BIOGRAPHICAL SKETCH

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NAME: **Zilberberg, Jenny**

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

POSITION TITLE: **Associate Scientist**

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
Universidad Simón Bolívar, Venezuela	**B.S.**	**05/1996**	**Chemical Engineering**
The Pennsylvania State University, University Park, PA	**M.S.**	**12/1998**	**Bioengineering**
The Pennsylvania State University, University Park, PA	**Ph.D.**	**08/2001**	**Bioengineering**
Thomas Jefferson University/HackensackUMC	**Postdoc**		**Cancer Immunotherapy**

A. Personal Statement

My research interest focuses on the development and biological characterization of tissue engineering platform to enable our understanding of the tumor microenvironment in cancers that reside in, or metastasize to, the bone/bone marrow niche. This transdisciplinary effort has resulted in the establishment of novel biomimetic models, which we showed to be suitable for: (1) the *ex vivo* preservation of multiple myeloma and (2) culturing primary murine and human osteocytes while maintaining *ex vivo* the production of sclerostin and FGF23, two key in vivo biomarker of primary osteocytes, for the first time to our best knowledge.

We are currently expanding the use of these platforms to discover novel molecular mechanisms of drug resistance and perform chemosensitivity studies of anti-cancer agents and immunotherapeutic treatments, using patient samples.

In addition, I have worked extensively on the development of novel immunotherapeutic treatments to potentiate the graft-versus-tumor effects of bone marrow transplantation without causing graft-versus-host disease, using various murine models of hematological malignancies, including acute myeloid leukemia and multiple myeloma.

Relevant publications:

- Q. Sun, S. Choudhary, C. Mannion, Y. Kissin, **J. Zilberberg***, and **W.Y. Lee***, “Ex Vivo Replication of Phenotypic Functions of Human Primary Osteocytes through 3D Bone Tissue Construction,” Bone,106:148-155 (2018).
- Q. Sun, S. Choudhary, C. Mannion, Y. Kissin, **J. Zilberberg***, and **W.Y. Lee***, “Ex Vivo Construction of Human Primary 3D-Networked Osteocytes,” Bone, 105, 245-252 (2017).
- S. Choudhary, Q. Sun, C. Mannion, Y. Kissin, **J. Zilberberg**, and **W.Y. Lee**, “Hypoxic 3D Cellular Network Construction Preserves Ex vivo the phenotype of Primary Human Osteocytes,” Tissue Engineering A, **24**, 458-468 (2018).
- Zhang W, **Lee WY***, **Zilberberg J*.** Tissue Engineering Platforms to Replicate the Tumor Microenvironment of Multiple Myeloma. Methods Mol Biol. 2017;1513:171-191.
- Q. Sun, Y. Gu, W. Zhang, L. Dziopa, **J. Zilberberg***, and **W.Y. Lee***, “Ex Vivo 3D Osteocyte Network Construction with Primary Murine Bone Cells,” Bone Research, 3, 152-163.3 (2015).

- W. Zhang, Y. Gu, Q. Sun, D.S. Siegel, P. Tolias, Z. Yang, **W.Y. Lee***, and **J. Zilberberg***, "Ex Vivo Maintenance of Primary Human Multiple Myeloma Cells through the Optimization of the Osteoblastic Niche," PLoS One 10(5): e0125995 (2015).
- Y. Gu, W. Zhang, Q. Sun, Y. Hao, **J. Zilberberg*,** and **W.Y. Lee***. Microbeads-Guided Reconstruction of 3D Osteocyte Network during Microfluidic Perfusion Culture. *Journal of materials chemistry. B, Materials for biology and medicine* **3**, 3625-3633, doi:10.1039/C5TB00421G (2015).
- W. Zhang, Y. Gu, Y. Hao, Q. Sun, K. Konior, H. Wang, **J. Zilberberg**, and **W.Y. Lee**, "Well Plate-Based Perfusion Culture Device for Tissue and Tumor Microenvironment Replication," Lab-on-a-Chip, 15, 2854-2863 (2015).
- Binsfeld M, Beguin Y, Belle L, Otjacques E, Hannon M, Briquet A, Heusschen R, Drion P, **Zilberberg J**, Bogen B, Baron F, Caers J. Establishment of a murine graft-versus-myeloma model using allogeneic stem cell transplantation. PLoS One. 2014 Nov 21;9(11):e113764.

