BIOGRAPHICAL SKETCH

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NAME: Joshua I. Warrick

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

POSITION TITLE: Associate Professor

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 |
| --- | --- | --- | --- |
| Wayne State University, Detroit, MI | BS | 06/2003 | Biochemistry |
| Wayne State University, Detroit, MI | MD | 06/2007 | Medicine |
| St. Joseph Mercy Hospital, Ann Arbor, MI | Internship | 06/2008 | Internal Medicine |
| Washington University, St. Louis, MO | Residency | 06/2012 | Anatomic and Clinical Pathology |
| University of Michigan, Ann Arbor, MI | Fellowship | 06/2013 | Urologic Pathology |
| University of Michigan, Ann Arbor, MI | Fellowship | 06/2014 | Surgical Pathology |

A. Personal Statement

I am a urologic pathologist with extensive experience with the histomorphologic diagnosis of tumors, particularly bladder cancer, and I direct the Urologic Pathology service at Penn State University College of Medicine. In addition to my clinical skills and experience, I have a sound understanding of computational biology and the data analysis platforms required to analyze genomic data.

**My research aims to merge traditional histomorphologic diagnosis of tumors with molecular diagnostics. This dual approach allows my team to leverage the strengths of each approach. The current proposal incorporates this dual approach to study the epigenetic determinants of clinical outcomes in non-muscle-invasive bladder cancer, a topic of great interest to my research group. Our group has had much success in research of urologic oncology. This success is made possible by our research team, which has great depth and breadth of experience and skill, including David DeGraff PhD (Cancer Biologist and Associate Professor of Pathology), Jay Raman (Urologist and Professor and Chair of Urology), Vonn Walter (Computational Biologist and Assistant Professor of Biochemistry and Molecular Biology), and Istvan Albert (Computational Biology and Research Professor of Bioinformatics, Department of Biochemistry and Molecular Biology), in addition to myself.**

B. Positions and Honors

**Positions and Employment**

July 2014 – June 2019 Assistant Professor, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

July 2019-Present Associate Professor, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

July 2017-Present Director of Urologic Pathology, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

July 2019-Present Director of Surgical Pathology and Histopathology Laboratory, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

Jan 2023-Present Division Chief of Anatomic Pathology, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

**Professional Memberships**

* College of American Pathologists
* United States and American Academy of Pathology

**Honors**

2007 Resident Teaching Award. Saint Joseph-Mercy Hospital, Department of Internal Medicine

2012 Honorable Mention for “*Tissue PCA3 Evaluation in Prostate Cancer by In-Situ Hybridization.*” University of Michigan Department of Pathology, Annual Anatomic, Molecular, and Hematopathology Research Day Abstract Award, 4th Annual.

2013 Third place for “Sequencing Multifocal Spatially Distinct Urothelial Carcinomas to Determine Tumor Clonality” University of Michigan Department of Pathology, Annual Anatomic, Molecular, and Hematopathology Research Day Abstract Award, 5th Annual.

2015 Resident Teaching Award, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

2015 Dean’s Award for Excellence in Teaching, 2015 Dean’s Award for Excellence in Teaching. Penn State Hershey Medical Center.

2016 Resident Teaching Award, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

2016 Dean’s Award for Excellence in Teaching, 2016 Dean’s Award for Excellence in Teaching. Penn State Hershey Medical Center.

2016 Best Paper of 2015, Virchows Archiv, for **“**Tumor evolution and progression in a case of multifocal invasive urothelial carcinoma.” European Congress of Pathology.

