UCI-18-64 : RPL-001-16 An Open-Label, Multicenter, Phase 1/2 Study of RP1 as a Single Agent and in Combination with PD1 Blockade in Patients with Solid Tumors.
PI 7/15/21-

Industry Sponsored Trial/ UCI-20-57: A Phase 3, Randomized, Open-label Study to Compare Adjuvant Immunotherapy of Bempegaldesleukin Combined with Nivolumab Versus Nivolumab After Complete Resection of Melanoma in Patients at High Risk for Recurrence (PIVOT-12).
PI $593,944 (T) 11/01/2020 - 10/31/2023

Industry Sponsored Trial/ UCI-19-140: A Randomized Phase II, Open-label, Active-controlled, Multicenter Study Investigating the Efficacy and Safety of UV1 Vaccination in Combination with Nivolumab and Ipilimumab as First-line Treatment of Patients with Unresectable or Metastatic Melanoma (UV1-202).
PI $338,316 (T) 09/01/2020 - 08/31/2023

Industry Sponsored Trial/ UCI-20-116: A RANDOMIZED, CONTROLLED, OPEN-LABEL, PHASE 2 STUDY OF CEMIPLIMAB AS A SINGLE AGENT AND IN COMBINATION WITH RP1 IN PATIENTS WITH ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA.
PI $493,338 (T) 11/01/2020 - 10/31/2023

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Fruehauf JP

Industry Sponsored Trial/ UCI-19-15 A Phase 2, Open-Label, Randomized, Multicenter Trial of Encorafenib + Binimetinib Evaluating a Standard-dose and a High-dose Regimen in Patients With BRAFV600-Mutant Melanoma Brain Metastasis
PI $299,658 (T) 11/5/19-10/21/22

Industry Sponsored Trial/ UCI-17-73: A Sequential 2-arm, Open-label Phase 1 Study to Evaluate the Effects of Encorafenib in Combination with Binimetinib on the Pharmacokinetics of Losartan, Midazolam, Caffeine, Omeprazole, and Dextromethorphan Administered in a Cocktail Approach and on the Pharmacokinetics of Rosuvastatin in Patients with BRAF V600-mutant Unresectable or Metastatic Melanoma or Other Advanced Solid Tumors.
PI $171,895.00 (T) 1/24/18 – 10/21/22

Industry Sponsored Trial/ UCI-16-102: A PHASE III, OPEN-LABEL, MULTICENTER, TWO-ARM, RANDOMIZED STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF COBIMETINIB PLUS ATEZOLIZUMAB VERSUS PEMBROLIZUMAB IN PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED BRAFV600 WILD-TYPE MELANOMA
PI $378,399.00 (T). 11/15/17 - 11/14/20

Industry Sponsored Trial/ UCI 17-09: A randomized, double-blind, placebo-controlled, phase III study comparing the combination of PDR001, dabrafenib and trametinib versus placebo, dabrafenib and trametinib in previously untreated patients with unresectable or metastatic BRAF V600 mutant melanoma
PI $507,335.00 (T). 08/01/17 - 07/31/20

Industry Sponsored Trial / UCI-16-92: A Phase III, Double-Blinded, Randomized, Placebo-Controlled Study of Atezolizumab Plus Cobimetinib and Vemurafenib versus Placebo plus Cobimetinib and Vemurafenib in Previously Untreated BRAFV600 Mutation-Positive Patients with Unresectable Locally Advanced or Metastatic Melanoma
PI $689,151.00 (T). 2/15/17 - 5/30/22

Industry Sponsored Trial / UCI 16-63
Phase III Randomized, Open-label Study to Evaluate Efficacy and Safety of Pembrolizumab (MK-3475) in Combination with Axitinib versus Sunitinib Monotherapy as a First-line Treatment for Locally Advanced or Metastatic Renal Cell Carcinoma (mRCC) (KEYNOTE-426)
PI $292,747.00 (T). 1/17/17- 07/5/20

Industry Sponsored Trial / UCI 15-12
A Phase III, Open-Label, Randomized Study of MPDL3280A (Anti-PD-L1 Antibody) in Combination with Bevacizumab versus Sunitinib in Patients with Untreated Advanced Renal Cell Carcinoma
PI $5,268,204 (T). 09/24/15 - 09/23/20

Industry Sponsored Trial / UCI 14-82: PHASE III, RANDOMIZED, DOUBLE-BLIND, MULTICENTER TRIAL OF AUTOLOGOUS DENDRITIC CELLS LOADED WITH IRRADIATED AUTOLOGOUS TUMOR CELLS IN GM-CSF (DC-TC) VS. AUTOLOGOUS PERIPHERAL BLOOD MONONUCLEAR CELLS IN GM-CSF (MC) FOR THE TREATMENT OF PATIENTS WITH METASTATIC MELANOMA
PI $216,091.00 (T). 06/25/15 - 06/24/20

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