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TITLE: Analysis of Novel Prostate Cancer Biomarkers and their Predictive Utility
in an Active Surveillance Protocol

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14. ABSTRACT The Research Project supported by this DOD PCRP Physician Research Training Award investigates novel biomarkers for prostate cancer detection and prediction of disease outcome. This first year of my DOD PCRP PRTA has been very productive from both a translational laboratory and clinical research standpoint. In this first annual reporting period, we have begun to investigate our list of biologically relevant candidate prostate cancer biomarkers and have demonstrated promising results. We have also begun to investigate the expression of these markers in prostate cancer tissue and normal prostate using immunohistochemistry. One of the investigated proteins, Tissue Inhibitor of Matrix Metalloproteinase Type 1 (TIMP-1) was found to have increased expression in men with Gleason 7 or greater prostate cancer compared to men with Gleason 3+3 disease. Immunohistochemical analysis for TIMP-1 demonstrated greater staining in prostate cancer compared with normal prostate tissue. These initial data suggest that this protein may represent a biomarker which can help distinguish intermediate and high risk disease from low risk disease. In addition to success in our laboratory work, we have also made significant accomplishments in developing a database of our cohort of 469 men on active surveillance for prostate cancer over the past 15 years. Our analysis of this database has demonstrated freedom from intervention of 77% at 5 years and 62% at 10 years. Cancer specific survival was 100% at 10 years and overall survival was 95% at 5 years and 88% at 10 years. We recently presented these data at the American Urological Association national meeting and are currently in the process of writing a manuscript to formally publish our results.					
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Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4-6
Key Research Accomplishments.....	6
Reportable Outcomes.....	7
Conclusion.....	7
References.....	8
Appendices.....	9

Introduction:

The Research Project supported by this DOD PCRP Physician Research Training Award investigates novel biomarkers for prostate cancer detection and prediction of disease outcome. The goals and objectives of this study are summarized by the Specific Aims: 1. Evaluate the relative levels of expression of our panel of candidate protein biomarkers in urine, tissue and serum from patients with prostate cancer compared with normal controls to identify prostate cancer specific biomarkers. 2. Evaluate the relative urine, tissue and serum levels of these prostate cancer specific biomarkers within our entire active surveillance (AS) cohort to identify accurate biomarkers predictive of indolent vs. progressive prostate cancer. These predictive biomarkers will then be integrated into a multivariate predictive model to optimize the exclusion and inclusion criteria for a safe and effective algorithm for the use of AS. The funding from this Physician Research Training Award provides salary support for Dr. Adam S. Feldman to secure protected time as a translational and clinical investigator in prostate cancer research. It also provides salary support for a Research Assistant for this project.

Body:

This first year of my DOD PCRP PRTA has been very productive from both a translational laboratory and clinical research standpoint. As discussed in my initial application, I used mass spectrometry (MS) to quantitatively compare the entire urinary proteome and identify differentially expressed proteins in the urine from men with prostate cancer as compared with those found in controls. Our MS analysis identified >1400 unique proteins in the urinary proteome. Comparative analysis revealed 55 potential prostate cancer specific proteins. Using bioinformatic database analyses, we narrowed this list of candidate biomarkers to 20 biologically relevant proteins, ranging from 10-80 kD in molecular weight.

We performed semi-quantitative Western blot to investigate expression of these identified proteins in a new cohort of voided urine specimens from PrCA and Controls. To date, we have investigated several of these proteins including Leukocyte Elastase Inhibitor, Annexin A1, Plastin-2 and Vimentin. One of the investigated proteins, Tissue Inhibitor of Matrix Metalloproteinase Type 1 (TIMP-1) has demonstrated some interesting results. In

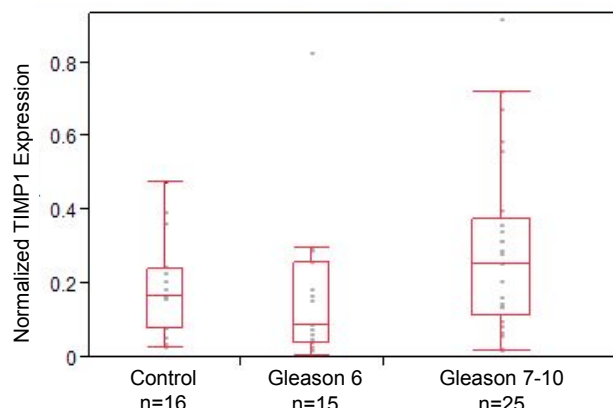


Figure 1: Elevated Expression of TIMP-1 in Gleason 7-10 disease.

urine specimens of 56 men with and without prostate cancer, we found that although there was no significant difference in expression of TIMP-1 between controls and men with Gleason 3+3 prostate cancer, there was a significant difference between expression in men with Gleason 3+3 disease and men with Gleason 7 or greater.¹ (Figure 1) These initial data suggest that this protein may represent

a biomarker which can help distinguish intermediate and high risk disease from low risk disease. Immunohistochemical analysis for TIMP-1 demonstrated greater staining in prostate cancer compared with normal prostate tissue. These data were presented at the American Urological Association (AUA) annual meeting and the AUA Foundation Research Forum this past May.

In addition to our encouraging results with TIMP-1, the success of our methods of discovery are supported by the fact that our list of candidate proteins contains several proteins known to play a biological role in other malignancies and potentially in prostate cancer as well. We are investigating the expression of these proteins in our list, however, we are also returning to our original list of 55 differentially expressed potential prostate cancer specific proteins to also investigate those which have not yet been demonstrated to have biological activity in prostate cancer. It may be that by investigating this list of proteins, we will be able to identify truly novel biomarkers in prostate cancer.

