Danielle W. Kimmel

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Education

Doctor of Philosophy, Chemistry **March 2012**
Vanderbilt University (Nashville, TN)
Advisor: Dr. David Cliffel
Dissertation: "Dynamic Metabolic Responses To Oxidative Stresses By Multianalyte Microphysiometry"

Master of Science, Chemistry **May 2009**
Vanderbilt University (Nashville, TN)
Advisor: Dr. Brian Bachmann
Dissertation: "Natural Products: History, Importance, and Isolation Methods With Two Case Studies From Actinomycete K-26 and Lysobacter Enzymogenes"

Bachelor of Science, Chemistry **May 2007**
University of Louisville (Louisville, KY)

Research Experience

Postdoctoral Research Assistant **Advisor: Dr. David Wright**
Vanderbilt University **(April 2015-present)**
Department of Chemistry

Summary: Malaria diagnostics for low-resource countries have innate problems, such as their inability to measure low concentrations of parasite in blood samples. By utilizing novel extraction procedures, commercially available rapid diagnostic tests (RDTs) can benefit from improved sensitivity. To enhance these RDTs, magnetic and electrochemical modifications must be investigated.

Postdoctoral Research Assistant **Advisor: Dr. David Cliffel**
Vanderbilt University **(January 2012-present)**
Department of Chemistry

Summary: Immune cells, such as macrophages, play a pivotal role in defense against disease due to their ability to phagocytize, oxidize, and dispose of potentially harmful agents. In order to fully understand disease onset and progression, dynamic energetics of macrophage response to assaults must be investigated.

Investigation of the Mechanism of Action for PGE_2 During Pregnancy:

- Developed and implemented an experimental protocol to examine human and murine macrophage response to two strains of Group B *streptococcus* (GBS) stimuli with and without PGE_2.
- Investigated the effects of GBS on two cell types, THP1 and RAW 264.7, to develop a model system for future Fetal Membrane on a Chip fabrication.
- Optimized a murine model of GBS infection using the multianalyte microphysiometer to study metabolic energetics.
- Acquired preliminary data for an RO1 proposal that will include multidisciplinary collaborations within Vanderbilt and lead to human placental sample usage in the proposed system.
- Presented data to internal collaborators in the infectious diseases department, as well as presentations at national meetings.

Role of LOX-1 in Atherogenic Development:

- Developed and implemented an experimental protocol for the multianalyte microphysiometer measurements of the metabolic response of macrophages when conditioned with anti-LOX-1 prior to oxLDL exposure.
- Compared commercially available sources of oxLDL to ensure maximum metabolic response prior to testing how anti-LOX-1, trehalose, CpG-DNA, and scrambled peptides affect the expected energetics of macrophages.
- Networked and collaborated with Novartis International to achieve milestones, further the scope of the project, and draft a manuscript for publication.

Multianalyte Microphysiometer Coupled IM-MS Development:

- Aided in troubleshooting the requirements to couple the multianalyte microphysiometer with an IM-MS for near real-time analysis of metabolism and excreted metabolites from immune cells over the course of oxidative stress assault.
- Cultured cells necessary for experimentation and provided groundwork and experimental design for the proof-of-concept experiments performed to test the coupled system.
- Collaborated with postdoctoral scholars and multiple principle investigators.
- Lead the efforts to collect data from each instrument and prepare a cohesive manuscript.

Preliminary Data for IL4 Role in Cancer Growth Proposal:

- Developed and implemented an experimental protocol for multianalyte microphysiometry to test the role of IL4 in cancer growth of three cancer cell lines: MC38 (colon), CT26 (colon), and 4T1 (breast).
- Measured the dynamic basal rates of each cell line with and without IL4 exposure.
- Examined the effect of limiting glucose availability to each cell line and the effect glucose starvation had on the expected basal and IL4 exposure metabolic rates.
- Collaborated with Vanderbilt University Medical Center cancer researchers, leading to a peer-reviewed publication.

