NAME: Charles Joel Rosser

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

POSITION TITLE: Professor, Associate Center Director of Translational and Clinical Research

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.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>Completion Date MM/YYYY</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Fairleigh Dickinson University</td>
<td>BS</td>
<td>05/1991</td>
<td>Biology</td>
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<tr>
<td>Rutgers School of Medicine</td>
<td>MD</td>
<td>05/1994</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of Phoenix</td>
<td>MBA</td>
<td>12/2008</td>
<td>Business Administration</td>
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A. Personal Statement

My primary basic/translational research interests involve molecular diagnostic and experimental therapeutics for genitourinary tumors. Related to molecular diagnostics, I wish to evaluate robust biomarkers for the non-invasive detection of BCa, a disease with prevalence in the US of 500,000. In addition, these validated biomarkers, or other identified targets, can be identified as druggable targets in the treatment of BCa. This has great potential since no new anti-cancer agents have been introduced into the treatment regimen of BCa for over 20 years.

I am an accomplished physician-scientist with over 15 years of experience as a practicing urologic oncologist. My science training was provided during my residency and surgical fellowship, where I spent over 3 dedicated years in basic science laboratories (1998-1999 Dr. Scott Cramer’s molecular biology laboratory at Wake Forest and 2000-2002 Dr. William Benedict’s cell biology laboratory at UT MD Anderson Cancer Center). Upon joining the faculty at University of Florida, I had the opportunity to have my own laboratory and to be mentored by Dr. Susan Boehlein (2003-2005), who is a molecular biologist. Starting in 2005, my laboratory was self-sustained with extramural grants geared towards molecular diagnostics and experimental therapeutics.

The attached proposal is part of the continuation of my effort to identify, validate and then bring to the clinic, a robust diagnostic signature for BCa in voided urine. Current urine-based BCa detection assays (e.g., urinary cytology, BTA-stat and NMP-22) are subpar. I took this opportunity to systematically address this issue in my laboratory. Within my laboratory, we began to employ gene expression arrays to identify unique genetic signature related to BCa. This was funded by a James and Esther King Biomedical – DOH State of Florida Young Investigator award (PI – Rosser). Next, I established collaborations to analyze our data with some novel selection algorithms which identified 44 key RNA transcripts. These RNA transcripts were tested with TaqMan Low Density Arrays and a 14 gene signature was validated. This was funded by a Flight Attendant Medical Research Institute Young Investigator award (PI- Rosser). Concomitantly, my laboratory teamed up with Dr. Steve Goodison to further characterize urines of BCa patients with proteomics. A unique glycoproteome was identified by our collaborators at the University of Michigan. The 9 biomarker proteome was then validated by ELISA and/or Western blot analysis. This was funded by a NIH/NCI R01 grant (PI – Goodison). Next, we collated our transcriptomic and proteomic data and derived a BCa associated diagnostic signature comprised of 10 biomarkers. To date we have validated this signature in four independent cohorts (n = 880) using commercial ELISA assays against our BCa associated diagnostic signature. This was funded by a James and Esther King Biomedical – DOH State of Florida Team Science award (PI – Rosser). Thus we are extremely confident in our results. Our signature has been submitted as a non-provisional patent (May

The text continues with details about the research and future plans.
Using the patent and our robust data, Nonagen Bioscience Corporation (Orlando/Jacksonville, FL) has procured NIH/NCI SBIR funding (phase I/II fast track) to explore RNA signature. But the protein signature, remains in the academic laboratory to further develop and refine into a multiplex assay capable of assuming its position among the diagnostic armamentarium of physicians. With the current NIH/NCI R01 grant, I am able to a) perform a phase III clinical trial using our multiplex assay and b) engage the FDA for insight into deliverables needed to have the multiplex assay FDA approved. Through another fruitful collaboration, this time with R&D (Minneapolis, MN), we have developed and optimized a multiplex ELISA assay for the Luminex platform that incorporates our 10 validated biomarkers. As Luminex has several FDA approved assays on its platform, our task of achieving FDA approval is made a bit easier since we do not have to work on the FDA reviewing the platform as they would for MSD since it has not been subjected to FDA review.

