BIOGRAPHICAL SKETCH

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NAME: Casiano, Carlos A.

eRA COMMONS USER NAME (credential, e.g., agency login): CCASIANO

POSITION TITLE: Professor of Microbiology, Molecular Genetics, and Medicine; Associate Director, Loma Linda University Center for Health Disparities and Molecular Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Puerto Rico, San Juan	BS	06/1981	Biology
University of Puerto Rico, San Juan	MS	06/1983	Biology/Tumor Biol.
University of California, Davis	PhD	04/1992	Microbiology/Biochem.
The Scripps Research Institute, La Jolla, CA	Postdoc Fellow	12/1997	Autoimmunity and Cancer / Cell Death

A. Personal statement

Over the past 20 years I have focused my research efforts on investigating biological and clinical aspects of tumor associated autoantigens (TAAs) in prostate cancer (PCa). This has allowed me to develop a broad expertise that combines molecular, biochemical, proteomics, immunological, and cellular approaches, as well as clinical studies with human biospecimens. My current research program focuses on the following aspects of PCa: 1) contribution of glucocorticoid-induced stress survival proteins to prostate tumor aggressiveness and chemoresistance; 2) targeting chemoresistance-associated proteins to sensitize PCa cells to taxane resistance; and 3) identification and characterization of novel PCa-associated autoantibodies and TAAs using immuno-proteomic approaches. I am especially interested in investigating these aspects in the context of PCa health disparities and contribute to the national goal of reducing these disparities. A currently NIH/NCI funded R21 grant in my laboratory investigates mechanisms by which glucococorticoid receptor (GR) signaling upregulates chemoresistance-associated proteins in PCa cells, and determine if these mechanisms operate more robustly in African American prostate tumors. Recent research efforts have also focused on uncovering mechanisms by which the transcription co-activator LEDGF/p75, a GR regulated stress protein, promotes taxane chemoresistance in PCa. Given LEDGF/p75 role in HIV integration into host chromatin, my lab is interested in targeting this protein with repurposed HIV-based inhibitors to overcome PCa chemoresistance. I also serve as Associate Director of the Loma Linda University Center for Health Disparities and Molecular Medicine (CHDMM), established in 2006 with NIH/NIMHD funding. In addition, I serve as faculty mentor, co-investigator, and Associate Program Director (APD) in the NIH/NIGMS R25 training grant that supports the LLU-NIH Initiative for Maximizing Student Development (IMSD) Program to enhance the research training and education of graduate students from underrepresented and disadvantaged backgrounds. I have a strong record of publications in the fields of molecular cancer research, autoimmunity, and cell death; extramural funding; academic leadership and mentoring; and productive collaborations with cancer biologists, clinicians, and behavioral health researchers. I have demonstrated the scientific expertise, core leadership, productivity, team-building skills, and commitment needed to continue leading NIH-funded research here at LLU and serving as Associate Director of the CHDMM. Recent relevant publications include:

1. Ortiz-Hernandez GL, Sanchez-Hernandez ES, **Casiano CA** (2020). Twenty years of research on the DFS70/LEDGF autoantibody-autoantigen system: many lessons learned but still many questions. AutoImmunity Highlights 11:(1)3,1-19. PMID: 32127038
2. Woods-Burnham L, Cajigas-Du Ross CK, Love A, Basu A, Sanchez-Hernandez ES, Martinez SR, Ortiz-Hernández GL, Stiel L, Durán AM, Wilson C, Montgomery S, Roy S, and **Casiano CA** (2018).

Glucocorticoids Induce Stress Oncoproteins Associated with Therapy-Resistance in African American and European American Prostate Cancer Cells. Scientific Reports 8:15063. PMID: 30305646

3. Cajigas-Du Ross CK, Martinez SR, Woods-Burnham L, Duran AM, Roy S, Basu A, Ramirez JA, Ortiz-Hernandez GL, Rios-Colon L, Chirsev E, Sanchez-Hernandez ES, Soto U, Greco C, Boucheix C, Chen X, **Unternaehrer J**, Wang C, and **Casiano CA** (2018). RNA sequencing reveals upregulation of a transcriptomic program associated with stemness in metastatic prostate cancer cells selected for taxane resistance. Oncotarget 9:30363-30384. PMID: 30100995.
4. Rios-Colon L, Cajigas-Du Ross C, Basu A, Elix C, Alicea-Polanco I, Sanchez TW, Radhakrishnan V, Chen CS, and **Casiano CA** (2017). Targeting the stress oncoprotein LEDGF/p75 to sensitize chemoresistant prostate cancer cells to taxanes. Oncotarget 8:24915-24931. PMID: 28212536