B. Positions and Honors

Positions and Employment

Associate Scientist 2017-present
Department of Biomedical Research, Hackensack University Medical Center, Hackensack, NJ

Associate Scientist 2017-present
John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ.

Visiting Assistant Professor 2012-present
Department of Chemistry, Chemical Biology and Biomedical Engineering, Stevens Institute of Technology, Hoboken, NJ.

Adjunct Assistant Professor 2015-present
Georgetown Lombardi Comprehensive Cancer Center, Georgetown University School of Medicine Washington, DC.

Instructor 2011-2012
John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ.

Research Associate 2007-2011
The Cancer Center, Hackensack University Medical Center, Hackensack, NJ

Postdoctoral Researcher 2005-2007
The Cancer Center, Hackensack University Medical Center, Hackensack, NJ.
Developed immunotherapeutic approaches for improving T cell-mediated anti-tumor responses while preventing graft-versus-host disease, including T cell graft selection and generation of cancer vaccines.

Postdoctoral Researcher 2004-2005
Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA.
Studied the role of regulatory T cells in preventing graft-versus-host disease

Postdoctoral Researcher 2001-2003
Institute for Medicine and Engineering, University of Pennsylvania
Philadelphia, PA
Used atomic force microscopy, molecular biology assays, and computational simulations to identify vascular areas of high stress and inflammation leading to cardiovascular disease.

Honors

- Inventors Award, New Jersey Inventors Hall of Fame. Research related to multiple myeloma cancers and ex vivo method to determine effectiveness of personalized treatment strategies. 2013
- Ruth L. Kirschstein National Research Service Award (5-T32-CA09683), Cancer Immunology. Training Program, Kimmel Cancer Center, Thomas Jefferson University. 2004
- Graduate Student Research Award, Biomedical Engineering Society Meeting, Seattle, WA. 2000
- Predoctoral Fellowship, The American Heart Association, Pennsylvania-Delaware Affiliation. 2000
- 1st Place, 14th Annual Graduate Exhibition, The Pennsylvania State University. Exhibit entitled: "Fluorescence and Pentosidine Content of Diabetic Foot Skin." 1999
- Scholarship for graduate studies from Fundación Gran Mariscal de Ayacucho, Caracas, Venezuela. 1996

Recent Professional Activities

- Reviewer, National Cancer Institute Special Emphasis Panel - Early Stage Innovative Molecular Analysis Technology Development for Cancer Research/IMAT Program.
- Reviewer, National Cancer Institute Clinical Research - Loan Repayment Program.
- Participant, The Industrial and Professional Advisory Council (IPAC) for the Department of Biomedical Engineering at Pennsylvania State University.
- Member, Institutional Animal Care and Use Committee at Hackensack University Medical Center (2012-2017)
- Ad Hoc Reviewer, Biology of Blood and Marrow Transplantation, Bone marrow Transplantation, PLOS ONE and Vaccine journals.
- Member, AACR (2017-present)

C. Contributions to Science

1. Understanding the role of leukocyte adherence and shear on venular permeability. As a graduate student in the bioengineering program at Penn State, I studied the impact of shear forces at the microvascular level on the development of inflammatory signals. This work led to the development of an *in vivo* method to determine venular permeability, which at the time had only been done through the execution of invasive techniques that were likely to bias the end result measurement of permeability. Using this methodology, I was able to shed light on the interplay between shear forces, leukocyte adherence, and nitric oxide production as key modulators of vascular permeability during both basal and inflammatory states. The resulting publications from this work are:

1. Harris NR, Whitt SP, **Zilberberg J**, Alexander JS, Rumbaut RE. Extravascular transport of fluorescently labeled albumins in the rat mesentery. Microcirculation. 2002; 9(3):177-87.
2. **Zilberberg J**, Harris NR. Synergism between leukocyte adherence and shear determines venular permeability in the presence of nitric oxide. Microvascular Research. 2001 Nov; 62(3):410-20.
3. **Zilberberg J**, Harris NR. Role of shear and leukocyte adherence on venular permeability in the rat mesentery. Microvascular Research. 2001 Nov; 62(3):215-25.

2. Development of novel models and computational techniques to understand the effect of leukocyte shear on endothelial mechanosignaling. As a postdoctoral fellow at the Institute for Medicine and Engineering at the University of Pennsylvania, I continued to study shear forces exerted by adhered leukocytes on the vascular endothelium using atomic force microscopy (AFM) and computational techniques to calculate the stimuli experienced by blood vessels as a function of the altered topography of inflamed vessels. The resulting publications from this experience are:

1. Simmons CA, **Zilberberg J**, Davies PF. A rapid, reliable method to isolate high quality endothelial RNA from small spatially-defined locations. Annals of Biomedical Engineering. 2004 Oct; 32(10):1453-9.

