BIOGRAPHICAL SKETCH

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NAME: Woodard, Lauren E., PhD

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POSITION TITLE: Assistant Professor, Division of Nephrology and Hypertension, Department of Medicine, Vanderbilt University

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
The University of Texas at Austin, Austin, TX	B.S.	05/2004	Biochemistry
Stanford University, Stanford, CA	Ph.D.	09/2009	Cancer Biology
Baylor College of Medicine, Houston, TX	Postdoctoral	09/2013	Nephrology

A. Personal Statement

I am developing new strategies to treat kidney disease through regenerative gene and cell therapies. My career development award from the Department of Veterans Affairs is to investigate the effect of expression of transcription factors to reprogram cells in the kidney into induced nephron progenitors (iNPs). We have made a transposon carrying reprogramming factors that were identified by our collaborators in Melissa Little's laboratory. We are using a novel technique to deliver the transposon to kidney cells of mice *in vivo*. This proposal addresses the ability of this transposon to ameliorate acute kidney injury in a mouse model. This builds on my work with Matthew Wilson during my postdoc in which I developed a novel way to transfect the kidneys of mice in a reproducible manner. The technique we developed is based on hydrodynamic tail vein injection, a method to transfect plasmid DNA into the livers of mice. I used hydrodynamic tail vein injection extensively during my graduate work with Michele Calos at Stanford University School of Medicine. I have 13 years of experience in the non-viral gene therapy field, including three oral presentations and a best poster award at American Society of Gene & Cell Therapy annual meetings. I am an expert at manipulating the mammalian genome and transfecting tissues *in vivo*. I am currently pursuing a research program to apply these skills to regenerative medicine. The kidney is a challenging yet worthy model for regenerative medicine projects: (1) reproducible gene transfer in the kidney will make it possible to pursue such new avenues of research (2) end-stage renal disease costs over $40 billion dollars in the United States alone and patients on dialysis have similar mortality rates to many cancers and (3) in the kidney we have our choice of models of acute injury, acute toxicity, and genetic abnormalities. Therefore, I seek to build on my experience in non-viral gene therapy by interacting with collaborators having expertise in regenerative medicine, stem cells, and acute kidney injury. Additionally, I have isolated human urine-derived stem cells, optimized their transfection, and am now tracking their cell fate following kidney injection in adult mice via pilot funding through the Vanderbilt O'Brien Kidney Center. Through strategies to gene-modify and reprogram kidney cells, I will develop new methods to treat kidney disease.

Reviews and Book Chapters

a. **Woodard, L.E.** and Calos, M.P. "Chapter 31: Nonviral genome modification strategies for gene therapy: transposon, integrase, and homologous recombination systems." Templeton, N.S., Ed. Gene and Cell Therapy: Therapeutic Mechanisms and Strategies, 3rd ed.; CRC Press: Boca Raton, **2009**.

b. **Woodard, L.E.** and Calos, M.P. "Chapter 8: DNA integrating vectors (transposon, integrase)." Herzog, R. and Zolotukhin, S., Ed. A Guide to Human Gene Therapy, 1st ed.; World Scientific: Mountain View, **2010**.
c. **Woodard, L.E.** and Calos, M.P. "Chapter 26: Nonviral genome modification strategies for gene therapy: Transposon, integrase, and nuclease systems." Templeton, N.S., Ed. Gene and Cell Therapy: Therapeutic Mechanisms and Strategies, 4th ed.; CRC Press: Boca Raton, **2015** 675-700.
d. **Woodard, L.E.** and Wilson, M.H. piggyBac-ing models and new therapeutic strategies. Trends Biotechnol. **2015**, 33(9):525-33. PMID: 26211958
e. **Woodard, L.E.**; Galvan, D. L. and Wilson, M.H. Site-directed genome modification with engineered zinc finger proteins. Smolke, C., Ed. Synthetic Biology: Parts, Devices and Applications, 1st ed.; Wiley-Blackwell. 2018: 33-43.

B. Positions and Honors

Positions and Employment

2000-2	Calculus/Chemistry/Physics/Biology Tutor, UT Learning Center, Austin, TX.
2000-4	Undergraduate Researcher/Beckman Scholar, The University of Texas at Austin, Austin, TX, Mentor: Karen S. Browning, Ph.D.
2002	Summer Undergraduate Research Program, UT MD Anderson Science Park, Smithville, TX, Mentor: Mark T. Bedford, Ph.D.
2002	Undergraduate Teaching Assistant, Undergraduate Physics for Pre-Meds, The University of Texas at Austin, Austin, TX, taught by Sacha Kopp, Ph.D.
2004-9	Graduate Student, Department of Genetics, Stanford University School of Medicine, Stanford, CA, Mentor: Michele P. Calos, Ph.D.
2009-13	Postdoctoral Fellow, Department of Medicine-Nephrology, Baylor College of Medicine, Houston, TX, Mentor: Matthew H. Wilson, M.D./Ph.D.
2013-18	Research Instructor (faculty), Department of Medicine-Nephrology/Hypertension, Vanderbilt University, Nashville, TN, Mentor: Matthew H. Wilson, M.D./Ph.D.
2015-	Research Health Scientist, Department of Veterans Affairs, TVHS Nashville, Research and Development
2018-	Assistant Professor (tenure track faculty), Department of Medicine-Nephrology/Hypertension, Vanderbilt University, Nashville, TN