B. Positions and Honors

Positions and Employment

1997-2003	Assistant Professor of Microbiology, Molecular Genetics, and Medicine, Loma Linda University School of Medicine (LLUSM)
2004-2012	Associate Professor (tenured) of Microbiology, Molecular Genetics, Biochemistry, and Medicine, LLUSM
2005-present	Associate Director and Founding Member, LLUSM Center for Health Disparities and Molecular Medicine (CHDMM)
2005-present	Director, Research Training and Education Core, LLUSM-CHDMM
2009-present	Associate Program Director, LLU-NIH Initiative for Maximizing Student Development (IMSD)
2012-present	Professor of Microbiology, Molecular Genetics, Biochemistry, and Medicine, LLUSM

Other Experience and Professional Membership

1992-present	Invited Speaker at national and international academic/scientific venues (n=85)
1993-present	Member, American Association for Cancer Research (AACR)
1998-present	Mentored Early Stage Investigators (ESIs) at the Assistant Professor level (5), postdoc/clinical fellows (10), graduate PhD students (13), and summer research medical students (8), undergraduate students (21), and high school students (17)
2000-present	Member of International Advisory Committee and co-chairperson of several scientific sessions, Dresden Symposium on Autoantibodies, Germany (occurs every other year)
2001-2005	Coordinator, LLU-NIH Undergraduate Research Minority Scholars Program
2004-2008	Member and Chair, AACR Minorities in Cancer Research Council (MICR)
2004-2006	Co-Chair, AACR Minority Scholar Award in Cancer Research Committee
2004-2013	Member of Several AACR Committees: Cancer Health Disparities Think Tank, Science Education Committee, Scientific Review Committee for 1st AACR Cancer Health Disparities Conference, Jane C. Wright Lectureship Selection Committee, Thomas Bardos Undergraduate Student Award Selection Committee, Centennial Grant/Fellowship Review Committee, Selection Committee for AACR Minority Faculty Scholar Awards
2005	Co-Chair, AACR-MICR Cancer Health Disparities Forum
2005-present	Mentor, AACR-MICR Annual Meeting Professional Advancement Sessions for ESIs
2006-present	Coordinator, Undergraduate Training Program in Health Disparities, and Apprenticeship Bridge to College Program in Health Disparities, LLU-CHDMM
2009-present	Editorial Board, *Autoimmunity Highlights* journal (Springer-Verlag)
2014-present	Co-leader of LLUH Project Change, an academia-community partnership to promote PCa education, screening, and shared decision making among African-American men
2019-present	Editorial Board, Nature- *Scientific Reports*

Honors, Awards, and Fellowships

1980-81	Undergraduate Research Assistantship, NIH/NIGMS MBRS Program, UPR San Juan
1981-82	NSF Graduate Fellowship, UPR San Juan
1984-85, 88-89	UC Davis Graduate Opportunity Fellowship
1986, 87	UC Davis Graduate Research Awards
1991-93	NIH/NIAMS Minority Postdoctoral Research Supplement Award
1993-96	Arthritis Foundation Postdoctoral Fellowship Award
1996-97	NIH/NIAMS NRSA Trainee in Molecular Aspects of Clinical Immunology

1994, 95, 96	NCI/AACR Minority Scientist Award
1998, 2002	NCI/AACR Minority Scholar Award in Cancer Research
2001, 02, 03	LLU Association of Latin American Students Award for Outstanding Leadership and Support of Minority Students and Diversity
2008	AACR-MICR Award in Recognition of Service and Commitment to Promoting the Professional Development and Achievements of Minority Scientists in Cancer Research
2012	LLU Hispanic Alumni Association Community Service Award- in recognition of years of service in promoting the development of Hispanic/Latino and other minority students at LLU
2018	LLUSM Distinguished Service Award - in recognition for exemplary service in promoting diversity, minority student development, and health disparities research
2019	LLUSM Bruce Wilcox Mentor of the Year Award – in recognition for excellence in mentoring graduate students