Graduate Research Assistant — **Advisor: Dr. David Cliffel**
Vanderbilt University — **(2009-2012)**
Department of Chemistry

Summary: Oxidative stresses, such as virulence factors, are able to incite immunological signaling cascades that recruit immune cells to an affected area. In many diseases, immune cells are incapable of reversing disease progression and can sometimes aid in disease development. In order to target earlier areas for therapeutic intervention, metabolic biosignatures of macrophage exposure must be measured to fully understand the role of oxidative stresses prior to disease.

Macrophage Metabolic Ramifications of Potential Therapeutics:

- Developed and implemented an experimental protocol for macrophage exposure to clinically relevant levels of oxLDL to mimic atherogenic behavior.
- Tested a novel therapeutic thought to attenuate the expected response of macrophage oxidative burst and subsequent foam cell formation due to engulfment of oxLDL.
- The increases in glucose consumption measured by my work validated the theory that PET imaging would be an effective way to monitor patients undergoing clinical trials for atherosclerotic development and treatment.
- Collaborated and met milestone deadlines associated with the funding provided by Novartis International and published the work in a peer-reviewed journal.
- Laid the methodological groundwork for future collaborations with multidisciplinary teams to study the effects of potential pharmaceuticals on a variety of cell types.
- Laid the groundwork for an additional collaboration with Novartis International to study the role of LOX-1 in atherosclerotic development.

Variations in Virulence Factors for Infectious Species:

- Developed and implemented an experimental protocol for measuring the metabolic responses of macrophages undergoing an assault from mycobacterial antigens, gram-negative effectors, and macrophage activators.
- Investigated the variation in infectious components before, during, and after their challenge to RAW 264.7 macrophages.
- Compared the roles of lipoarabinomannan as the mycobacterial antigen associated with tuberculosis infection, lipopolysaccharide as the gram-negative effector, and phorbol myristate acetate as a known macrophage activator.
- Collaborated with other analytical chemists to produce a peer-reviewed publication.

Screening Metabolic Effects of Potential Anti-Cancer Compounds:

- Developed and implemented a multianalyte microphysiometry protocol for screening the metabolic effects of anti-cancer compounds, apoptolidin-A1 and oligomycin-A1, as exposed to robust lung cancer cells.
- Cultured H292 cells as the platform to test anti-cancer compounds.
- Investigated both known and unknown compounds to compare the metabolic efficacy of potential therapeutic.
- Networked and collaborated with faculty and staff in the cancer research center at Vanderbilt University.

Graduate Research Assistant **Advisor: Dr. Brian Bachmann**
Vanderbilt University **(2007-2009)**
Department of Chemistry

Summary: Natural products-based drug development has provided numerous, widely used therapeutics for thousands of years. To fully explore secondary metabolites, competitive environments, such as caves, must be probed for potential bacteria species. Actinomycetes are a

gram-positive species, known to produce clinically relevant secondary metabolites, and live in competitive environments capable of producing novel compounds.

Natural Product Isolation from Actinomycetes:

- Developed extraction methodology for secondary metabolite isolation from multiple strains of locally collected Actinomycetes.
- Extensive bacterial culture experimentation to select an appropriate medium that favored growth of interesting metabolites.
- Utilized column chromatography, HPLC, and NMR to elucidate targets of interest.

Undergraduate Research Assistant **Advisor: Dr. K. Grant Taylor**
University of Louisville **(August 2006-December 2006)**
Department of Chemistry

Protein Expression and Purification

- Aided in organic synthesis of a potential osteoporosis therapeutic.
- Prepared and maintained freshly distilled solvents.

Undergraduate Research Assistant **Advisor: Drs. Craig A. Grapperhaus**
University of Louisville **and Francis P. Zamborini**
Department of Chemistry **(May 2004-August 2004)**

- Inorganically synthesized a carbon dioxide capturing Ni containing compound, cyclam acetate.
- Built self-assembled monolayer scaffolding onto a gold substrate to contain the cyclam acetate for a pollution-cleaning device.
- Participated in an undergraduate, campus-wide summer research program.