One unexpected technical difficulty that we have encountered over the past year was in our technique for protein isolation for Western blot analysis. For MS analysis urinary protein was isolated using Trichloroacetic Acid-Deoxycholate (TCA-DOC) precipitation. This method was ideal for biomarker discovery using this method. For consistency of evaluation, we initially used this method of protein isolation for Western blot analysis as well. In our initial attempts at analyses, we were unable to produce high quality Western blots from our urinary protein. After several rounds of troubleshooting, it became evident that it was the TCA-DOC method of urinary protein isolation which was responsible for these poor quality blots. We switched to a simple centri-filtration method for protein isolation and our quality has since been much more reliable.

In addition to success in the laboratory, we have had significant success in identifying our cohort of men on active surveillance (AS) for low risk prostate cancer. Through billing and pathology records we identified our cohort of 469 men on AS between 1997 and 2009. Although AS had been practiced throughout this entire period, in 2008 our group agreed upon formal guidelines for AS at our institution. Inclusion criteria included Gleason ≤ 6 , Gleason 7 in select patients with low volume, no more than 3/12 cores positive with $\leq 20\%$ in each core, and PSA < 10 . Our AS follow-up protocol involves PSA

Reason for intervention	n=116	%
Pathologic progression	52	44.8
PSA progression	35	30.2
Patient preference	14	12.1
DRE progression	6	5.2
Metastasis	3	2.6
Other	6	5.2

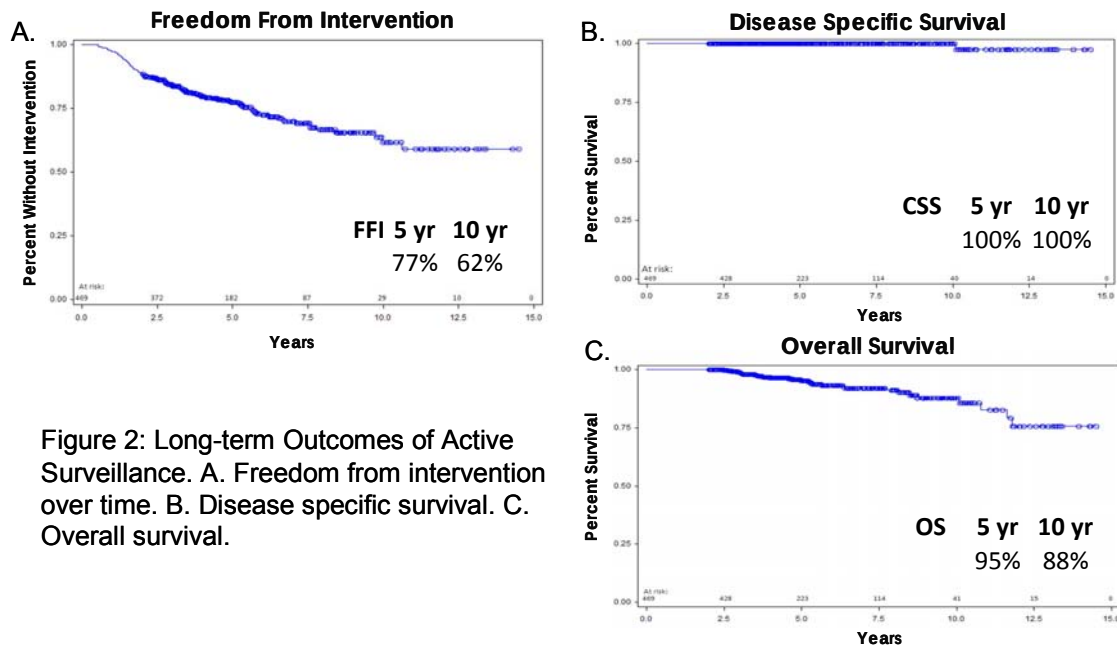
Table 1: Reason for intervention in men under active surveillance.

testing and a digital rectal examination every four months for one year, followed by every six months for two years, and then annually. Those on AS also have a mandatory repeat 12-core biopsy 12-18 months after initial diagnosis. Additional biopsies are at the discretion of the treating physician.

In this cohort, the mean follow-up was 5.6 years and the patients had a mean of 1.5 post-diagnosis biopsies. On first re-biopsy, fifty-five (17.9%) experienced an increase in their Gleason score and

fifty-two (16.8%) experienced cancer-volume progression, defined as an increase from less than

33% to 33% or more. A total of 116 patients (24.7%) converted to active treatment during follow-up. Of these, 52 (44.8%) had an intervention due to pathologic progression, whereas 35 (30.2%) had PSA increase and 14 (12.1%) chose to have an intervention because of their own preference. (Table 1) At five years post-diagnosis, freedom from intervention in our cohort was 77%, and at 10 years this was 62%. At both five and 10 years, the cancer-specific survival rate was 100%. The overall survival rate was 95% at five years and 88% at 10 years. (Figure 2) These data were presented at the American Urological Association (AUA) annual meeting in May and at the Canadian Urological Association annual meeting in June.^{2,3}



In addition to significant research accomplishments, I continue to meet my goals within the training program of this grant. I meet regularly with my two mentors, Drs. Matthew Smith and Bruce Zetter. In our regular meetings, we not only discuss research progress, but also focus on career planning and guidance. I attend regular urologic oncology clinical and research conferences at our institution and both attend and present at regional and national scientific meetings. I attend regular laboratory research meetings both for our own research progress, as well as reviewing other associated research in the current literature.

Key Research Accomplishments:

- Identification of panel of biologically relevant proteins in urine which may be prostate cancer specific.
- Preliminary demonstration that one of our identified proteins, TIMP-1, appears to be more highly expressed in the urine of men with intermediate or high risk disease.

- Development and analysis of a large database of our series of men with low risk prostate cancer on active surveillance.

