## **BIOGRAPHICAL SKETCH**

NAME: Dome, Jeffrey S.

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

POSITION TITLE: Vice President, Center for Cancer and Blood Disorders, Chief of Oncology

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<br>(if applicable) | Completion<br>Date<br>MM/YYYY | FIELD OF STUDY |
|--|---------------------------|-------------------------------|----------------|
| University of Pennsylvania, Philadelphia, PA   | BA                        | 1987                          | Biochemistry   |
| University of Pennsylvania, Philadelphia, PA   | MD                        | 1991                          | Medicine       |
| Erasmus University, Rotterdam, The Netherlands | PhD                       | 2009                          | Medicine       |

## A. Personal Statement

I am a pediatric oncologist with a research interest in pediatric solid tumors, most notably renal tumors. I am Professor of Pediatrics at the George Washington University School of Medicine and Health Sciences, Vice President of the Center for Cancer and Blood Disorders and Chief of Oncology at the Children's National Health System, and Institutional PI for the Children's Oncology Group (COG) studies at my center. I was a member of the National Wilms Tumor Study Committee for 5 years before it merged into the Children's Oncology Group (COG) in 2002. I served as Vice-Chair of the COG Renal Tumor Committee and Chair of the Renal Tumor Biology Sub-Committee from 2002-2006. From 2006-2016, I served as Chair of the Renal Tumor Committee. As Committee Chair, I oversaw the grant applications, protocol development, and conduct of numerous biology studies and five major therapeutic studies, with more than 600 patient enrollments annually. I also serve as Study Chair of the AREN0321 high-risk renal tumor study and have served as PI or co-Investigator on several early phase clinical trials for pediatric solid tumors. In addition to my clinical research, I led a translational research program in telomere biology of Wilms tumor, osteosarcoma, rhabdoid tumor, and neuroblastoma, which was funded by grants from the NIH and private foundations. Additionally, I hold other leadership positions in pediatric oncology, including member of the COG Executive Committee (2017-present), member of the COG Scientific Council (2018-present), and Chair of the American Board of Pediatrics Subboard of Pediatric Hematology/Oncology (2018-present).

I am well-suited for the role of SIOP Treasurer based on more than a decade of SIOP membership and meeting attendance, membership on the Scientific Program Advisory Committee (SPAC), and service as Chair of the Local Organizing Committee (LOC) for the 2017 SIOP Congress in Washington, DC. As the LOC Chair, I developed a successful and productive relationship with the SIOP Executive Board, the SIOP secretariat, and the professional staff from Kenes. In my administrative roles at Children's National, I have had the opportunity to gain experience with budgetary oversight, fundraising, and making difficult fiscal decisions. Importantly, in my roles in COG I led numerous international collaborations and fostered relationships to enhance the care of children around the globe in the true spirit of SIOP's vision.

## **B. Positions and Honors**

#### **Positions and Employment**

| 1991 - 1994 | Yale-New Haven Hospital, Department of Pediatrics, Resident Physician, New Haven, CT         |
|-------------|--|
| 1994 - 1997 | Johns Hopkins University School of Medicine, Department of Pediatrics and Oncology,          |
|             | Clinical Fellow (Pediatric Hematology/Oncology), Baltimore, MD                               |
| 1997 - 1998 | Assistant Faculty, Johns Hopkins University School of Medicine, Department of Pediatrics and |
|             | Oncology Baltimore MD  |

1998 - 2004 Assistant Member, Department of Hematology-Oncology, St. Jude Children's Research Hospital, Memphis, TN

- 1998 2005 Assistant Professor, Department of Pediatrics, University of Tennessee Memphis Health Sciences Center, Memphis, TN
- 2004 2006 Associate Member, Department of Hematology-Oncology, St. Jude Children's Research Hospital, Memphis, TN
- 2005 2006 Associate Professor, Department of Pediatrics, University of Tennessee Memphis Health Sciences Center, Memphis, TN
- 2006 Present Chief, Division of Oncology, Center for Cancer and Blood Disorders, Children's National Health System, Washington, DC
- 2007 2010 Associate Professor with tenure, Department of Pediatrics, George Washington University School of Medicine, Washington, DC
- 2007- Present Adjunct Investigator, Pediatric Oncology Branch, National Cancer Institute, Washington, DC
- 2010- Present Professor with tenure, Department of Pediatrics, George Washington University School of Medicine
- 2012 2017 Chief, Division of Hematology, Center for Cancer and Blood Disorders, Children's National Health System
- 2016- Present Vice President, Center for Cancer and Blood Disorders, Children's National Health System