Other Experience and Professional Memberships

2005-	Member, **American Society of Gene and Cell Therapy (ASGCT)**
2014-	Member, **American Society of Nephrology**
2018	Poster Reviewer, ASGCT Annual Meeting, Synthetic/Molecular Conjugates and Physical Methods for Delivery of Gene Therapeutics
2018-	Member, ASGCT Physical Delivery, Therapeutics & Vector Development Committee

Honors

2000-4	George L. Clark/MCorp Scholarship
2003-4	Louis M. Pearce Unrestricted Endowed Presidential Scholarship
2003-4	Chemistry & Biochemistry Department Scholarship
2003-4	Pirrung Family Scholarship
2003-4	Undergraduate Research Fellowship Awards (2)
2003-4	Beckman Scholar
2004	Dean's Honored Graduate, College of Natural Sciences
2004	Highest Honors and Special Departmental Honors/Magna Cum Laude (4.0 GPA)
2005	NSF Graduate Fellowship Honorable Mention
2007	Jain Foundation Forum Prize
2009-10	Training Grant, Nephrology Division, Baylor College of Medicine
2011	Training Grant, Hematology, Baylor College of Medicine
2014	Outstanding Poster Presentation Award, ASGCT Annual Meeting
2015-	VA Career Development Award (CDA-2)

C. Contribution to science

1. **phiC31 integrase system for therapeutic applications.** During my thesis work at Stanford, we delivered transgenes to the liver and used the phiC31 integrase enzyme to irreversibly integrate transgenes in a sequence-specific manner. We improved the specificity of the enzyme, discovered basic information about how it functions in mammalian cells, and delivered the Factor IX gene successfully to knockout mice.

a. Keravala, A.; Lee, S.; Thyagarajan, B.; Olivares, E.C.; Gabrovsky, V.E.; **Woodard, L.E**. and Calos, M.P. Mutational derivatives of ϕC31 integrase with increased efficiency and specificity. *Mol. Ther*. **2009**, *17,* 112-20. PMC2834998
b. **Woodard, L.E.;** Hillman, R.T.; Keravala, A.; Lee, S. and Calos, M.P. Effect of nuclear localization and hydrodynamic delivery-induced cell division on ϕC31 integrase activity. *Gene Ther.* **2010,** *17,* 217-26. PMC2820593
c. Chavez C.L.; Keravala, A.; **Woodard, L.E.;** Hillman, R.T.; Stowe, T.R.; Chu, J.N. and Calos, M.P. Kinetics and longevity of phiC31 integrase in mouse liver and cultured cells. *Hum. Gene Ther.* **2010** *21*, 1287-97. PMC2974851
d. Keravala, A.; Chavez, C.L.; Hu, G.; **Woodard, L.E.;** Monahan, P.E. and Calos, M.P. Long-term phenotypic correction in factor IX knockout mice by using phiC31 integrase-mediated gene therapy. *Gene Ther.* **2011**, *18*, 842-8.

2. ***TcBuster* transposon system in mice and humans.** During my postdoc at Baylor College of Medicine, I found the *TcBuster* transposon to be comparable to *piggyBac* and *Tol2* transposons for non-viral gene transfer in mammalian cells. Currently, we are studying how *TcBuster* transposase self-regulates through formation of transposase aggregates. We currently seek to further elucidate the mechanism of transposase regulation to create enhanced mutants.

a. **Woodard, L.E.;** Li, X.; Malani, N.; Kaja, A.; Hice, R.H.; Atkinson, P.W.; Bushman, F.D.; Craig, N.L.; and Wilson, M.H. Comparative analysis of the recently discovered *hAT* transposon *TcBuster* in human cells. *PLoS One.* **2012,** *7,* e42666. PMC3499496
b. **Woodard, L.E.;** Downes, L.M.; Lee, Y.C.; Kaja, A.; Terefe, E.S.; and Wilson, M.H. Temporal self-regulation of transposition through host-independent transposase rodlet formation. *Nucleic Acids Res.,* **2017,** *45*, 353–366. PMC5224482

