Doctoral Dissertation Announcement

Valery Lozada-Fernández

“Nicotinamide Riboside-Conditioned Microbiota Deflects High Fat Diet-Induced Weight Gain in Mice”

Candidate for Doctor of Philosophy in Microbiology and Immunology
Graduate School of Biomedical Sciences
Medical College of Wisconsin

Tuesday, March 23\textsuperscript{rd}, 2021
11:00 am
Zoom link: \url{https://mcw-edu.zoom.us/j/94860607438?pwd=NmRUUGIzbGRxU1R3eTI3VVFPYkpiZz09}

Committee members:
John R. Kirby, PhD
Dara Frank, PhD
Nita Salzman, MD, PhD
John Auchampach, PhD
Christopher Kristich, PhD
Graduate Studies:
Prokaryotic Biology (Module I and II)
Graduate Microbial Genetics
Pathogenic Bacteriology
Bacterial Diversity
Bioinformatics
Conduct in Research
Cellular Microbiology
Mucosal Pathogenesis
Advanced Bacterial Physiology
Ethics and Integrity in Science
Biostatistical Computing
Seminar
Reading and Research
Research Ethics Discussion
Doctoral Dissertation
Dissertation Abstract

The gut microbiome plays an essential yet under-investigated role in energy homeostasis of the host and influences the development of obesity and obesity-related conditions. Studies have shown that nicotinamide riboside (NR) supplementation into a diet-induced obesity (DIO) mouse model can reduce weight gain and increase energy expenditure. NR is a vitamin B₃ derivative and an NAD⁺ precursor with the potential of treating human diseases that arise from mitochondrial degeneration, such as obesity and type II diabetes. Gut bacteria produce vitamin B₃ in the colon and are capable of salvaging and metabolizing vitamin B₃ derivatives. However, it is unknown how dietary supplementation of NR alters the gut microbiome and if those alterations contribute to the deflection of weight gain and other benefits seen on the host. In this dissertation, we fed males a high fat diet (HFD) or a western diet (WD) supplemented with or without 0.4% NR to investigate the effects on physiology and gut microbiome profile of the host. Subsequently, we performed a fecal material transfer (FMT) to establish a link between NR-conditioned microbiota and NR-induced deflection of weight gain. FMT from NR-treated donors to naïve mice fed a HFD was sufficient to deflect weight gain by reducing energy efficiency and thus increasing energy expenditure. We found that NR-treated mice had an altered gut microbial composition relative to controls and fecal transplant resulted in a distinct functional metabolic profile characterized by enrichment of butyrate producing Firmicutes. The NR-treated donors and subsequent FMT recipients share similar enrichment of metagenomic biomarkers relative to controls. WD-fed mice treated with NR deflect diet-induced weight gain via a different mechanism than HFD-fed mice since it does not increase energy expenditure, but it does alter body composition differently. By implementing a machine learning approach we created a random forest classifier that can accurately classify fecal samples by diet and treatment. Lastly, this classifier helped identify discriminant microbial responses to diets and to NR treatment.
Curriculum Vitae
Valery V. Lozada-Fernández
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Department of Microbiology and Immunology
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EDUCATION
01/2017-05/2021 PhD Candidate, Microbiology and Immunology, Medical College of Wisconsin, Milwaukee, WI.
08/2015-12/2016 Microbiology Graduate Student, The University of Iowa, Iowa City, IA.
08/2010-06/2014 B.S. Industrial Microbiology, University of Puerto Rico, Mayagüez, PR.

RESEARCH AND PROFESSIONAL EXPERIENCE
01/2017-Present Graduate Student Dissertation Project, Medical College of Wisconsin, Milwaukee, WI. “Nicotinamide Riboside-Conditioned Microbiota Deflects High Fat Diet-Induced Weight Gain in Mice”. Advisor: Dr. John R. Kirby.

The goal of my dissertation research is to determine how dietary nicotinamide riboside (NR) supplementation shifts the gut microbiome of C57BL/6j male mice fed a 60% high fat diet (HFD). Specifically, I want to determine how the gut microbiome contributes to weight loss and improved metabolism in mice. I have found that dietary NR supplementation for 168 days alters the gut microbiome compositional and functional profiles and enriches for butyrate-producing members of the Firmicutes phylum. Additionally, a fecal material transplant (FMT) from NR-treated mice into naïve recipients fed a 60% HFD is sufficient to reduce HFD-induced weight gain and increase energy expenditure. Lastly, FMT-NR mice exhibit similar enriched microbial and functional biomarkers as the NR-treated donors, suggesting that the gut microbiome contributes in part to the improved metabolism observed upon NR supplementation.

09/2020-Present 2020 Scientist Mentoring & Diversity Program (SMDP) Scholar

09/2017-12/2019 Instructor for the CMR Microbiome Informatics Workshop 2019: 16S rDNA Sequencing, Medical College of Wisconsin, Milwaukee, WI.

11/2018 Intellectual Property Business Basics Workshop, Milwaukee, WI.

08/2018-10/2018 Scientific Writing Course, Medical College of Wisconsin, Milwaukee, WI.

06/2018 SciPhD Workshop, Medical College of Wisconsin, Milwaukee, WI.

09/2017 Microbiome Informatics Workshop 2017: 16S & Metagenomics Sequencing, Medical College of Wisconsin, Milwaukee, WI.