Reportable Outcomes:

- **Feldman AS**, Banyard J, Fergus M, Jedrychowski M, Huttlin E, Gygi S, Smith M, Zetter B. Identification of novel prostate cancer biomarkers using mass spectrometry. Presented at the AUA Foundation Research Forum, May 2012.
- **Feldman AS**, Banyard J, Fergus M, Jedrychowski M, Huttlin E, Gygi S, Smith M, Zetter B. Discovery and analysis of prostate cancer biomarkers in a standard non-post-DRE voided urine specimen. Abstract presented at the American Urological Association national meeting, May 2012.
- Carrasquillo R, Preston M, Coen J, Zietman A, Smith M, Wu CL, McDougal WS, **Feldman AS**. Gleason upgrading and Increased Cancer Volume on Repeat Prostate Biopsy in Patients on Active Surveillance. Abstract presented at the American Urological Association national meeting, May 2012.
- Preston M, Carrasquillo R, Coen J, Zietman A, Smith M, Wu CL, McDougal WS, **Feldman AS**. Need for Intervention and Survival in a Cohort of Patients on Active Surveillance for Low-risk Prostate Cancer. Abstract presented at the American Urological Association national meeting, May 2012.

Conclusion:

In summary, this first year of my DOD PCRP PRTA has been very productive. In this first annual reporting period, we have begun to investigate our list of biologically relevant candidate prostate cancer biomarkers and have demonstrated promising results. We have also begun to investigate the expression of these markers in prostate cancer tissue and normal prostate using immunohistochemistry. In addition to success in our laboratory work, we have also made significant accomplishments in developing a database of our large cohort of men on active surveillance for prostate cancer over the past 15 years. Analysis of this database has already begun to produce data, which we have presented at national meetings. We are currently in the process of writing a manuscript to publish our results.

This work is very relevant to current clinical practice in prostate cancer and meets any potential “so what” criteria. New diagnostic and predictive biomarkers with improved performance characteristics than prostate specific antigen (PSA) are sorely needed. The work funded by this grant directly addresses that challenge and we are already beginning to produce results toward that goal. In addition, it is clear that we have historically over-treated low risk prostate cancer. Active surveillance is a management strategy for low risk disease which will help ameliorate the problem of overtreatment. Our large database of men on active surveillance will help us to understand the safety, efficacy and outcomes of this strategy and will help us better select men for AS in the future. Biomarker analysis within this cohort will also help us better understand who truly has very low risk disease and can safely avoid radical treatment.

References:

1. **Feldman AS**, Banyard J, Fergus M, Jedrychowski M, Huttlin E, Gygi S, Smith M, Zetter B. Identification of novel prostate cancer biomarkers using mass spectrometry. Presented at the AUA Foundation Research Forum, May 2012.
2. Carrasquillo R, Preston M, Coen J, Zietman A, Smith M, Wu CL, McDougal WS, **Feldman AS**. Gleason upgrading and Increased Cancer Volume on Repeat Prostate Biopsy in Patients on Active Surveillance. Abstract presented at the American Urological Association national meeting, May 2012.
3. Preston M, Carrasquillo R, Coen J, Zietman A, Smith M, Wu CL, McDougal WS, **Feldman AS**. Need for Intervention and Survival in a Cohort of Patients on Active Surveillance for Low-risk Prostate Cancer. Abstract presented at the American Urological Association national meeting, May 2012.

Curriculum Vitae

Date Prepared: June 28, 2012

Name: Adam S. Feldman, M.D., M.P.H.

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Place of Birth: New York, NY

Education

1994	B.A. - Biological Basis of Behavior	University of Pennsylvania
1996	M.A. (Alpha Epsilon Lambda) - Medical Sciences	Boston University School of Medicine
2000	M.D. (Alpha Omega Alpha)	University of Massachusetts Medical School
2009	M.P.H. – Clinical Effectiveness	Harvard School of Public Health

Postdoctoral Training

07/00-06/01	Intern in Surgery, Massachusetts General Hospital
07/01-06/02	Resident in Surgery, Massachusetts General Hospital
07/02-06/05	Resident in Urology, Massachusetts General Hospital
07/05-06/06	Chief Resident in Urology, Massachusetts General Hospital
07/06-06/08	Fellow in Urologic Oncology, Massachusetts General Hospital

Faculty Academic Appointments

2000-2006	Clinical Fellow in Surgery, Harvard Medical School, Boston, MA
2006-2010	Instructor in Surgery, Harvard Medical School, Boston, MA
2010-	Assistant Professor of Surgery, Harvard Medical School, Boston, MA

Appointments at Hospitals/Affiliated Institutions

07/06-	Assistant in Urology, Massachusetts General Hospital, Boston, MA
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Major Administrative Leadership Positions

2011	Scientific Program Chair, American Urological Association, New England and Mid-Atlantic Sections, Annual Meeting
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Other Professional Positions

- 2012 American Urological Association Representative, Lower Anogenital Squamous Terminology Standardization (LAST) Consensus Conference, 2012
- 2012 Member: Scientific Program Committee, American Urological Association, New England Section Annual Meeting

Professional Societies

- 1998- Massachusetts Medical Society, Member
- 2002- American Urological Association, Member
- 2004- American Association of Clinical Urologists, Member

Editorial Activities

- 2006- Ad-Hoc Reviewer, International Braz J Urol
- 2007- Ad-Hoc Reviewer, Journal of Urology
- 2010- Ad-Hoc Reviewer, Urology
- 2010- Ad-Hoc Reviewer, Prostate Cancer and Prostatic Diseases
- 2010- Ad-Hoc Reviewer, Urologic Oncology
- 2011- Ad-Hoc Reviewer, BJU International
- 2012- Ad-Hoc Reviewer, Molecular Cancer Research