I have demonstrated a record of successful and productive research projects in an area of high relevance for our current proposal. Since leading independent research programs under a restrained funding condition over the past ten years, I have served as a senior and corresponding author for 67 publications (mainly basic or translational research), in addition to one manuscript under revision and one manuscript in preparation. Over the past 12 years, I have garnered over $6 million in extramural funding (e.g., ACS, DOD, DOH State of Florida and NIH). Furthermore, I have served as PI on over 50 clinical trials (i.e., investigator initiated, cooperative or pharmaceutical) and served as a senior leader in NCI-designated cancer center. Given my background, extremely successful track record of acquiring funding, fostering fruitful collaboration, publishing seminal results and commitment to eliminate BCa, the existence of invaluable patient resources and the clear support from the institution(s), this proposal has an extremely high probability of success and thus identifying a novel multiplex assay for the non-invasive diagnosis of BCa. The parent NIH/NCI R01 grant entitled ‘Multiplexed Protein Biomarker-Based Assay for the Detection of Bladder Cancer’ CA198887 received a score of 3rd percentile in its review in 2016. We are currently in that award’s 4th year, thus limiting our eligibility for the NIH/NCI R01 Supplemental ‘Revision Applications for Validation of Biomarker Assays Developed Through NIH-Supported Research Grants (R01) PAR-17-003’ to our final and last year of the parent award. In the parent award we have: a) recruited to the 2 prospective multicenter clinical trials and are on pace to complete enrollment in 2021 and b) performed an interim analysis demonstrating <5% of data missing within the database and persistent, accurate assay performance (sensitivity 87% and specificity 86%).

The purpose of this NIH/NCI R01 supplemental award is to ‘accelerate the pace of translation of NCI-supported methods/assays/technologies to the clinic’. We are well position to accelerate our discovery (i.e., our multiplex bead-based immunoassay – Luminex platform for BCa detection assay) to the clinic, as this assay is more sensitive and specific than the current multiplex electrochemoluminescent – MSD platform in the parent R01 grant.

B. Positions and Honors

Positions and Employment

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<th>Year</th>
<th>Position</th>
<th>Institution</th>
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<tr>
<td>2003-2009</td>
<td>Assistant Professor, Urology, Pharmacology/Therapeutics</td>
<td>University of Florida</td>
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<tr>
<td>2009</td>
<td>Associate Professor (tenured)</td>
<td>University of Florida</td>
</tr>
<tr>
<td>2009-2013</td>
<td>Chief, Urologic Oncology</td>
<td>MD Anderson Orlando</td>
</tr>
<tr>
<td>2009-2013</td>
<td>Professor, Surgery</td>
<td>Univ. Central Florida</td>
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<tr>
<td>2013-present</td>
<td>Professor (tenured)</td>
<td>Univ. Hawaii</td>
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<td>2013-present</td>
<td>Program Director, Clinical &amp; Translational Research</td>
<td>Univ. Hawaii</td>
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<tr>
<td>2015-2016</td>
<td>Director, Clinical Trials Office</td>
<td>Univ. Hawaii</td>
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<tr>
<td>2015-2019</td>
<td>Associate Center Director Clinical Research</td>
<td>Univ. Hawaii</td>
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<tr>
<td>2019-</td>
<td>Professor, Medical Director</td>
<td>Cedars-Sinai</td>
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Other Experience and Professional Memberships

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<th>Year</th>
<th>Experience/Professional Membership</th>
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<tr>
<td>1998-</td>
<td>Active Member, American Association for Cancer Research</td>
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<tr>
<td>2005-</td>
<td>Fellow, American Board of Urology</td>
</tr>
<tr>
<td>2006-</td>
<td>Fellow, American College of Surgeons</td>
</tr>
<tr>
<td>2009-</td>
<td>Active Member, American Society of Clinical Oncologist</td>
</tr>
<tr>
<td>2009-</td>
<td>A reviewer of BMC Cancer</td>
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2009–2014 Section Editor, BMC Urology
2010–2016 Section Editor, BMC Cancer
2008–2014 Congressionally Directed Medical Research Programs - Pathobiology Study Section
2012–2016 Congressionally Directed Medical Research Programs - Cell Biology Study Section
2017–present NCI – CBSS Study Section
2011–present A reviewer of PLoS One, Molecular Cancer Therapeutics, Oncotarget