Advisory Service

1999-present	Reviewer for over 40 peer-reviewed biomedical journals
2000-present	Member and Chair, NIH/NIGMS SCORE Molecular Genetics Review Panel
2001-2003	NRC-HHMI Pre-doctoral Fellowship-Cell Biology Review Panel
2001-present	Ad-Hoc Grant Reviewer for Canadian Institutes of Health, Belgian FWO-National Fund for Scientific Research, Belgian Cancer Foundation, Ireland Health Research Board, Italian Cariplo Foundation, Pennsylvania ORAU/ORISE Grant Final Performance Review, Florida Department of Health Grant Review Process, Puerto Rico Science and Technology Trust
2006	NIH/NIGMS MBRS-IMSD Special Emphasis Review Panel
2008-2017	NIH/NCI-CRCHD Special Emphasis Panel on P20-U54 Partnerships to Advance Cancer Health Equity (PACHE)
2008-present	Member and Chair, Department of Defense Prostate Cancer Research Program Grant Review Panels
2009-present	Member and Chair, Program Steering Committee, NIH/NCI-CRCHD U54-PACHE Ponce Health Sciences University-Moffitt Cancer Center Partnership
2010	External Scientific Advisory Committee, NIH/NIGMS SCORE Program, University of Puerto Rico School of Medicine
2017-2019	NIH/NIGMS Study Section for Postdoctoral Research Associate (PRAT) Program
2018	NIH/NCI P20 Pre-SPORE Cancer Health Disparities Study Section
2020	NIH/NCI SPORE Review Panel

C. Contributions to Science

1. **Discovery of Cell Cycle-Regulated Centromere Protein CENP-F as a Tumor Associated Antigen (TAA) and Cancer Biomarker.** My early contributions to the field of cancer research began while I was a postdoctoral fellow at The Scripps Research Institute, La Jolla. I used cancer patient autoantibodies to co-discover and characterize a novel cell cycle-regulated, mitosis-associated protein called centromere-associated protein F (CENP-F). I was the first investigator to demonstrate the presence of autoantibodies to this protein in cancer patients, and to establish CENP-F as a TAA and tumor proliferation marker. Increased CENP-F tissue expression and circulating anti-CENP-F autoantibodies are now considered as cancer biomarkers. Representative publications include:
    a. **Casiano CA**, Landberg G, Ochs R, and Tan EM (1993). Autoantibodies to a novel cell cycle-regulated autoantigen that accumulates in the nuclear matrix during S phase and is localized to kinetochores and spindle midzone during mitosis. J. Cell Science 106: 1045-1056. PMID: 7907337
    b. **Casiano CA**, Humbel RL, Peebles C, Covini G and Tan EM (1995). Autoimmunity to the cell cycle-dependent centromere protein p330^{d}/CENP-F in disorders associated with cell proliferation. J. Autoimmunity 8: 575-586. PMID: 7492351
    c. Landberg G, Erlanson M, Roos G, Tan EM, and **Casiano CA** (1996). Nuclear autoantigen p330^{d}/CENP-F: a marker for cell proliferation in human malignancies. Cytometry 25: 90-98. PMID: 8875058
    d. Rattner JB, Rees J, Whitehead CM, **Casiano CA**, Tan EM, Humbel RL, Conrad K, and Fritzler MJ (1997). High frequency of neoplasia in patients with autoantibodies to centromere protein CENP-F. Clinical and Investigative Medicine 20: 308-319. PMID: 20933614

