Lauren E. Woodard, Ph.D.

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Education:

- **College: The University of Texas at Austin (Austin, TX), B.S., May 2004 (Biochemistry)**
- **Professional or graduate: Stanford University (Stanford, CA), Ph.D., July 2009 (Cancer Biology Program)**
    - Safety and Utility of Phage Integrases for Gene Therapy
- **Postgraduate Training: Postdoctoral Fellowship, Nephrology T32 and Hematology T32**
    - **Baylor College of Medicine, Matthew H. Wilson, September 2009-September 2013**

Academic Appointments:

- *Summer Undergraduate Research Program.* Mark Bedford, Ph.D., The University of Texas M.D. Anderson - Science Park, Department of Carcinogenesis, 2002.
- *Honors thesis.* Karen Browning, Ph.D., The University of Texas at Austin, Department of Chemistry and Biochemistry, 2000-2004.
- *Doctoral thesis.* Michele Calos, Ph.D., Stanford University School of Medicine, Department of Genetics, 2004-2009.
- *Postdoctoral Fellowship.* Matthew Wilson, M.D., Ph.D., Baylor College of Medicine, Department of Medicine, Division of Nephrology, 2009-2013.
- *Research Instructor.* Matthew Wilson, M.D., Ph.D., Vanderbilt University Medical Center, Department of Medicine, Division of Nephrology and Hypertension, 2013-2018.
- *Assistant Professor.* Vanderbilt University Medical Center, Department of Medicine, Division of Nephrology and Hypertension, 2018-present.
- *Research Scientist.* Department of Veterans Affairs, Research and Development Service, 2015-present.

Professional Organizations:

- American Society of Gene (and Cell) Therapy, 2005-present
    - Physical Delivery, Therapeutics & Vector Development Committee, 2018-2021
- American Society of Nephrology, 2014-present

Teaching Activities:

- Courses for Research Fellows, Nephrology Division, Baylor College of Medicine
    - Nephrology Journal Club, Presented Paragas et al. *The Ngal reporter mouse detects the response of the kidney injury in real time*, March 2011
    - Basic Research Concepts, Lecture *Using Luciferase Imaging for Live Animal Gene Expression Analysis*, October 2012
- Undergraduate Education
    - Tutor, University of Texas Learning Center, Calculus, Chemistry, Physics and Biology, December 2000-June 2002

        - One on one teaching of diverse subjects with different instructors
        - Emphasis on developing individual learning skills to allow students to master material themselves
    - Undergraduate Teaching Assistant, Physics for Pre-Med Students, Dr. Sacha Kopp, Fall 2002
        - Provided individual assistance during graduate TA office hours
        - Edited homework questions to ensure clarity
    - Teaching Assistant, Cancer Biology 101, Dr. Joseph Lipsick, Spring 2005
        - Created critical thinking-based test questions and graded exams
        - Headed a small discussion section reviewing seminal and current primary cacner research papers with undergraduates
        - Held office hours and tutored individual students
    - University of Houston-Downtown Scholar's Academy, Invited Speaker, *Professional etiquette for Graduate School Interviews*, November 2011
    - Beckman Foundation Symposium, Invited Panelist, *Career Trajectory – Academia,* August 2016
- Elementary Education/Community Involvement
    - SEED co-educator at Costano Elementary, East Palo Alto, Fall 2006-Spring 2007
        - Taught an interactive 4th grade science class twice a month at an underperforming school
        - Designed experiments, created worksheets and teaching props

Research Program:

Dr. Woodard is developing a regenerative treatment for acute kidney injury based on recent advances in reprogramming to change cell fate. Specifically, nuclear reprogramming technology will be employed to create a population of induced nephron progenitor cells. The nephron progenitor cells of the kidney are the only cell type known to be capable of differentiation into all parts of the nephron. Unfortunately, these cells are only found in the cap mesenchyme and are not normally present in the adult kidney. Collaborators Little and colleagues have identified six factors that can convert tubule cells into induced nephron progenitor cells. To capitalize on recent advances in nuclear reprogramming technology for the treatment of acute kidney injury, we will create an artificial population of induced nephron progenitors. This population will be created in situ, or in place, following the delivery of the reprogramming genes to kidney cells of mice in vivo. Others have used in situ reprogramming to successfully treat mouse models of diabetes and cardiac ischemia, suggesting that in situ reprogramming technology may also be useful for protection from ischemia reperfusion injury in the kidney. The reprogramming genes will be carried into the existing kidney cells using a newly developed gene transfer technique. An inducible piggyBac transposon will be used to integrate the genes into the genomes of renal cells and reprogramming will be initiated upon doxycycline induction. Markers of nephron progenitor cells that are not found normally in adult kidneys (Six2, Cited1) will be examined to determine the number and location of induced nephron progenitors in the treated kidneys. Following acute kidney injury, measures of kidney function such as serum creatinine and long-term fibrosis will be assayed to determine the effect of the induced nephron progenitor population on the severity and recovery from injury. Finally, we will determine how the induced nephron progenitor cells protect from acute kidney injury by performing fate-mapping studies in a double transgenic mouse model. These double transgenic mice express a tamoxifen-inducible Cre recombinase from the Cited1 promoter and contain a LacZ transgene that will express LacZ only after Cre recombination. Therefore, only cells that are progeny of the Cited1+ induced nephron progenitor cells will express LacZ. This will allow tracking of the nephron progenitor cell fate by visualization of all LacZ+ cells following acute kidney injury. We hypothesize that the induced nephron progenitors may function to ameliorate acute kidney injury by migrating to sites of damage and replacing the damaged cells, thereby restoring injured nephrons. This would represent a novel mechanism of recovery from acute kidney injury. In conclusion, in situ reprogramming to create induced nephron progenitors represents a potentially powerful treatment for acute kidney injury.