Honors and Prizes

- 1996 Alpha Epsilon Lambda - Graduate Honors Society, Boston U. School Of Medicine
- 2000 Senior Scholar - Department of Surgery, U. Of Massachusetts Medical School
- 2000 Alpha Omega Alpha Honor Medical Society, U. Of Massachusetts Medical School
- 2003 Resident Abstract Travel Award, American Urological Association - New England Section
- 2005 Merit Award for Outstanding Abstract, The ASCO Foundation Grants Program – Multidisciplinary Prostate Cancer Symposium
- 2006 Gerald P. Murphy Scholar, American Urological Association
- 2008 Merit Award for Outstanding Abstract, The ASCO Foundation Grants Program – Multidisciplinary Genitourinary Cancers Symposium
- 2009 AUA Foundation Research Forum – AUA New England Section Nominee
- 2008 Prostate Cancer Foundation Young Investigator Award
- 2011 CINE Golden Eagle Award – CBS Public Service Announcement on Prostate Cancer
- 2011 Best Poster - Annual Meeting of the American Urological Association, Washington, D.C.
- 2012 AUA Foundation Research Forum – AUA New England Section Nominee

Report of Funded and Unfunded Projects

Funding Information

Past:

- 1997 Student Institutional Grant, Joseph P. Healy Grant, Pre-clinical Intercultural Program, University of Massachusetts Medical School

- Summer intercultural immersion program in clinical medicine in

Latino community in Miami, FL

1997-1998	Project Director	Institutional Grant, Community Service Grant funding Creating Our Future Program, University of Massachusetts Medical School • Program in which medical students tutored and mentored children of homeless families in Worcester, MA
2007-2008	P.I.	Claire and John Bertucci Prostate Cancer Research Fund, A Proteomic Approach to Prostate Cancer Biomarker Discovery • Use proteomic techniques for urine biomarker discovery in men with prostate cancer • \$25,000 award
2007-2009	P.I.	Company – Predictive Biosciences; Evaluation of Urine Based Protein Biomarkers in Bladder Cancer • Analyze urinary proteins as novel diagnostic and surveillance markers in bladder cancer • Sponsored Research Agreement
2009-2010	P.I.	Claire and John Bertucci Prostate Cancer Research Fund - Active Surveillance for Prostate Cancer: Management Patterns, Outcomes, and Quality of Life • Funding supports research personnel for data mining and management • \$25,000 award
Current: 2008-	P.I.	Prostate Cancer Foundation – Young Investigator Award; Proteomic Discovery and Analysis of Novel Biomarkers in Prostate Cancer • Use proteomic mass spectrometry techniques for identification of novel prostate cancer biomarkers in urine and serum
2009-	Investigator	\$75,000 per year for 3 years. A Phase II Randomized Study for Patients With Muscle-Invasive Bladder Cancer Evaluating Transurethral Surgery and Concomitant Chemoradiation by Either BID Irradiation Plus 5-Fluorouracil and Cisplatin or QD Irradiation Plus Gemcitabine Followed by Selective Bladder Preservation and Gemcitabine/Cisplatin Adjuvant Chemotherapy (RTOG 0712).
2009-	Investigator	Harvard Catalyst Pilot Grant Program NIH UL1 RR 025758-02 Clinical and Translational Science Center Grant Sonoelastography for Tumor-Targeted Prostate Biopsy • This study is a pilot study of the utility of sonoelastography for targeting biopsy to foci of cancer in the prostate.

2011-	P.I.	Department of Defense Prostate Cancer Research Program - Physician Research Training Award; Analysis of Novel Prostate Cancer Biomarkers and Their Utility in an Active Surveillance Protocol
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- The research project will investigate novel biomarkers in prostate cancer detection and prediction of disease outcome.

\$130,000 per year for 5 years

Unfunded Projects

Past:

1991	Research Assistant	Isolation and sequencing of a conserved domain of the DnaJ family of chaperonins. Department of Surgical Research, Children's Hospital, Boston, MA.
1994-1995	Research Assistant	Evaluation of Critical Pathways for CHF, DVT, and Normal Vaginal Delivery with 24 hour LOS. Brigham and Women's Hospital, Boston, MA.
1994-1995	Research Assistant	Adverse Drug Events Prevention Study Group. Brigham and Women's Hospital, Harvard School of Public Health.
1999-2000	Research Fellow	Characterization of Angiogenic Markers in the Rat Genitourinary System. Laboratory for Cellular Therapeutics and Tissue Engineering, Department of Urology, Children's Hospital, Boston, MA.
2002-2004	Investigator	Development of bladder cancer in a murine model for Cables knock-out mice exposed to N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). Laboratory of Urology/Pathology, Massachusetts General Hospital, Boston, MA.
2002-2004	Investigator	The Role of Cables, a novel cell-cycle regulatory protein in human transitional cell carcinoma and prostate cancer. Laboratory of Urology/Pathology, Massachusetts General Hospital, Boston, MA.
2004-2005	Investigator	Proteomic analysis of voided urine specimens for biomarker discovery and validation in prostate and bladder cancer. Laboratory of Urology/Pathology, Massachusetts General Hospital. Department of Vascular Biology, Children's Hospital, Boston, MA.
2007-2008	Investigator	Laparoscopic and Open Radical prostatectomy after laparoscopic inguinal hernia repair. Massachusetts General Hospital, Boston, MA.
2010	Investigator	Outcomes of Organ Sparing Surgery in Penile Cancer. Massachusetts General Hospital, Boston, MA.

Current:

2006-	P.I.	A comparison of nephron sparing techniques: percutaneous radiofrequency ablation (RFA) vs. open and laparoscopic partial nephrectomy. Massachusetts General Hospital, Boston, MA.
2009-	P.I.	Active Surveillance in Prostate Cancer: Retrospective analysis of quality of life and outcomes and development of a prospective cohort. Massachusetts General Hospital, Boston, MA.
2010-	Investigator	Renal Biopsy for Small Renal Masses. Massachusetts General Hospital, Boston, MA.
2010-	Investigator	Multi-Institutional Bladder Cancer Quality Care Initiative for non-metastatic muscle invasive transitional cell carcinoma of the bladder.