2. **Development of TAA Panels for Cancer Immunodiagnosis.** My interest in TAAs led me to join multi-institutional collaborative studies to pioneer the development of TAA panels to enhance cancer diagnosis in multiple cancer types, including PCa. Some of the TAA panels that we designed are currently being investigated for their potential as diagnostic and prognostic tools in various cancer types. Representative publications include:
    a. Zhang JY, **Casiano CA**, Peng X-X, Koziol J, Chan EKL, and Tan EM (2003) Enhancement of antibody detection in cancer using panel of recombinant tumor-associated antigens. Cancer Epidemiology, Biomarkers, and Prevention 12:136-143. PMID: 12582023
    b. Koziol JA, Zhang JY, **Casiano CA**, Peng XX, Chan EKL, Feng AC, and Tan EM (2003) Recursive partitioning as an approach to selection of immune markers for tumor diagnosis. Clinical Cancer Research 9:5120-5126. PMID: 14613989
    c. **Casiano CA**, Mediavilla-Varela M, and Tan EM (2006). Tumor-associated Autoantigen Arrays for the Serological Diagnosis of Cancer. Molecular Cellular Proteomics 5:1745-1759. PMID: 16733262
    d. Dai L, Li J, Ortega R, Qian W, **Casiano CA**, and Zhang JY (2014). Preferential autoimmune response in prostate cancer to Cyclin B1 in a panel of tumor-associated antigens. J. Immunol Research 2014:827827. PMID: 24860838

3. **Delineating Proteolytic Mechanisms in Cell Death.** My study of TAAs raised the question of whether intracellular proteins targeted by autoantibodies are functionally and structurally modified by proteases during cell death, which could provide insights into their function in cancer and their targeting by the immune system. To address this question, we used autoantibodies from patients with cancer and systemic autoimmune diseases to delineate proteolytic mechanisms targeting specific autoantigens during apoptotic and necrotic cell death. These studies increased our understanding of the fate of intracellular autoantigens during cell death and how their cell death-associated cleavage alters their molecular function and contributes to the elicitation of autoantibody responses. Representative publications include:
    a. **Casiano CA**, Martin SJ, Green DR, and Tan EM (1996) Selective cleavage of nuclear autoantigens during CD95 (Fas/APO-1)-mediated T cell apoptosis. J. Experimental Medicine 184: 765-770. PMID: 8760832
    b. **Casiano CA**, Ochs RL, and Tan EM (1998). Distinct cleavage products of nuclear proteins in apoptosis and necrosis revealed by autoantibody probes. Cell Death Differentiation 5:183-190. PMID: 10200463
    c. Wu X, Daniels T, Molinaro C, Lilly MB, and **Casiano CA** (2002). Caspase cleavage of the nuclear autoantigen LEDGF/p75 abrogates its pro-survival function: implications for autoimmunity in atopic disorders. Cell Death and Differentiation 9:915-925. PMID: 12181742
    d. Brown-Bryan TA, Leoh LS, Ganapathy V, Pacheco FJ, Mediavilla-Varela M, Fillipova M, Linkhart T, Gijsberg R, Debyser Z, and **Casiano CA** (2008). Alternative splicing and caspase-mediated cleavage generate antagonistic variants of the stress response oncoprotein LEDGF/p75. Molecular Cancer Research 6:1293-1307. PMID: 18708362

4. **Discovery of LEDGF/p75 as a Stress Oncoprotein in Prostate Cancer.** During my initial studies on PCa, we discovered that LEDGFp75 (also known as the DFS70 autoantigen) is targeted by autoantibodies in certain patients with PCa. Since then, my research group has been at the forefront of the study of this protein in cancer and autoimmunity, and was the first to demonstrate its overexpression in PCa, implicate it in PCa chemoresistance, and target it for PCa sensitization to chemotherapy. Representative peer-reviewed publications include:
    a. Mediavilla-Varela M, Pacheco FJ, Almaguel F, Daniels TR, Padilla A, Perez J, Leoh LS, Sahakian E, Wall NR, Lilly MB, De Leon M, and **Casiano CA** (2009). Docetaxel-induced prostate cancer cell death involves concomitant activation of caspase and lysosomal pathways and is attenuated by LEDGF/p75. Molecular Cancer 8:68. PMID: 19715609
    b. Basu A, Rojas H, Banerjee H, Cabrera I, Perez K, and **Casiano CA** (2012) Expression of the stress oncoprotein LEDGF/p75 in human cancers: a study of 21 tumor types. PLoS One 7:e30132.
    c. Leoh LS, van Heertum B, De Rijck J, Filippova M, Rios-Colon L, Basu A, Martinez SR, Tungteakkuhn SS, Filippov V, Crist F, De Leon M, Debyser Z, and **Casiano CA** (2012). The stress oncoprotein LEDGF/p75 interacts with the methyl CpG binding protein MeCP2 and influences its transcriptional activity. Molecular Cancer Research 10:378-91. PMID: 22275515
    d. Basu A, Cajigas-Du Ross C, Rios-Colon L, Daniels T, Leoh LS, Mediavilla-Varela M, Rojas H, Banerjee H, Martinez SR, Acevedo-Martinez S, and **Casiano CA** (2016). LEDGF/p75 overexpression