Cumulative listing of all grants: title, source, dollar amount, inclusive dates, percent effort.

- Beckman Scholar, UT-Austin, *Cloning and Expression of Arabidopsis eIF4G, a Subunit of Arabidopsis eIF4F*, 2003-2004, two summers and one academic year of personal and research funding at the undergraduate level, ~$17,000 in total

- Undergraduate Research Fellowship Awards, 2003 and 2004, *Cloning and Expression of Arabidopsis eIF4G, a Subunit of Arabidopsis eIF4F,* awarded by competition through the UT-Austin University Co-op, $1000 each for research supplies
- Nephrology T32 Training Grant, October 2009 - October 2011, salary + benefits
- Hematology T32 Training Grant, October 2011 – October 2012, salary + benefits
- VA career development CDA-2 award, In Situ *Reprogramming of Induced Nephron Progenitor Cells for Kidney Regeneration,* January 1, 2015 – December 31, 2019, $870,485
- Vanderbilt O'Brien Kidney Center Pilot and Feasibility Grant, *Generation and evaluation of transposon-modified urine-derived stem cells*, July 1, 2017 – June 30, 2018, $40,000

Publications and Presentations:

1. Articles in refereed journals:

    1. Keravala, A.; Lee, S.; Thyagarajan, B.; Olivares, E.C.; Gabrovsky, V.E.; **Woodard, L.E**. and Calos, M.P. Mutational derivatives of phiC31 integrase with increased efficiency and specificity. *Mol. Ther*. **2009**, *17,* 112-20.
    2. **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 phiC31 integrase activity. *Gene Ther.* **2010,** *17,* 217-26.
    3. 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.
    4. **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.
    5. 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.
    6. 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.
    7. **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(11), e42666
    8. Doherty, J.E.; **Woodard, L.E.;** Bear, A.S.; Foster, A.E.; Wilson, M.H. Transient Transgene Repression Post-Gene Delivery Improves Long-Term Expression *In Vivo*. *FASEB J.* **2013**, *27,* 3753-3762.
    9. Patrick, R.M.; Mayberry, L.M.; Choy, G.; **Woodard, L.E.;** Liu, J.S.; White, A.; Mullen, R.A.; Tanavin, T.M.; Latz, C.A.; and Browning, K.S. Two Arabidopsis thaliana loci encode novel eIF4E isoforms that are functionally distinct from the conserved plant eIF4E. *Plant Physiol.* **2014**, *164*, 1820-1830.
    10. 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.
    11. Liang, M.; **Woodard, L.E.;** Liang, A.; Luo, J.; Wilson, M.H.; Mitch, W.E.; and Cheng, J. Protective role of insulin-like growth factor-1 receptor in endothelial cells against unilateral ureteral obstruction-induced renal fibrosis. *Am. J. Pathol.* **2015,** *185,* 1234-50.
    12. **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.
    13. 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**, *45,* 8411-8422.

14. **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.
15. **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.
16. 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.

2. Books, book chapters, invited review articles:

1. **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**.
2. **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**.
3. **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.
4. **Woodard, L.E.** and Wilson, M.H. piggyBac-ing models and new therapeutic strategies. Trends Biotechnol. **2015**, *33*, 525-33.
5. **Woodard, L.E.**; Galvan, D. 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.