Report of Local Teaching and Training

Teaching of Students in Courses

2006-present Urologic Surgery

	Attending	30 Medical Students 8 Residents	<i>contact time</i> 10 hours/week for 50 week(s)	<i>prep time</i> none reported
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2008-2010 Patient Doctor II

	Attending	5 Medical Students	<i>contact time</i> 8 hours/year for 1 year(s)	<i>prep time</i> none reported
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2010 HMS2 Pathophysiology

	Attending	25 Medical Students	<i>contact time</i> 3 hours/year for 1 year(s)	<i>prep time</i> 3 hours
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Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

2007 Surgical Chief's Rounds - Department of Surgery - Injuries to the Urogenital Tract

	Lecturer	25 Residents	<i>contact time</i> 1 hour	<i>prep time</i> 5 hours
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2008-present Ambulatory Teaching Rounds - Department of Medicine – Uro-oncology for the primary care physician; Management of Small Renal Masses

	Lecturer	30 Residents	<i>contact time</i> 4 hours/year	<i>prep time</i> 10 hours/year
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2010 General Surgery Teaching Rounds – Department of Surgery – Bladder Cancer Review

	Lecturer	25 Residents	<i>contact time</i> 0.5 hour	<i>prep time</i> 3 hours
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Clinical Supervisory and Training Responsibilities

2006-present Urological Surgery – Training of Residents 15 hours/week

2008-present Sub-specialty Faculty Advisor for the Acute Care Surgery fellow 10 hours/year

Laboratory and Other Research Supervisory and Training Responsibilities

2007-present Supervision and mentoring of Research Fellow 5 hours/week

Formal Teaching of Peers (e.g., CME and other continuing education courses)

1996-1997 Worcester, MA Teaching Assistant/Tutor in Biochemistry, University of Massachusetts Medical School

Responsibility: Tutor fellow medical students in Biochemistry.

2009 Las Vegas, NV Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?"

2009 Scottsdale, AZ Faculty (CME Course): Maximizing Bone Health for Patients With

2010	San Francisco, CA	Prostate Cancer: Establishing the "Who, What, Why & How?" Faculty (CME Course): Master Class on Integrating Novel Antiresorptive Agents into the treatment of Prostate Cancer
2010	Boston, MA	Faculty (CME Course): Trauma and Critical Care Symposium – Penile and Genitalia Trauma
2011	Boston, MA	Faculty (CME Course): Society of Translational Oncology Prostate Cancer Symposium – Prostate Cancer: Progress and Promise
2011	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Case Studies in Urology <i>[Invited Lecture]</i>

Report of Regional, National and International Invited Teaching and Presentations

Local Invited Presentations and Courses

2008	Boston, MA	Comparative Analysis of Nephron Sparing Techniques. Update on Urologic Oncology – Massachusetts General Hospital, Harvard Medical School <i>[Invited Lecture]</i>
2008	Boston, MA	Prostate Cancer: Diagnosis and Management. Prostate Cancer Support Group, Massachusetts General Hospital <i>[Invited Lecture]</i>
2011	Boston, MA	Controversies Around the Management of Small Renal Masses – DF/HCC Kidney Cancer Program <i>[Invited Lecture]</i>
2011	Boston, MA	Proteomic Discovery of Novel Biomarkers in Prostate Cancer – Massachusetts General Hospital Department of Urology Centennial Academic Program <i>[Invited Lecture]</i>
2011	Cambridge, MA	Management of Small Renal Masses – Harvard University Health Services Grand Rounds <i>[Invited Lecture]</i>
2011	Boston, MA	Incidental Radiologic Findings: "Incidental Renal Masses" – Massachusetts General Hospital Medical Grand Rounds <i>[Invited Lecture]</i>
2012	Concord, MA	Controversies in the Management of the Small Renal Mass – Emerson Hospital Medical Grand Rounds <i>[Invited Lecture]</i>

Regional Invited Presentations and Courses

2009	Dedham, MA	Urologic Oncology: An Overview. Massachusetts Health Information Management Association <i>[Invited Lecture]</i>
2010	Mt. Kisco, NY	Controversies in the Management of Small Renal Masses <i>[Invited Lecture]</i>
2011	Dedham, MA	Penile Cancer. Urology Nursing Society <i>[Invited Lecture]</i>

National Invited Presentations and Courses

2007	Hollywood, FL	Radical prostatectomy after inguinal hernia repair. The American Hernia Society <i>[Invited Lecture]</i>
2009	Boston, MA	Renal Cell Carcinoma: Surgical Management at Massachusetts General Hospital. Exchange Experience Program on Renal Cancer <i>[Invited Lecture]</i>

2009	Las Vegas, NV	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?" <i>[Invited Lecture]</i>
2009	Scottsdale, AZ	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?" <i>[Invited Lecture]</i>
2010	San Francisco, CA	Faculty (CME Course): Master Class on Integrating Novel Antiresorptive Agents into the treatment of Prostate Cancer. <i>[Invited Lecture]</i>
2010	Boston, MA	Faculty (CME Course): Trauma and Critical Care Symposium – Penile and Genitalia Trauma. <i>[Invited Lecture]</i>
2011	Boston, MA	Faculty (CME Course): Society of Translational Oncology Prostate Cancer Symposium – Prostate Cancer: Progress and Promise
2011	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Case Studies in Urology <i>[Invited Lecture]</i>

International Invited Presentations and Courses

2011	Mallorca, Spain	5 th International Urology Forum – The Potential of Nanoparticle Enhanced Imaging in the Accurate Detection of Lymph Node Metastases <i>[Invited Lecture]</i>
2012	Mallorca, Spain	6 th International Urology Forum – Renal Mass Biopsy <i>[Invited Lecture]</i>