attenuates oxidative stress-induced necrosis and upregulates ERp57/PDIA3/GRp58 in prostate cancer. PLoS One 11:e0146549. PMID: 26771192

5. **Identifying Novel Determinants of Prostate Cancer Health Disparities.** More recently our team has examined the differential tissue expression of proteins, and profile the differential circulation of serum anti-TAA autoantibodies and exosome vesicles in African American and European American patients with and without PCa. Our proteomic approaches are revealing differences in serum autoantibody responses and exosomal protein patterns between these patient groups. This is a relatively new research direction that is already yielding intriguing results and manuscripts. Representative publications include:
    a. Khan S, Simpson J, Turay D, Mirshahidi S, Gonda A, Sanchez TW, **Casiano CA***, and Wall NR (2017). Racial Differences in the Expression of Inhibitors of Apoptosis (IAP) Proteins in Extracellular Vesicles from Prostate Cancer Patients. PLoS One. 12:e0183122. PMID: 28981528 ****shared senior authorship***
    b. Sanchez TW, Zhang G, Dai L, Li J, Mirshahidi S, Wall NR, Wilson C, Yates C, Montgomery S, Zhang JY, and **Casiano CA** (2016) Immunoproteomic profiling of autoantibodies in African American men with prostate cancer: evidence for an autoantibody response to glycolysis and plasminogen associated proteins. Molecular and Cellular Proteomics 15:3564-80. PMID: 27742740
    c. Turay D, Khan S, Diaz-Osterman CJ, Curtis MP, Khaira B, Neidigh JW, Mirshahidi S, **Casiano CA**, and Wall NR (2016) Proteomic profiling of serum-derived exosomes from ethnically diverse prostate cancer patients. Cancer Investigation 4:1-10. PMID: 26536157
    d. Dai L, Li J, Lei N, Xing M, Sanchez TW, **Casiano CA*,** and Zhang JY (2016). Using serological proteomics analysis to identify anti-nucleophosmin 1 autoantibody in sera from European American and African American prostate cancer patients as potential biomarker. Prostate 76:1375-86. ****shared senior authorship.*** PMID: 27418398

Complete List of Published Work in My NCBI Bibliography: PubMed Peer Reviewed Publications (77) and Other Citations/Book Chapters (16) at: **https://www.ncbi.nlm.nih.gov/sites/myncbi/1bW--X1C53D5l/bibliography/48971263/public/?sort=date&direction=ascending**

D. Research Support

Ongoing

NIH/NCI 1R21CA226654-01A1 Casiano CA (PI) 04/01/19-03/31/21
"Glucocorticoid Signaling, Taxane Resistance, and Prostate Cancer Disparity Mortality"

NIH/NCI 3R21CA226654-01 Supplement Casiano CA (PI) 08/01/19-03/31/21
"Administrative Diversity Supplement to Glucocorticoid Signaling, Taxane Resistance, and Prostate Cancer Disparity Mortality"

5R25GM060507 De Leon M (PI) 4/01/01-12/31/22
"LLU-NIH Initiative for Maximizing Student Development"
Role: Co-investigator and Associate Program Director

Recently completed support

NIH/NIMHD 1P20MD006988 Casiano CA (PI) 7/01/12-01/31/19
"Immunoseroproteomics Profiling in Prostate Cancer: Focus on Health Disparities"
An R01 application resulting from this project was submitted but not funded; revised application planned for resubmission.

NIH/NIMHD 1P20MD006988 De Leon M (PI) 7/01/12-01/31/20
"Loma Linda University Center for Health Disparities Research"
Role: Co-investigator and Associate Center Director

1S10OD019960-01 Wang CH (PI) 04/15/15-04/14/16
"High Throughput DNA Sequencer"
Role: Co-Investigator