## **Other Positions**

- 2001 2006 Children's Oncology Group Member, Biopathology and Translational Research Committee
- 2002 2004 Children's Oncology Group Member, Young Investigator Committee
- 2002 2006 Children's Oncology Group, Chair, Renal Tumor Biology Committee
- 2002 2006 Children's Oncology Group, Vice Chair, Renal Tumor Committee
- 2002 2006 Children's Oncology Group, Chair, Renal Tumor Biology Committee
- 2005 NIH Study Section ZRG1 F09, Fellowship: Oncological Sciences
- 2006 2009 ASCO Foundation Grants Selection Committee
- 2006 2016 Children's Oncology Group, Chair, Renal Tumor Committee
- 2010 Present Alex's Lemonade Stand Foundation Scientific Review Board
- 2010 Present International Society of Pediatric Oncology (SIOP), Scientific Program Committee
- 2013 Present American Board of Pediatrics, Sub-board member and Chair-elect, Hematology/Oncology
- 2013 Present CureSearch Foundation, grant reviewer
- 2013 Present Pablove Foundation, Advisory Board and grant reviewer
- 2013 Present American Board of Pediatrics, Subboard of Pediatric Hematology/Oncology Board Member
- 2016 2017 International Society of Pediatric Oncology (SIOP), Board Member, Chair, Organizing Committee for annual congress
- 2017 Present Children's Oncology Group, Executive Committee (elected)
- 2018 Present Children's Oncology Group, Scientific Council
- 2018 Present American Board of Pediatrics, Chair Hematology/Oncology Subboard

#### Honors

| 1983         | Westinghouse Science Talent Search Semi-finalist                          |
|--------------|---|
| 1984         | Benjamin Franklin Scholar, University of Pennsylvania                     |
| 1987         | Mortar Board Senior Honor Society   |
| 1987         | Phi Lambda Upsilon Honorary Chemistry Society                             |
| 1994         | American Cancer Society Clinical Fellow                                   |
| 1997         | American Society of Clinical Oncology Young Investigator Award            |
| 1997         | Herman and Walter Samuelson Fellow, Johns Hopkins University              |
| 1998         | Giulio D'Angio Award, International Conference on Childhood Renal Tumors  |
| 2007         | Society for Pediatric Research, Elected                                   |
| 2009-present | Best Doctors in America   |
| 2011         | Thomas Willson and Lenore Williams McKnew Professor of Pediatric Oncology |
| 2016-present | Washingtonian Magazine Best Doctors                                       |
| 2016-present | Northern Virginia Magazine Best Doctors                                   |

#### **C.** Contributions to Science

Telomere biology of pediatric cancer

I was one of the first investigators to study telomerase as a prognostic marker and therapeutic target for pediatric cancers. My laboratory identified high telomerase expression as a prognostic marker for Wilms tumor and demonstrated that approximately 50% of human osteosarcomas use the alternative lengthening of telomerase (ALT) mechanism, rather than telomerase, to maintain telomeres. In osteosarcoma, tumors that had telomerase expression had inferior event-free survival compared to tumors that use ALT. My laboratory was one of the first laboratories to demonstrate that telomere shortening elicits a DNA damage response similar to that seen with double-strand breaks. This response disappears once senescence is reached, indicating that the telomere-induced damage response induces, but is not required to maintain, senescence. We also demonstrated that telomere shortening alters the kinetics of the cellular response to ionizing radiation. Most recently, we demonstrated that the telomerase inhibitor imetelstat inhibits growth of malignant rhabdoid tumor cell lines and xenografts. My laboratory developed an antibody directed against TERT that has been considered to be the most specific anti-TERT antibody and is widely used in laboratories around the world. In recent years, I have limited my research on telomere biology to focus on studies of the treatment and biology of pediatric renal tumors (see below).