Publications

1. **Kimmel, DW**; LeBlanc, G; Meschievitz, ME; Cliffel, DE. Electrochemical Sensors and Biosensors. *Anal. Chem*. 2012, **84**(2), 685-707.
2. Harry, RS; Hiatt, LA; **Kimmel, DW**; Carney, CK; Halfpenny, KC; Cliffel, DE; Wright, DW. Metabolic Impact of 4-Hydroxynonenal on Macrophage Function and Activation. *Chem Res Toxicol*. 2012, **84**(2): 685-707.
3. **Kimmel, DW**; Dole, WP; Cliffel, DE. Macrophage Metabolic Responses to Oxidized LDL by Multianalyte Microphysiometry and Effects of an ApoA-1 Mimetic. *Biochem. Biophys. Res. Commun*. 2013, **431**(2): 181-5.
4. **Kimmel, DW**; Meschievitz, ME; Hiatt, LA; Cliffel, DE. Multianalyte Microphysiometry Investigation of Macrophage Metabolic Responses to Phorbol Myristate Acetate, Lipopolysaccharide, and Lipoarabinomannan. *Electroanalysis*. 2013, **25**(7): 1706-1712.
5. Shinawi, TF; **Kimmel, DW**; Cliffel, DE. Multianalyte Microphysiometry Reveals Changes in Cellular Bioenergetics Upon Exposure to Fluorescent Dyes*. Anal. Chem.* 2013, **85**(24): 11677-11680.
6. Lima, EA; Snider, RM; Reiserer, RS; McKenzie, JR; **Kimmel, DW**; Eklund, SE; Wikswo JP; Cliffel, DE. Multichamber Multipotentiostat System for Cellular Microphysiometry. *Sensors and Actuators B: Chemical*. 2014, **204**: 536-543.
7. Venmar, KT; **Kimmel, DW**; Cliffel, DE; Fingleton, B. IL4 Receptor α Mediates Enhanced Glucose and Glutamine Metabolism to Support Breast Cancer Growth. *Biochim Biophys Acta*. 2015, **1853**(5):

1219-1228.

Publications in Preparation

8. **Kimmel, DW**; Dole, WP; Cliffel, DE. Lectin-Like OxLDL Receptor-1 (LOX-1) Antibodies Modulate Macrophage Response to OxLDL. Submission planned for Spring 2015.
9. McKenzie, JR; Sherrod, SD; **Kimmel, DW**; McLean, JA; Wikswo, JP; Cliffel, DE. Interfacing Multianalyte Microphysiometry with Ion-Mobility Mass Spectrometry. Submission planned for Spring 2015.
10. **Kimmel, DW**; Rogers, LM; Aronoff, DM; Cliffel, DE. Eicosanoid Regulation of Fetal Membrane Innate Immunity. Submission planned for Summer 2015.

Honors and Awards

- Vanderbilt Graduate School travel grant 2012
- Vanderbilt Graduate School travel grant 2011
- Scholarship and Creative Activity Summer Institute research grant 2004

Teaching

Vanderbilt University (Nashville, TN)

General Chemistry Laboratory TA, Fall 2009

- Guided undergraduate general chemistry laboratory experiments.
- Performed general laboratory responsibilities to ensure safety, graded quizzes and exams, and held weekly office hours to field student questions.

Organic Chemistry TA, Fall 2007 – Spring 2009

- Guided undergraduate organic chemistry laboratory experiments.
- Performed general laboratory responsibilities to ensure safety, graded quizzes and exams, and held weekly office hours to field student questions.

Mentorship and Management

Over the course of my graduate and postdoctoral research at Vanderbilt, I have mentored numerous graduate students on rotation projects, as well as two graduate students on their graduate projects. I have also been involved with and lead numerous multidisciplinary collaborations, resulting in peer-reviewed publications. Throughout my research career, I have managed the research for several grant funded projects, driven by milestone completion.