2. Davies PF, **Zilberberg J**, Helmke BP. Spatial microstimuli in endothelial mechanosignaling. Circulation Research. 2003; 92:359-370.

3. Unraveling the immunobiology of graft-versus-host disease/ development of novel immunotherapeutic approaches for the treatment of hematological cancers. In 2005, I joined Dr. Robert Korngold's cancer immunology laboratory at HackensackUMC as a postdoctoral fellow. My efforts led to the development of novel preclinical immunotherapeutic approaches for the treatment of hematological cancers. In this regard, allogeneic blood and marrow transplantation (allo-BMT) is an important therapeutic tool for the treatment of various types of hematologic disorders, and offers potential for providing immunotherapy for several other forms of cancer. Parts of my scientific efforts are geared toward graft-versus-host disease (GVHD) immunobiology and the development of novel immunotherapeutic against this major complication of allo-BMT. My work in this field has led to the identification of potential therapeutic modalities and therapeutic targets to ameliorate GVHD as highlighted by the following publications:

1. **Zilberberg J*,** Matos J*, Dziopa E, Dziopa L, Yang Z, Kirk CJ, Assefnia S, Korngold R. Inhibition of the immunoproteasome subunit LMP7 with ONX 0914 ameliorates graft-versus-host disease in an MHC-matched minor histocompatibility antigen-disparate murine model. Biol Blood Marrow Transplant. 2015 Sep;21(9):1555-64. doi: 10.1016/j.bbmt.2015.06.010. Epub 2015 Jun 18.

2. **Zilberberg J**, Feinman R, Korngold R. Strategies for the identification of T cell recognized tumor antigens in hematological malignancies for improved graft-versus-tumor responses following allogeneic blood and marrow transplantation. Biology of Blood and Marrow Transplantation. 2014. DOI: http://dx.doi.org/10.1016/j.bbmt.2014.11.001.

3. Binsfeld M, Beguin Y, Belle L, Otjacques E, Hannon M, Briquet A, Heusschen R, Drion P, **Zilberberg J**, Bogen B, Baron F, Caers J. Establishment of a murine graft-versus-myeloma model using allogeneic stem cell transplantation. PLoS One. 2014 Nov 21;9(11):e113764.

4. Fanning SF*, **Zilberberg J***, Stein J, Vazzana K, Berger SA, Korngold R, and Friedman TM. Unraveling GVHD and GVL responses using TCR Vβ spectratype analysis and tumor pre-sensitization in a murine bone marrow transplantation model. J Immunol. 2013 Jan 1; 190(1):447-5.

5. **Zilberberg J**, Friedman TM, Dranoff G, Korngold R. Treatment with GM-CSF secreting myeloid leukemia cell vaccine prior to autologous-BMT improves the survival of leukemia-challenged mice. Biol Blood Marrow Transplant. 2011 Mar; 17(3):330-40.

6. Friedman TM, Goldgirsh K, Berger S, **Zilberberg J**, Filicko-O'Hara J, Flomenberg N, Donato M, Rowley SD, Korngold R. Overlap between in vitro donor antihost and in vivo posttransplantation Vβ use: A new paradigm for designer allogeneic blood and marrow transplantation. Blood, 2008 Oct; 112 3517-3525.

7. **Zilberberg J**, McElhaugh D, Gichuru LN, Korngold R, Friedman TM. Inter-strain tissue-infiltrating T cell responses to minor histocompatibility antigens involved in graft-versus-host disease as determined by Vβ size spectratype analysis. Journal of Immunology. 2008 April:180(8): 5352-5359.

8. Friedman TM, Azhipa O, **Zilberberg J**, Tkachuk Y, Hsu JW, Rowley SD, Goldberg, SL, Preti RA, Korngold R, Pecora AL. Reconstitution of T cell subset repertoire diversity following antigen mismatched bone marrow transplantation. Biology of Blood and Marrow Transplantation. 2006 Oct;12(10):1092-5.