- 1. Sanders RP, Drissi R, Billups CA, Daw NC, Valentine MB, **Dome JS**. Telomerase expression predicts unfavorable outcome in osteosarcoma, *J Clin Oncol*. 2004; 22: 3790-3797. PMID: 15365076.
- 2. Drissi R, Wu J, Hu Y, Bockhold CA, **Dome JS**. Telomere shortening alters the kinetics of the DNA damage response after ionizing radiation in human cells. *Cancer Prev Res*. 2011; 4(12): 1973-1981. PMC3232288
- 3. Hu Y, Bobb D, Lu Y, He J, **Dome JS**. Effect of telomerase inhibition on preclinical models of malignant rhabdoid tumor. *Cancer Genetics*. 2014; 207(9): 403-411. PMID: 25441685
- Hu Y, Bobb D, He J, Hill DA, <u>Dome JS</u>. The HSP90 inhibitor alvespimycin enhances the potency of telomerase inhibition by imetelstat in human osteosarcoma. Cancer Biol Ther. 16(6):949-57, 2015. PMC:4622625

### **Biology of Pediatric Renal Tumors**

As Chair of the Children's Oncology Group Renal Tumor Biology Committee (2002-2006) and Chair of the overall COG Renal Tumor Committee (2006-2016), I have helped design and conduct numerous studies to elucidate the biology of pediatric renal tumors. Research has been conducted in my own laboratory and with external collaborators.

- 1. **Dome JS**, Bockhold CA, Li SM, Baker SD, Green, DM, Perlman EJ, Hill DA, and Breslow NE. High telomerase RNA expression is an adverse prognostic factor for favorable histology Wilms tumor, *J Clin Oncol*. 2005; 23: 9138-9145. PMID:16172460
- Turnbull C, Perdeaux ER, Pernet D, Naranjo A, Renwick A, Seal S, Munoz-Xicola RM, Hanks S, Slade I, Zachariou A, Warren-Perry M, Ruark E, Gerrard M, Hale J, Hewitt M, Kohler J, Lane S, Levitt G, Madi M, Morland B, Neefjes V, Nicholdson J, Picton S, Pizer B, Ronghe M, Stevens M, Traunecker H, Stiller CA, Pritchard-Jones K, **Dome J**, Grundy P, Rahman N. A genome-wide association study identifies susceptibility loci for Wilms tumor. *Nat. Genet.* 2012; 44(6), 681-4. PMC3400150
- 3. Gratias EJ, **Dome JS**, Jennings LJ, Chi YY, Tian J, Anderson J, Grundy P, Mullen EA, Geller JI, Fernandez CV, Perlman EJ. Association of Chromosome 1q Gain With Inferior Survival in Favorable-Histology Wilms Tumor: A Report From the Children's Oncology Group. J Clin Oncol 34(26): 3189-3194, 2016.
- 4. Gadd S, Huff V, Walz AL, Ooms AHAG, Armstrong AE, Gerhard DS, Smith MA, Auvil JMG, Meerzaman D, Chen QR, Hsu CH, Yan C, Nguyen C, Hu Y, Hermida LC, Davidsen T, Gesuwan P, Ma Y, Zong Z, Mungall AJ, Moore RA, Marra MA, **Dome JS**, Mullighan CG, Ma J, Wheeler DA, Hampton OA, Ross N, Gastier-Foster JM, Arold ST, Perlman EJ. A Children's Oncology Group and TARGET initiative exploring the genetic landscape of Wilms tumor. Nat Genet. Oct;49(10):1487-1494,2017.

#### **Treatment of Pediatric Renal Tumors**

I have spent many years developing treatments for high-risk pediatric renal tumors, including anaplastic Wilms tumor, bilateral Wilms tumor, malignant rhabdoid tumor, clear cell sarcoma of the kidney and renal cell carcinoma. Important contributions to the field include the observation that augmentation of therapy improves outcomes for patients with anaplastic Wilms tumor, camptothecins (topotecan and irinotecan) are highly active in Wilms tumor, bilateral Wilms tumor is usually amenable to bilateral partial nephrectomies with good clinical outcomes, pediatric renal cell carcinoma has distinct biology and clinical behavior compared to adult renal cell carcinoma and recurrent clear cell sarcoma of the kidney is responsive to ifosfamide/carboplatin/etoposide chemotherapy. These and other observations have influenced how pediatric renal tumors are treated throughout the world.