3. **Safety of non-viral gene transfer.** The majority of my thesis work comprised the development of a gold-standard assay to test our gene therapy as an oncogene in a mouse model of liver cancer. Additionally I contributed to studies analyzing the ability of *piggyBac* to have undesired genomic effects in human cells. Although these systems cut and paste DNA, in the process creating double strand breaks and/or chromosomal translocations in some contexts, they appear remarkably safe for therapeutic applications. We made transposon integration site-specific by fusion of the transposase to DNA-binding domains including zinc fingers, TALE, and dCas9. Finally, we showed that T lymphocytes can be utilized as peptide delivery factories for production of erythropoietin, a potentially safer method of gene delivery than modifying cells *in situ*.

a. **Woodard, L.E.;** Keravala, A.; Jung, W.E.; Wapinski, O.L.; Yang, Q.; Felsher, D.W. and Calos, M.P. Impact of hydrodynamic injection and phiC31 integrase on tumor latency in a mouse model of MYC-induced hepatocellular carcinoma. *PLoS One.* **2010**, *5,* e11367. PMC2820593
b. Saha, S.; **Woodard, L.E.;** Charron, E.M.; Welch, R.C.; Rooney, C.M.; and Wilson, M.H. Evaluating the potential for undesired genomic effects of the piggyBac transposon system in human cells. *Nucleic Acids Res.* **2015**, *43,* 1770-82. PMC4330379
c. Luo, W.; Galvan, D.; **Woodard, L. E.;** Dorset, D.; Levy, S.; and Wilson, M.H. Comparative analysis of chimeric ZFP-, TALE-, and Cas9-piggyBac transposases for integration into a single locus in human cells. *Nucleic Acids Res.* **2017**, *7*, 44904. PMC5737283
d. O'Neil, R.T.; Saha, S.; Veach, R.A.; Welch, R.C.; **Woodard, L.E.;** Rooney, C.M.; and Wilson, M.H. Transposon-modified antigen-specific T lymphocytes for sustained therapeutic protein delivery *in vivo. Nat Commun,* **2018**, *9*, 1325. PMC5893599

4. **Kidney-specific gene transfer.** We have successfully translated hydrodynamic tail vein injection from liver to kidney by direct injection of the renal pelvis of mice. This technique is truly kidney-specific and non-viral.

a. Liang, A.; Wang, Y.; **Woodard, L.E.;** Wilson, M.H.; Sharma, R.; Awasthi, Y.C.; Du, J.; and Cheng, J. *In vivo* Manipulation of Glutathione S-transferase A4 Prevents Obstruction-induced Renal Tubular Cell Damage. *J. Pathology.* **2012,** *228,* 448-458. PMC3760987

b. Liang, M; **Woodard, L.E.;** Liang, A.; Luo, J.; Wilson, M.H.; Mitch, W.E.; Cheng, J. Protective Role of IGF-1R in Endothelial Cells against UUO-Induced Renal Fibrosis. *Am. J. Pathol.* **2015**, *185,* 1234-50. PMC4419212
c. **Woodard, L.E.;** Cheng, J.; Welch, R.C.; Williams, F.M.; Luo, W.; Gewin, L.S.; and Wilson, M.H. Kidney-specific transposon-mediated gene transfer *in vivo*. *Scientific Reports.* **2017,** *7,* 44904. PMC5357952
d. **Woodard, L.E.;** Welch, R.C.; Williams, F.M.; Luo, W.; Cheng, J.; and Wilson, M.H. Hydrodynamic renal pelvis injection for non-viral expression of proteins in the kidney. *J. Vis. Exp.*, **2018**, *1*, 131. PMC5907682

5. **Transposon reprogramming to induced nephron progenitors.** In collaboration with Melissa Little and Jessica Vanslambrouck, we have established an inducible transposon system for expression of three transcription factors which are sufficient for direct reprogramming of HK2 and RPTEC human tubule cells in tissue culture. These reprogrammed induced nephron progenitors are able to differentiate into different segments of the tubule when incorporated into kidney organoids. This work has been presented in oral presentations at the 2014 and 2016 American Society of Nephrology and 2017 International Society for Stem Cell Research annual meetings.
a. Inventors: Vanslambrouck, J.M.; **Woodard, L.E.;** Wilson, M.H.; and Little, M.H. Genetically Induced Nephron Progenitors. US and Worldwide patents filed May **2018**.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1ZgUeh6Ql9ekC/bibliography/51219066/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

VA CDA-2 BX002797 Woodard (PI) 01/2015-01/2020
In situ reprogramming of induced nephron progenitor cells for kidney regeneration
This career development award includes a focused career development program for Dr. Woodard in regenerative medicine and a research program focused on the in situ reprogramming of induced nephron progenitor cells for kidney regeneration, including tests in a mouse model of acute kidney injury.
Role: PI

Vanderbilt O'Brien Kidney Center Pilot Funds DK114809 02 Harris and Pozzi (PI) 07/2017-06/2019
Generation and evaluation of transposon-modified urine-derived stem cells
This pilot and feasibility study addresses the potential for human urine-derived stem cells to be isolated, genome-modified and engraft after kidney injection into immunocompromised mice.
Role: PI

Research Support Completed During the Last Three Years
None