4. Development of ex vivo models that recapitulate the 3D bone/bone marrow tumor microenvironment. In an effort to translate my research into the field of personalized medicine, I established an important collaboration in 2010 with Woo Lee, Ph.D, at Stevens Institute of Technology to develop novel *in vitro* microfluidic platforms to study blood cancers and solid tumors. Our unique approach to recapitulate the bone/bone marrow tumor microenvironment has led to a number of publications and patents detailed in the personal statement section. Beyond the aforementioned publications in the Personal Statement, the resulting publications from this work are:

1. W. Zhang, W.Y. Lee, D. Siegel, P. Tolias and **J. Zilberberg**. Patient-specific 3D microfluidic tissue model for multiple myeloma. Tissue Engineering C: Methods, 20, 663-670 (2014).

2. W.Y. Lee, **J. Zilberberg**, W. Zhang, D, Siegel, P.Tolias, and H. Wang. An ex vivo human multiple myeloma cancer niche and its use as a model for personalized treatment of multiple myeloma. Application No: 13/827,170. Issued Date: 02/23/2016. Patent No. 9267938.

6. Development of cancer targeting peptides:siRNA structures against multiple myeloma and prostate cancer. I recently formed a collaboration with David Sabatino, Ph.D., an expert in RNA and peptide chemical biology to establish and evaluate novel chemistry for delivery of a variety of different types of cargo. In particular, we are focusing on siRNAs against GRP78, a chaperone protein that serves as main sensor for misfolded proteins in the endoplasmic reticulum and triggers the unfolded protein response. Our work has resulted in one manuscripts currently under revision and two accepted for publication:

1. S.S. Shah, C.N. Cultrara, S.D. Kozuch, M.R Patel, J.A. Ramos; U. Samuni*, **J. Zilberberg***, and D. Sabatino*. Direct Transfection of Fatty Acid Conjugated siRNAs and Knockdown of the Glucose-Regulated Chaperones in Prostate Cancer Cells. *Accepted for publication in Bioconjugate Chemistry,* September 20th, 2018.
2. S. Kozuch, C. Cultrara, A. Beck, C. Heller, S.S. Shah, M. Patel, **J. Zilberberg*,** D. Sabatino*. Enhanced Cancer Theranostics with Self-Assembled, Multi-Labeled siRNAs. *Accepted for publication in ACS Omega,* September 26th, 2018.

D. Research Support

Active

NIH-NCI 1R33CA212806-01A1: "Ex vivo culture platform validation for preservation of patient derived multiple myeloma cells", 09/01/2017-8/31/2020. The goal of this project is to develop and validate an ex vivo multiple myeloma (MM) culture platform that utilizes patient biospecimens for screening patient-specific treatment options. *Role:* PI with Lee (multiple PI grant).

Celularity: "Evaluation of the immunotherapeutic effects of PiNK cells on patient multiple myeloma cells using 3D-tissue perfusion culture technology – A pilot study", 05/01/2018-11/31/2018. The goal of this pilot project is to evaluate the killing capability of PiNK cells against patient derived multiple myeloma using reconstructed osteoblastic niche co-culture and 3D-tissue perfusion culture technology. *Role:* PI with Lee (multiple PI grant).

Emerald Foundation Inc.: "Mitigating adhesion between myeloma cells and the tumor microenvironment to abrogate drug resistance", 12/31/2016-12/31/2019. The goal of this project is to determine the feasibility of manipulating patient derived multiple myeloma cells interactions with the endosteal niche to abrogate drug resistance. *Role:* PI.

Completed Research Support

NSF-DMR 1409779: Biomimetic Assembly of Microphysiological Lacunocanalicular Network," 08/01/2014-07/31/2018. *Role:* PI with Lee (multiple PI grant).

NIH-NCI 1R21CA174543-01A1: "Microfluidic Approach for the Development of a Three-Dimensional Bone Marrow Microenvironment Model to Test Personalized Multiple Myeloma Treatments," 06/06/2014-05/31/2018. *Role:* PI with Lee (multiple PI grant).

NIH-NIAMS 1R21AR065032: "Microfluidic 3D culture of primary osteocytes," 09/01/2013-8/31/2015. *Role:* Co-Investigator. *Role:* PI with Lee (multiple PI grant).

Onyx Pharmaceutical Research Proposal: "Effect of ONX 0914 and PR-825 on graft-vs.-host responses and regulatory T cells," 04/01/13-04/01/14. *Role:* Co-Investigator.

NIH/NHLBI 1R21HL102886-02: "Stable shRNA-mediated gene silencing of the beta 7 integrin to ameliorate graft-vs.-host disease," 7/01/10-6/30/13. *Role*: PI.