Report of Clinical Activities and Innovations

Current Licensure and Certification

2002	Diplomate, National Board of Medical Examiners
2004	Massachusetts Registered Physician

Practice Activities

Urology/Urologic Oncology, Laparoscopy and Endourology	Massachusetts General Hospital
Attending Urologic Surgeon, Polycystic Kidney Disease Clinic	Massachusetts General Hospital

Report of Technological and Other Scientific Innovations

Patents

1. Zetter BR, Feldman AS, McDougal WS. Methods for diagnosis and prognosis of epithelial cancers. U.S. provisional Patent Application. 2006 Mar 8.
 - Potential use of biomarkers as diagnostic or prognostic markers in bladder cancer. These are currently under investigation and are not yet being used in clinical care
 - My contribution was and is the discovery and analysis of the patented biomarkers

Report of Education of Patients and Service to the Community

Activities

1996-1998	Director (1997-1998) Volunteer (1996-1997), Creating Our Future Program - Worcester Family Health and Social Services Center
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Educational Material for Patients and the Lay Community:

- 2010 **Feldman AS.** Essay on Prostate Cancer. CBS Cares: Prostate Cancer Campaign. cbscares.com.
- 2011 **Feldman AS.** Essay on Testicular Cancer. CBS Cares Valentine's Day Campaign on Testicular Cancer. cbscares.com.
- 2011 **Feldman AS.** Patient information: Blood in the urine (hematuria) in adults. UpToDate 19.3. October 14, 2011.

Report of Scholarship

Peer Reviewed Publications in print or other media:

Research Investigations:

1. Eisner BH, **Feldman AS**, Chapin BF, Dretler SP. "Blind coning"--using the Stone Cone for removal of intramural ureteral calculi. *Urology*. 2007;69(4):773-5.
2. Banyard J, Bao L, Hofer MD, Zurakowski D, Spivey KA, **Feldman AS**, Hutchinson LM, Kuefer R, Rubin MA, Zetter BR. Collagen XXIII expression is associated with prostate cancer recurrence and distant metastases. *Clin Cancer Res*. 2007;13(9):2634-42.
3. **Feldman AS**, Banyard J, Wu C-L, McDougal WS, Zetter BR . Cystatin B as a tissue and urinary biomarker of bladder cancer recurrence and disease progression. *Clin Cancer Res*. 2009;15(3):1024-31.
4. Tanrikut C, **Feldman AS**, Altemus M, Paduch DA, Schlegel PN. Adverse effect of paroxetine on sperm. *Fertility and Sterility*. 2009. June 10, Epub ahead of print.
5. Kubota K, Anjum R, Yu Y, Kunz RC, Andersen JN, Kraus M, Keilhack H, Nagashima K, Krauss S, Pawletz C, Hendrickson RC, **Feldman AS**, Wu CL, Rush J, Villen J, Gygi SP. Sensitive multiplexed analysis of kinase activities and activity-based kinase identification. *Nature Biotechnology*. 2009; 27(10): 933-40.
6. Pandharipande PV, Gervais DA, Hartman RI, Harisinghani MG, **Feldman AS**, Mueller PR, Gazelle GS. Renal mass biopsy to guide treatment decisions for small incidental renal tumors: a cost-effectiveness analysis. *Radiology*. 2010; 256(3):836-46.
7. Coen JJ, **Feldman AS**, Smith MR, Zietman AL. Watchful waiting for localized prostate cancer in the PSA era: what have been the triggers for intervention? *BJU Int*. 2010 Sep 22. Epub ahead of print.
8. Psutka SP, **Feldman AS**, Rodin D, Olumi AF, Wu CL, McDougal WS. Men With Organ-confined Prostate Cancer and Positive Surgical Margins Develop Biochemical Failure at a Similar Rate to Men With Extracapsular Extension. *Urology*. 2011 Mar 14. [Epub ahead of print]
9. **Feldman AS**, McDougal WS. Long Term Outcome of Excisional Organ Sparing Surgery for Carcinoma of the Penis. *J Urol*. 2011 Oct;186(4):1303-7.
10. Gershman B, Zietman AL, **Feldman AS**, McDougal WS. Transperineal Template-Guided Prostate Biopsy for Patients with Persistently Elevated PSA and Multiple Prior Negative Biopsies. *Urologic Oncology: Seminars and Original Investigations*. Accepted for publication. 2012.
11. Fernandez CA, Milholland JM, Zwarthoff EC, **Feldman AS**, Karnes JR, Shuber AP. A noninvasive multi-analyte diagnostic assay: combining protein and DNA markers to stratify bladder cancer

patients. Research and Reports in Urology. 2012 Feb 22. [EPub]

Other peer-reviewed publications:

1. **Feldman AS**, Bauer SB. Diagnosis and management of dysfunctional voiding. Curr Opin Pediatr. 2006;18(2):139-47.
2. **Feldman AS** and McDougal WS. Inguinal Node Dissection for Penile Carcinoma. AUA Update. 2008.
3. **Feldman AS**, McDougal WS, Harisinghani MG. The potential of nanoparticle-enhanced imaging. The Journal of Urologic Oncology, Seminar Section. 2008;26(1):65-73.
4. Kaufman DS, Shipley WU, **Feldman AS**. Bladder Cancer. The Lancet. 2009; 374(9685):239-49.
5. Eisner BH and **Feldman AS**. Nanoparticle imaging for genitourinary cancers. Cancer Biomark. 2009;5(2):75-9.
6. Siddiqui MM, **Feldman AS**. Advances in the evaluation and management of lymph node involvement in urothelial carcinoma of the bladder. Expert Rev Anticancer Ther. 2010;10(12):1855-9.