2017 Resident Teaching Award, Department of Pathology, The Pennsylvania State University, College of Medicine, Hershey, PA

**C. Contribution to Science**

**1. Biology and outcomes of non-invasive bladder cancer:** Most bladder cancers are diagnosed at the non-invasive stage of disease evolution. Most of these recur after treatment, and a subset progress to invasive disease, which is often lethal. It is difficult to predict outcomes in the disease. Treatments are also limited. Under my leadership at Penn State University, as senior/corresponding author, our group showed that mitotic index (the number of mitotic figures per 10 high-powered microscope fields) predicts clinical behavior of non-invasive bladder cancer, independent of tumor grade (Zaleski et al, *Human Pathol*, 2019). Also under my leadership as principal/corresponding author, our group showed that non-invasive papillary urothelial carcinoma frequently losses expression of the cell cycle inhibitor p16 (encoded by *CDKN2A*), and this loss is mutually exclusive of loss the cell cycle inhibitor RB1 (Warrick et al, *Eur Urol*, 2019). We further showed loss of these cell cycle genes is propagated as the tumors evolve to conventional and rare variants of invasive urothelial carcinoma. We have most recently elucidated a transcriptional network of cell cycle dysregulation in noninvasive bladder cancer, which appears to act independent of mutations in genes that control the cell cycle (Warrick et al, *Sci Rep*, 2022).

1. Zaleski M, Gogoj A, Walter V, Raman JD, Kaag M, Merrill SB, Drabick J, Joshi M, Holder S, DeGraff DJ, **Warrick JI.** “Mitotic activity in non-invasive papillary urothelial carcinoma: its value in predicting tumor recurrence and comparison with the contemporary 2-tier grading system.” *Hum Pathol*. 2019;84:275-282. PMID: 30359638.
2. **Warrick J,** Sjodahl G, Kaag M, Raman J, Merrill S, Shuman L, Chen G, Walter V, DeGraff D. “Intratumoral heterogeneity of bladder cancer by molecular subtypes and histologic variants.” *Eur Urol.* 2019;75(1):18-22.
3. **Warrick J,** Knowles M, Hurst C, Shuman J, Raman J, Walter V, Putt J, Dyrskjøt L, Groeneveld C, Castro M, Robertson AG, DeGraff DJ. A transcriptional network of cell cycle dysregulation in noninvasive papillary urothelial carcinoma. *Scientific Reports.* 2022. 12(1):16538.

**2. Transcription factors and molecular subtypes of bladder cancer**. Invasive bladder cancer is biologically and clinically diverse. This is well-captured by recurrent patterns of gene expression, which have been termed “molecular subtypes.” For example, invasive cancers are termed “luminal” if they express high levels of genes involved in urothelial differentiation and “basal-squamous” if they express high levels of genes involved in squamous differentiation. As a close collaboration with David DeGraff, in which we co-led our research team as co-corresponding authors, we showed that the transcription factors FOXA1, GATA3, and PPARɣ cooperate to drive a luminal expression signature in bladder cancer (Warrick et al, *Sci Rep*, 2016). I further led studies by our group as principal/corresponding author that evaluated evolution of molecular subtypes in clinical cases of invasive bladder cancer, including one that showed molecular subtypes often differ in histologically distinct regions of invasive bladder cancer, while patterns of p16 and RB1 loss are remarkably consistent among tumor regions (Warrick et al, *Eur Urol*, 2019). This publication received great attention in the field of Urologic Oncology, because it raised concern for sampling error in clinical tests of bladder cancer that assigned molecular subtype, which were being marketed to guide therapy. We recently expanded on this work, demonstrating that histologically distinct regions of bladder cancer often differ profoundly in inflammatory microenvironment, gene expression, and mutational drivers (Warrick et al, *Nat Commun*, 2023).

1. **Warrick JI**, Walter V, Yamashita H, Shuman L, Amponsa VO, Zheng Z, Yue F, Iyyanki T, Kawasawa YI, Kaag M, Guo W, Raman JD, DeGraff DJ. FOXA1, GATA3 and PPARɣ cooperate to drive luminal subtype in bladder cancer: a molecular analysis of established human cell lines. *Sci Rep*. 2016;7;6:38531. PMCID: PMC5141480
2. **Warrick J,** Sjodahl G, Kaag M, Raman J, Merrill S, Shuman L, Chen G, Walter V, DeGraff D. Intratumoral heterogeneity of bladder cancer by molecular subtypes and histologic variants. *Eur Urol.* 2019;75(1):18-22.
3. **Warrick J,** Hu W, Yamashita H, Walter V, Shuman L, Craig J, Gellert L, Castro M, Robertson AG, Kuo F, Ostrovnaya I, Sarungbam J, Chen Y, Gopalan A, Sirintrapun S, Fine S, Tickoo S, Kim K, Thomas J, Karan N, Gao SP, Clinton T, Lenis A, Chan T, Chen Z, Rao Z, Hollman T, Li Y, Socci N, Chavan S, Viale S, Mohibullah N, Bochner B, Pietzak E, Teo M, Iyer G, Rosenberg J, Bajorin D, Kaag K, Merrill S, Joshi M, Adam R, Taylor III J, Clark P, Raman J, Reuter V, Chen Y, Funt S, Solit D, DeGraff DJ, Al-Ahmadie H Lineage plasticity and immune heterogeneity are coordinately dysregulated by FOXA1 repression in bladder cancers with squamous differentiation. *Nat Commun.* 2022. 13(1):6575.

## Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=joshua+warrick>

D. Research Support

**Ongoing Research Support**

IRG-17-175-04 Warrick & Walter (MPI) 07/01/2018 - 06/30/2020

American Cancer Society – Institutional Review Grant

Title: Social Determinants, Incidence, Outcomes, and Molecular Biology of Urinary Bladder Cancer in Central Pennsylvania

Project goal: Identify biological differences in bladder cancer by socioeconomic status in a cohort from Central Pennsylvania

Role: MPI

RSG-16-219-01-TBG Stairs (PI) 01/01/2017 - 12/31/2020

American Cancer Society

Title: Mechanisms of Squamous Cell Carcinoma Invasion

Project goal: By identifying and understanding these pathways we will, in the future, be able to develop therapeutics that target these pathways that are likely to increase the effectiveness of current therapies.

Role: Collaborator

RSG-17-233-01-TBE DeGraff (PI) 01/01/2018 - 12/31/2021

American Cancer Society

Title: Transcriptional Control of Bladder Cancer Progression

Project goal: We hypothesize inactivation of PPARG promotes SqD and the emergence of a clinically aggressive basal molecular subtype through increased expression of the transcription factors TFAP2A; and (2) overexpression of TFAP2A and/or TFAP2C promote SqD and the aggressive phenotype of basal BC

Role: Co-Investigator

No number DeGraff (PI) 10/1/2019 - 09/30/2020

W. W. Smith Charitable Trust

Title*:* Cancer Cell Intrinsic Immune Checkpoint Circuits

Project goal: The objective of this project is to test the hypothesis that FOXA1 regulates immune checkpoint (ID) pathway components and associated therapeutic response in urothelial carcinoma (UC) via IRF1-dependent mechanisms.

Role: Co-Investigator

**Completed Research Support**

4100072562-EQU Warrick (PI) 01/01/2016 – 06/30/2019

Pa Tobacco Settlement Funds (TSF)

Title: Cancer Risk Stratification of Endometrial Hyperplasia by Next Generation Sequencing

Project Goal: This project aims to perform next generation sequencing on a series of endometrial hyperplasia cases to determine if mutational profile in endometrial hyperplasia is predictive of cancer risk

Role: PI

SAP #4100072562 Matters (PI) 01/01/2016 – 06/30/2018

PA Tobacco Settlement Funds (TSF)

Title: Calcium phosphosilicate nanoparticles: Imaging and drug delivery for prostate tumors

Project goal: to develop tumor-targeted CPSNPs can be used to increase sensitivity/specificity of detecting early stage cancers as well as improve the delivery of standard chemotherapeutics with fewer side-effects.

Role: Co-Investigator

W81XWH-16-1-0117 Hempel (PI) 05/01/2016 – 04/30/2018

U. S. Army Medical Research and Development Command

Title: Clinical Significance and Mechanistic Insights into Ovarian Cancer Mitochondrial Dysfunction

Project Goal:”The proposal addresses the unexplored clinical relevance and mechanisms behind mitochondrial dysfunction in EOC, which has the potential to affect a significant proportion of ovarian cancer cases. In addition, this body of work will for the first time investigate a potential dominant negative Drp1 variant in a pathophysiological context, and directly explore if this is a novel mechanism for EOC chemoresistance.

Role**:** Co-Investigator