- Dome JS, Cotton CA, Perlman EJ, Breslow NE, Kalapurakal JA, Ritchey ML, Grundy PE, Malogolowkin M, Beckwith JB, Shamberger RC, Haase GM, Coppes MJ, Coccia P, Kletzel M, Macklis R, Green DM. Treatment of Anaplastic Histology Wilms Tumor: Results from the Fifth National Wilms Tumor Study. J Clin Oncol. 2006; 20: 2352-2358. PMID:16710034
- Metzger MM, Stewart CF, Freeman BB, Billups CA, Hoffer FA, Wu J, Coppes MJ, Grant R, Chintagumpala M, Mullen EA, Alvarado C, Daw NC, **Dome JS**. Topotecan is active against Wilms tumor: Results of a multiinstitutional phase II study. *J. Clin Oncol.* 2007; 25:3130-3136. PMID:17634492
- Dome JS, Graf N, Geller JI, Fernandez CV, Mullen EA, Spreafico F, Van den Heuvel-Eibrink M, Pritchard-Jones K. Advances in Wilms Tumor Treatment and Biology: Progress Through International Collaboration. J Clin Oncol. 33(27):2999-3007, 2015. PMC 4567702
- Ehrlich P, Chi YY, Chintagumpala MM, Hoffer FA, Perlman EJ, Kalapurakal JA, Warwick A, Shamberger RC, Khanna G, Hamilton TE, Gow KW, Paulino AC, Gratias EJ, Mullen EA, Geller JI, Grundy PE, Fernandez CV, Ritchey ML, **Dome JS**. Results of the First Prospective Multi-institutional Treatment Study in Children With Bilateral Wilms Tumor (AREN0534): A Report From the Children's Oncology Group. Ann Surg. 266(3):470-478, 2017

# Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/jeffrey.dome.1/bibliograpahy/47345339/public/

#### D. Research Support Ongoing

U10 CA180886 (Adamson, PI) 3/1/14-2/28/18, 10% effort Children's Oncology Group Study Chair Grant, Institutional Workload Intensity Role: Co-Investigator This grant supports my role as Insitutional PI for Children's Oncology Group studies at Children's National Health System

U10 CA180884 (Adamson/Skapek, PI) 3/1/2014 – 2/28/2019, 2% effort COG NCTN Solid Malignancy Integrated Translational Science Award Role: Co-Investigator This grant supports Dr. Dome's efforts on the COG Solid Malignancy Integrated Translational Science Committee

RO1 CA219013-01 (Kalapurakal, PI) 7/1/2017- 6/30/2022, 5% effort Retrospective NCI Phantom-Monte Carlo Dosimetry for Late Effects in Wilms Tumor Role: Co-Investigator This grant supports Dr. Dome's efforts determining the effect of organ-specific radiation exposure on late effects in survivors of Wilms tumor

## Completed

U10 CA98543 (Perlman) NIH/NCI Therapeutically Applicable Research to Generate Effective Treatments (TARGET) Initiative High-Risk Wilms Tumor Project This grant supports gene expression, DNA copy number, DNA methylation, and DNA sequencing analysis of high risk Wilms tumor, including anaplastic Wilms tumor and recurrent favorable histology Wilms tumor. Role: Co-Investigator

U10 CA98543 (Adamson) 03/01/03 - 02/28/14 NIH/NCI Children's Oncology Group Study Chair Grant This grant supported Dr. Dome's role as Study Chair of AREN0321, a therapeutic study for high-risk renal tumors Role: Co-Investigator U10 CA98543 (Adamson) 03/01/09 - 02/28/16 NIH/NCI Children's Oncology Group Study Chair Grant This grant supports Dr. Dome's involvement as Disease Committee Chair of the COG Renal Tumor Committee. Role: Co-Investigator

Children's Cancer Foundation (Dome) 10/1/09-9/30/2011 Telomerase as a Therapeutic Target for Pediatric Cancer This grant supports the study of a novel telomerase inhibitor, GRN163L alone and in combination with other targeted therapy in pediatric pre-clinical models. Role: Principal-Investigator

 R21 CA98543, (Dome)
 9/1/2005-8/31/2009

 NIH/NCI
 Telomere Maintenance Mechanisms in Osteosarcoma

 The objective of this study was to 1) identify the prognostic significance of telomere maintenance mechanism (telomerase expression vesus Alternative Lengthening of Telomeres (ALT)) in osteosarcoma and 2) identify genes and biomarkers for the ALT pathway.

 Role: Principal-Investigator

Glaxo Smith Kline (Dome) 9/1/05-8/31/07 Phase II Study of Topotecan for Recurrent Wilms Tumor This grant supported a multi-institutional phase II study of topotecan for recurrent Wilms tumor. Role: Principal-Investigator

P01 CA23099 (Houghton) 7/01/02-6/30/07 NIH Clinical phase I-II Studies in Children and Adolescents This grant supported early phase clinical studies for patients with pediatric solid tumors Role Co-Investigator

RO1 CA087903 (Dome)8/01/00-7/31/05Telomerase as a prognostic indicator for Wilms tumorThis grant supported a confirmatory study of telomerase activity and mRNA expression as a prognostic markerfor favorable histology Wilms tumor.Role- Principal Investigator