Non-peer reviewed scientific or medical publications/materials in print or other media:

1. **Feldman AS**, Gargollo PC, Grocela JA. Genitourinary Trauma. In: Sheridan RL, Ed. The Trauma Handbook of the Massachusetts General Hospital. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. p. 584-508.
3. **Feldman AS** and Dahl DM. , 2006. June, 2-6, 2006. Laparoscopic Radical Prostatectomy. US Oncological Disease 2006. 2006: pp. 56-58.
10. **Feldman AS**, Mueller PR, McDougal WS. Radiofrequency Ablation. In: Ahmed HU, et al. Eds. Interventional Techniques in Uro-Oncology. Oxford, UK: Wiley; 2011. p. 68-85.
11. **Feldman AS**, Hsu C, Kurtz M, Cho KC. Etiology and evaluation of hematuria in adults. In: UpToDate 19.2. June 17, 2011.
12. Psutka SP, Daha A, McGovern FM, McDougal WS, Mueller PR, Gervais D, **Feldman AS**. Complication rates increase with radiofrequency ablation of large, central renal tumors. AUA News. November 2011. p. 9-10.

Thesis

1. **Feldman AS**. Developmental Lead Exposure and Cognition. Boston, MA: Boston University School of Medicine;1996.

Abstracts, Poster Presentations and Exhibits Presented at Professional Meetings:

1. **Feldman A**, Soker S, Lu X, Atala A. Characterization of the normal expression of angiogenic markers in the rat genitourinary system. Presented at Senior Scholars Presentation Day, University of Massachusetts Medical School. 2000.
2. Soker S, Machado MG, Lu X, **Feldman A**, Atala A. Localization of VEGF and its receptors in corpus cavernosa. Presented at American Urological Association. 2000.
3. **Feldman A**, Kirley S, McDougal WS, Zukerberg LR, Wu CL. The role of cables, a putative tumor suppressor gene in urothelial carcinoma. Presented at American Urological Association, New

- England Section, 2002. The role of cables, a putative tumor suppressor gene in urothelial carcinoma. Presented at American Urological Association, New England Section. 2002.
4. **Feldman A**, Kirley S, McDougal WS, Zukerberg LR, Wu CL. Expression of cables, a cell cycle regulatory gene is lost in human prostate cancer and suppresses prostate cancer cell growth. Presented at American Urological Association. 2003.
 5. **Feldman A**, Tang Z, Kirley S, McDougal WS, Zukerberg LR, Wu CL. Expression of cables, a cell cycle regulatory gene is lost in invasive transitional cell carcinoma of the bladder. Presented at American Urological Association. 2003.
 6. **Feldman A**, Kirley S, McDougal WS, Zukerberg LR, Wu CL. The expression of cables, a cell cycle regulatory gene is progressively lost in human prostate cancer as Gleason score increases. Presented at American Urological Association. 2004.
 7. **Feldman AS**, Hutchinson LM, McDougal WS, Zetter BR. Proteomic analysis of voided urine, bladder cancer tissue and cell lines for biomarker discovery in transitional cell carcinoma. Presented at the Scientific Advisory Committee Meeting, Massachusetts General Hospital. 2005.
 8. **Feldman AS**, Hutchinson LM, McDougal WS, Zetter BR. Biomarker profiling and novel approach to biomarker normalization for prostate cancer diagnosis using post-DRE voided urine specimens. Presented at the Multidisciplinary Prostate Cancer Symposium. 2005.
 9. **Feldman AS**, Hutchinson LM, McDougal WS, Zetter BR. Proteomic analysis of post-DRE voided urine specimens for prostate cancer biomarker discovery. Presented at the Multidisciplinary Prostate Cancer Symposium. 2005.
 10. **Feldman AS**, Gervais D, Cutie CJ, Mueller PR, McDougal WS. A comparison of nephron sparing techniques: percutaneous radiofrequency ablation (RFA) vs. open and laparoscopic partial nephrectomy. Presented at the Society of Urologic Oncology, 2005 and American Urological Association. 2006.
 11. **Feldman AS**, Banyard J, Wu CL, McDougal WS, Zetter BR. Proteomic discovery and analysis of Cystatin B, a novel biomarker in transitional cell carcinoma. Presented at the American Urological Association and ASCO GU Cancer Symposium. 2007.
 12. **Feldman, AS**, Gartner C, Holleman A, Daha A, Gygi SP, Stampfer MJ, Zetter BR, Smith MR. Proteomic discovery and analysis of novel biomarkers in prostate cancer. Presented at the Prostate Cancer Foundation Scientific Retreat. 2008.
 13. Tanrikut C, **Feldman AS**, Altemus M, Paduch DA, Schlegel PN. Antidepressant-associated changes in semen parameters. Presented at the American Society of Reproductive Medicine. 2008.
 14. Psutka SD, **Feldman AS**, Rodin D, Wu C-L, McDougal WS. Positive Surgical Margins Do Not Affect Disease Recurrence in Patients with T3a Prostate Cancer. Presented at the American Urological Association, New England Section, 2008 and American Urological Association, 2009.
 15. Chapin BF, **Feldman AS**, Dahl, DM. Hydrodissection of the neurovascular bundles in laparoscopic radical prostatectomy: impact on positive surgical margins. Presented at the American Urological Association, New England Section. 2008 and American Urological Association, 2009.
 16. Kubota K, Anjum R, Yu Y, **Feldman A**, Wu CL, Rush J, Villen J, Gygi S. Toward simultaneously assessing the activation state of the kinome including substrate-kinase relationship. Presented at the American Society of Mass Spectrometry, 2009.
 17. Osbourne AL, Daha AK, Cutie CJ, Dahl DM, **Feldman AS**. Comparison of Laparoscopic and Open Partial Nephrectomy. A retrospective review at the Massachusetts General Hospital. Presented at the American Urological Association, New England Section, 2009.
 18. Daha AK, Osbourne AL, Cutie CJ, Gervais DA, Dahl DM, **Feldman AS**. Choice of Nephron