Honors
2000–2002 American Foundation of Urologic Disease Scholarship for the Use of Mutated RB Gene in an Adenoviral Vector in the Treatment of Superficial Bladder Cancer
2008 Society of Basic Urologic Research, Young Investigator
2011 American Urologic Association Exchange Scholar
2014 Weinman Innovator Award Recipient

C. Contribution to Science

1. My laboratory made significant contributions to understanding factors that influence the development of radio-resistant prostate cancer tumors. These concepts included the role of Bcl-2, COX2 and Akt, and the value of using small molecule inhibitors against these targets to restore radiation sensitization.

2. My laboratory played a major role in describing the biological effects of Bcl-2 on tumoral angiogenesis. Specifically, we went on to identify that Bcl-2 stimulates the expression of CXCL1 in tumor epithelial and tumor endothelial. Each of these preclinical observations has led to clinical evaluation. We are now completing preclinical toxicology studies as we bring a novel therapeutic to the clinic in mid 2016.

3. My laboratory has a long-standing interest in the identification and validation of urine-based BCa-associated diagnostic signature. We were the first to a) perform gene expression profiling of shed urothelia cells in the urine, b) perform global proteomics on the enriched glycoproteome of voided urine, c) integrate our gene expression data from shed urothelia and glycoproteome data from voided urine, and d) develop and validate a multiplex assay to detect a unique BCa-associated diagnostic signature.
in voided urine. Promising approaches currently under evaluation include comparing the multiplex assay to voided urinary cytology in large multicenter prospective studies.


4. My most recent area of research focus has been exploring the biologic significance of angiogenin, plasminogen activator inhibitor -1, Chemokine (C-X-C motif) ligand 1 and sphingosine kinase 1 in human tumorigenesis. These studies have been done in collaboration with Dr. Steve Goodison. Upon unraveling the biologic significance, we will begin devising methodologies to target these molecules in hopes of bringing novel therapeutics to the clinic for BCa.


This project will profile and validate candidate biomarkers for bladder cancer detection via urinalysis.

The project is geared to refine a miRNA bladder cancer prognostic signature.

STTR (Rosser) 7/1/2012-6/30/2013
Bankhead Coley – DOH State of Florida
Bladder cancer detection assay
The project involves generation of antibodies towards our urine-based bladder cancer signature with the goal of incorporating these antibodies into a protein-based detection assay.

Team Science Project (Rosser) 7/1/2010-6/30/2013
James and Esther King Biomedical – DOH State of Florida
A Multidisciplinary Approach to Improve Patient Outcome in Bladder Cancer - A tobacco-related disease
The project involves novel gene expression profiling methods to identify bladder cancer.

Exploratory Hypothesis (Rosser) 4/1/2012-6/30/2013
Department of Defense
Role of mycoplasmal ABC transporter (p37) in metastatic prostate cancer
The project will shed light on the role Mycoplasma genitalium protein p37 plays in the pathogenesis and progression of human prostate cancer.

R01 (Goodison) 9/1/2007-8/30/2012
NIH/NCI
Towards a non-invasive molecular test for bladder cancer
The project is geared to identify and validate a glycoprotein signature of bladder cancer from a voided urine sample.

Research Scholar Award (Rosser) 7/1/2006-6/30/2009
American Cancer Society
The role of p37 in prostate cancer invasion
The project investigates the role of specific infectious agents in prostate cancer.

New Investigator Award (Rosser) 6/1/2005-5/31/2008
James and Esther King Biomedical – DOH State of Florida
Genomic analysis of voided urine to detect bladder cancer
The project involves novel gene expression profiling methods to identify bladder cancer-specific markers for non-invasive screening.

Young Investigator Award (Rosser) 7/1/2008 - 6/30/2011
Flight Attendant Medical Research Institute
Genomic Analysis of Urine to Detect Bladder Cancer
This project will profile and validate candidate biomarkers for bladder cancer detection via urinalysis.