Selected Poster and Oral Presentations

- Kimmel, DW; Zamborini, FP; Grapperhaus, CA. Scholarship and Creative Activity Summer Institute research symposium, Louisville, KY, 2004. Poster presentation.
- Kimmel, DW; Dole, WP; Cliffel, DE. “Multianalyte Microphysiometry of Macrophage Metabolism Triggered By Oxidized Low Density Lipoprotein.” Pittcon, Atlanta, GA 2011. Poster presentation.

- Kimmel, DW; Dole, WP; Cliffel, DE. "Multianalyte Microphysiometry of Macrophage Metabolism Triggered By Oxidized Low Density Lipoprotein." Melbourne Symposium, Nashville, TN, 2011. Poster Presentation.
- Kimmel, DW; Dole, WP; Cliffel, DE. "Multianalyte Microphysiometry of Macrophage Metabolism Triggered by Oxidized Low Density Lipoprotein." Vanderbilt Institute of Chemical Biology Symposium, Nashville, TN, 2011. Poster presentation.
- Kimmel, DW; Meschievitz, ME; Hiatt, LA; Cliffel, DE. "The Metabolic Effects of Mycobacterial and Gram-Negative Bacterial Exposure." Pittcon, Orlando, FL, 2012. Oral presentation.
- Kimmel, DW; Cliffel, DE. "Dynamic Metabolic Measurements Using Multianalyte Microphysiometry." SLAS, San Diego, CA, 2014. Poster presentation.
- Kimmel, DW; Cliffel, DE. "Metabolic Activity of PGE2 in Macrophages During LPS Exposure." Pittcon, Chicago, IL, 2014. Poster presentation.
- Kimmel, DW; Rogers, LM; Aronoff, D; Cliffel, DE. "Multianalyte Microphysiometry of Group B streptococcus Exposure." SERMACS, Nashville, TN, 2014. Poster presentation.
- Kimmel, DW; Rogers, LM; Aronoff, D; Cliffel, DE. "Multianalyte Microphysiometry Investigation of Virulence Differences Between Group B *streptococcus* Strains." Pittcon, New Orleans, LA 2015. Oral Presentation.
- Cliffel, DE; McKenzie, JR; Kimmel, DW. "Instrumenting Organs on a Chip with Real-Time Electrochemical Sensors." Pittcon, New Orleans, LA 2015. Oral presentation.
- Rogers, LM; Kimmel, DW; Sutton, JA; Montenegro, JR; McLean, JA; Cliffel, DE; Manning, SD; Aronoff, DM. "A Virulent cps V Group B *streptococcus* Strain Alters Macrophage Metabolism and Activation." Science in the Service of Women's Health, San Francisco, CA 2015. Poster presentation.
- Kimmel, DW; Rogers, LM; Aronoff, DM; Cliffel, DE. "The Role of Prostaglandin E2 in Modulating Macrophage Metabolism During Infection With Group B *Streptococcus*." Infection and Immunology Symposium, Nashville, TN 2015. Poster presentation.
- Rogers, LM; Kimmel, DW; Sutton, J; Montenegro, JR; McLean, JA; Cliffel, DE; Manning, S; Aronoff, DM. "A Hypervirulent *cps* V GBS Strain Alters Macrophage Metabolism and Activation." Infection and Immunology Symposium, Nashville, TN 2015. Poster Presentation.

Technical Skills

- BSL2+ certified
- Murine and human cell culture – biosafety levels 1 and 2
- Bacterial cell culture
- High Performance Liquid Chromatography (prep scale and analytical)
- Basic use and interpretation of UV-vis and NMR
- Limited use of developmental software (e.g. LabVIEW)
- Fluent in multianalyte microphysiometer measurements
- Microfluidics and electrochemical enzyme sensing
- Sensor development and fabrication
- Organic extractions, column chromatography
- Experimental development and application
- Department of Transportation hazmat training