3. Presentations at Scientific Meetings*

Oral presentations

- *Identification of new Protein Arginine Methyltransferase substrates*
  - M.D. Anderson Science Park Summer Undergraduate Research Program, 2002
- *The cloning and characterization of* Arabidopsis *translation initiation factor eIF4G.*
  - UT-Austin Undergraduate Research Focus Group, 2003
- *Cellular localization and cell cycle dynamics of phiC31 integrase.*
  - Stanford Cancer Biology Program Retreat, 2006
  - **American Society of Gene Therapy Annual Meeting, 2006**
- *Evaluation of the liver cancer risk associated with a novel gene therapy for Hemophilia B.*
  - Stanford Cancer Biology Program Retreat, 2007
- *Safety first: testing phiC31 integrase gene therapy in a liver cancer model.*
  - Stanford Current Issues in Genetics, 2008
- *Translation of gene therapy using phiC31 integrase and hydrodynamic delivery into large animals.*
  - Stanford Cancer Biology Research Talks, 2008
- TcBuster *transposase and gene delivery to mouse kidneys.*
  - BCM Nephrology Division Research Seminar, 2011
- *Robust long-term gene expression in mouse liver via the novel transposon* TcBuster
  - **American Society of Gene and Cell Therapy Annual Meeting, 2011**
- *Transfecting mouse kidney cells* in vivo *by high-pressure direct injection*
  - BCM Nephrology Division Research Seminar, 2012
  - BCM Cell and Gene Therapy Retreat, 2011
- *Kidney-specific hydrodynamic injection of* piggyBac *transposons*
  - BCM Cell and Gene Therapy Retreat, 2012
- *The TcBuster transposon: a new tool for genome modification*

    - BCM Cell and Gene Therapy Research Seminar, 2013
- *Gene delivery to the adult mouse kidney*
    - University of Alabama-Birmingham and Vanderbilt Joint Nephrology Retreat, 2015
- *How to change the genome of your favorite cell: Transposase, Integrase, and Nuclease Systems*
    - Vanderbilt Renal Research Conference, 2015
- *In situ reprogramming of induced nephron progenitor cells for kidney regeneration*
    - BCM Nephrology Division Research Seminar, 2015
    - Translational Research Forum, 2016
- *Cellular reprogramming with* piggyBac *transposons*
    - Vanderbilt Renal Research Conference, 2016
- *Regenerating the kidney via transposon-based reprogramming to induced nephron progenitors*
    - Vanderbilt Stem and Progenitor Cell Interest Group (SPRING)
- *Kidney-directed hydrodynamic injection of Slc3a1 piggyBac transposon lowers urinary cystine in a mouse model of cystinuria type I*
    - **American Society of Gene and Cell Therapy Annual Meeting, 2018**

Poster presentations

- *Diet-dependent development of chronic kidney disease in a mouse model of cystinuria type I*
    - **American Society of Nephrology Kidney Week Meeting, 2017**
    - Vanderbilt Translational Biology Research Forum, 2017
- *Kidney-specific Gene Transfer by Hydrodynamic Renal Pelvis Injection*
    - **American Society of Nephrology Kidney Week Meeting, 2016**
- *The hAT-family Negative Dosage Effect occurs via Transposase Aggregation at High Transposase Protein Concentrations*
    - Vanderbilt Cell Dynamics Symposium, 2016
- *Generation of Transgene-Only Gene-Modified Human Cells Via Transposition*
    - **American Society of Gene and Cell Therapy Meeting, 2015**
- *Transposon mediated long-term kidney-specific transgene expression after gene transfer* in vivo
    - **American Society of Nephrology Kidney Week Meeting, 2014**
- *Kidney-Directed Hydrodynamic Injection of Plasmid DNA in Mice*
    - **American Society of Gene and Cell Therapy Meeting, 2014**
    - ***Outstanding Poster Presentation Award***
- *Mutation of the DDE Catalytic Triad in* TcBuster *Transposase Disrupts Function and Localization*
    - **American Society of Gene and Cell Therapy Meeting, 2014**
- *Transient transgene repression post-gene delivery improves long-term expression* in vivo
    - **American Society of Gene and Cell Therapy Meeting, 2012**
- *Activity, integration preferences, and localization of* TcBuster*; a novel hAT transposon system*
    - Cell and Gene Therapy Retreat, 2010
    - **American Society of Gene and Cell Therapy Meeting, 2010**
- *Mesoangioblast stem cells modified with phiC31 integrase repair dystrophic muscle tissue.*
    - Cancer Biology Program Retreat, 2008
- *Evaluation of hepatocyte proliferation and liver cancer risk associated with hydrodynamic injection and phiC31 integrase.*
    - Comprehensive Cancer Research Training Program, 2008
    - Genetics Department Program Retreat, 2008
    - **American Society of Gene Therapy Annual Meeting, 2008**
- *Gene therapy for hemophilia with phiC31 integrase.*
    - **American Society of Gene Therapy Annual Meeting, 2006**
- *Oral gene therapy with phiC31 integrase.*
    - Cancer Biology Program Retreat, 2005
- *The cloning and characterization of* Arabidopsis *translation initiation factor eIF4G.*
    - Undergraduate Poster Session, UT-Austin, 2004
    - **American Chemical Society Regional Conference, 2004**

*Bold indicates that presentation abstract was peer-reviewed.