- Sparing Technique correlates with change in GFR: Percutaneous Radiofrequency Ablation (RFA) vs. Open and Laparoscopic Partial Nephrectomy. Presented at the American Urological Association, New England Section, 2009.
19. Chapin BF, **Feldman AS**, Psutka SD, Dahl DM. Predictors of Post-Prostatectomy Incontinence: A Multivariate Analysis. Presented at the American Urological Association, New England Section, 2009.
 20. **Feldman AS**, Jedrychowski M, Huttlin E, Gartner C, Holleman A, Gygi SP, Zetter BR, Smith MR. Proteomic discovery of novel biomarkers in prostate cancer using mass spectrometry. Presented at the Prostate Cancer Foundation Scientific Retreat. 2009.
 21. Psutka SP, Daha A, Gervais D, **Feldman AS**. Salvage radiofrequency ablation achieves effective local control of recurrent renal cell carcinoma. Presented at the American Urological Association, New England Section, 2010 and Society of Urologic Oncology, 2010.
 22. Psutka SP, Daha A, McGovern FM, McDougal WS, Mueller PR, Gervais D, **Feldman AS**. Radiofrequency ablation of centrally located renal tumors is associated with increased rates of Clavien grade 3-5 complications. Presented at the American Urological Association, 2011.
 23. Siddiqui MM, Heney N, McDougal WS, **Feldman AS**. Private vs. public insurance: is there a difference in survival in bladder urothelial carcinoma? Presented at the American Urological Association, New England Section, 2010 and American Urological Association, 2011.
 24. Psutka SP, Daha A, Gervais D, **Feldman AS** Salvage radiofrequency ablation achieves local control of recurrent renal cell carcinoma. Presented at the Society of Urologic Oncology, 2010.
 25. Deshmukh SM, Sequeira L, McGovern FJ, Dahl D, Olumi A, Eisner B, McDougal WS, Mueller P, Samir A, **Feldman AS**. Percutaneous Biopsy of Suspicious Cystic Renal Masses: What is the Diagnostic Yield? Presented at the American Urological Association, 2011.
 26. Deshmukh SM, Sequeira L, McGovern FJ, Dahl D, Olumi A, Eisner B, McDougal WS, Mueller P, Samir A, **Feldman AS**. Percutaneous Renal Mass Biopsy: If they're positive, they're positive, but if they're negative, be careful: A Correlation Between Renal Biopsy and Surgical Pathology. Presented at the American Urological Association, 2011.
 27. Gershman B, **Feldman A**, Zietman A, McDougal WS. Transperineal template-guided prostate biopsy for persistently elevated PSA following multiple negative biopsies. Presented at the American Urological Association, 2011.
 29. Everly RA, Kunz RC, McAllister FE, **Feldman AS**, Wu CL, Gygi SP. Measuring Kinase Activity Phenotypes in Normal and Cancerous Human Prostate Tissue Using KAYAK. Presented at American Society for Mass Spectrometry, 2011.
 30. Psutka SP, Olumi AF, **Feldman AS**, Saylor P, Kaufman D, Lee RJ. Pathologic down-staging with gemcitabine and cisplatin neoadjuvant chemotherapy for muscle-invasive urothelial carcinoma of the bladder. Presented at the American Urological Association, New England Section, 2011 and 2012 Genitourinary Cancers Symposium
 31. Psutka SP, McGovern FJ, Mueller PM, McDougal WS, Gervais D, **Feldman AS**. Durable oncologic outcomes after radiofrequency ablation for T1 renal cell carcinoma in poor surgical candidates. Presented at the American Urological Association, New England Section, 2011 and 2012 Genitourinary Cancers Symposium
 32. Deshmukh SM, Chapin BF, Eisner BH, Eswara J, McGovern FJ, McDougal WS, Mueller P, Samir A, **Feldman AS**. Renal Oncocytoma diagnosed by Percutaneous biopsy can be safely followed but must not be forgotten. Presented at the American Urological Association, New England Section, 2011
 33. Psutka SP, **Feldman AS**, Lee RJ, Olumi AF. Short-term complications after cystectomy in patients

treated with neoadjuvant chemotherapy is only associated with comorbidity. Presented at the American Urological Association, New England Section, 2011

34. Siddiqui MM, Lee RJ, Wu S, Wu CL, **Feldman AS**. Perioperative systemic chemotherapy confers a cancer-specific survival benefit in T3 urothelial carcinoma of the renal pelvis. Presented at the American Urological Association, New England Section, 2011
35. **Feldman AS**, Banyard J, Fergus M, Jedrychowski M, Huttlin E, Gygi S, Smith M, Zetter B. Identification of novel prostate cancer biomarkers using mass spectrometry. Presented at the AUA Foundation Research Forum, May 2012.
36. **Feldman AS**, Banyard J, Fergus M, Jedrychowski M, Huttlin E, Gygi S, Smith M, Zetter B. Discovery and analysis of prostate cancer biomarkers in a standard non-post-DRE voided urine specimen. Abstract presented at the American Urological Association national meeting, May 2012.
37. Carrasquillo R, Preston M, Coen J, Zietman A, Smith M, Wu CL, McDougal WS, **Feldman AS**. Gleason upgrading and Increased Cancer Volume on Repeat Prostate Biopsy in Patients on Active Surveillance. Abstract presented at the American Urological Association national meeting, May 2012.
38. Preston M, Carrasquillo R, Coen J, Zietman A, Smith M, Wu CL, McDougal WS, **Feldman AS**. Need for Intervention and Survival in a Cohort of Patients on Active Surveillance for Low-risk Prostate Cancer. Abstract presented at the American Urological Association national meeting, May 2012.