06/2017-07/2017 The Community Research Education and Engagement for Data Science (CREEDS) Summer Program, Icahn School of Medicine at Mount Sinai, New York, NY.
08/2015-12/2016 Graduate Student Research Project, The University of Iowa, Iowa City, IA. “Opposing effects of Risperidone and Nicotinamide Riboside in the murine gut microbiome”. Research advisor: Dr. John R. Kirby

08/2016-12/2016 Graduate Teaching Assistant, The University of Iowa, Iowa City, IA. Course: General Microbiology Laboratory (MICR2158). Advisor: Dr. Marcia Cordts

07/2014-07/2015 Post-Baccalaureate Research Education Program (PREP) Scholar, Case Western Reserve University, Cleveland, OH. “The role of the exoU genomic island in the pathogenesis of the Pseudomonas aeruginosa 19660 keratitis”. Advisors: Dr. Eric Pearlman and Dr. Arne Rietsch

08/2011-08/2013 Undergraduate Student Research, University of Puerto Rico, Mayagüez, PR. “Distribution of Vancomycin Resistant Enterococci in isolates from River, Beach, Clinical, Human Fecal and Animal Fecal isolates”. Advisor: Dr. Luis Ríos-Hernández

06/2013-08/2013 Summer Undergraduate Course Creating Excellence in Scientific Study (Success) Program, The Ohio State University, Columbus, OH. “Post-Translational Modifications on Histones”. Advisor: Dr. Michael Freitas

06/2012-08/2012 Short-Term Training Program to Increase Diversity in Health-Related Research (STREAMS) Program, Wright State University, Dayton, OH. “The oxysterol responsive nuclear receptor LXRα binds to fatty acid derivatives”. Advisor: Dr. Heather Hostetler

06/2011 EXTRACURRICULAR AND VOLUNTEER ACTIVITIES

05/2018- Present American Association for the Advancement of Science (AAAS)

02/2018-05/2018 Mentor for middle school students participating of WSTEM Program, Milwaukee, WI.

07/2017-05/2018 Writer for the Milwaukee Area Science Advocate (MASA) Non-Profit Group, Milwaukee, WI.

07/2017 Organizational Committee for the National Domestic Violence Awareness Campaign, Medical College of Wisconsin, Milwaukee, WI.

11/2012- Present American Society of Microbiology

11/2013-12/2015 Minorities in Cancer Research, Student Association

03/2013-06/2014 Sociedad de Microbiólogos de Puerto Rico

06/2013-08/2013 Volunteering and Doctor Shadowing at the Columbus Free Clinic, OH

04/2009 Close Up Program, Washington D.C

05/2008-05/2010 Venture Scout- Boys Scout of America, Crew 1972, San Germán, PR

AWARDS

06/2019 Graduate School Minority Scholar Award, Medical College of Wisconsin, Milwaukee, WI.

03/2018 Outstanding Poster Presentation, 2nd Annual GSA Student Symposium, Medical College of Wisconsin, Milwaukee, WI.

08/2015-12/2017 Alfred P. Sloan Foundation Graduate Scholarship, The University of Iowa, Iowa City, IA

05/2015 Outstanding Oral Presentation in the Post-Baccalaureate Education Program (PREP), Case Western Reserve University, Cleveland, OH

08/2011 Dean’s List, Faculty of Arts and Science, University of Puerto Rico, Mayagüez, PR
Howard Hughes Medical Institute (HHMI) travel award to attend the American Society of Microbiology (ASM) General Meeting in Denver, CO

Outstanding Oral Presentation in the Undergraduate Research Symposium, University of Puerto Rico, Mayagüez, PR

Minority Access to Research Careers (MARC) Scholar, University of Puerto Rico, Mayagüez, PR

Outstanding Poster Presentation in Biochemistry and Interdisciplinary, Annual Biomedical Research Conference for Minority Students (ABRCMS), San José, CA

MEETINGS AND CONFERENCES ABSTRACTS

Keystone eSymposia: Harnessing the microbiome for disease and therapy. Virtual Conference. Poster: “Nicotinamide riboside-conditioned microbiota deflects weight gain and increases energy expenditure in mice”. Awarded the eSymposia Student Aid to cover the registration fee.

Cold Spring Harbor Laboratories. Microbiome Virtual Conference. Poster: “Nicotinamide riboside-conditioned microbiota is sufficient to deflect diet-induced weight gain”.

4th Annual GSA Student Symposium, Medical College of Wisconsin, Milwaukee, WI. Poster: “NR Supplementation Remodels the Gut Microbiota, which is Sufficient to Ameliorate High Fat Diet-Induced Weight Gain”. Cancelled due to COVID-19.

29th Annual Graduate School Research Poster Session, Medical College of Wisconsin, Milwaukee, WI. Poster: “Ameliorating High-Fat Diet-Induced Weight Gain via a Fecal Material Transplant”.

Molecular Genetics of Bacteria and Phages Meeting 2019, University of Wisconsin, Madison, WI. Poster: “Ameliorating High-Fat Diet-Induced Weight Gain via a Fecal Material Transplant”.

3rd Annual GSA Student Symposium, Medical College of Wisconsin, Milwaukee, WI. Poster: “Nicotinamide Riboside Supplementation Remodels the Gut Microbiome and is Sufficient to Ameliorate High Fat Diet-Induced Weight Gain”.

2018 Changemakers in Science, Advancing a Healthier Wisconsin Endowment, Medical College of Wisconsin, Milwaukee, WI.

7th Conference on Beneficial Microbes, University of Wisconsin, Madison, WI. Poster: “Gut Microbiome Alterations Upon Nicotinamide Riboside Supplementation”.

2018 MCW’s Redox Symposium, Medical College of Wisconsin, Milwaukee, WI.

2nd Annual GSA Student Symposium, Medical College of Wisconsin, Milwaukee, WI. Poster: “Gut Microbiome Alterations Upon Nicotinamide Riboside Supplementation”.

27th Annual Graduate School Poster Session, Medical College of Wisconsin, Milwaukee, WI.

2017 Changemakers in Science, Advancing a Healthier Wisconsin Endowment, Medical College of Wisconsin, Milwaukee, WI.

1st Annual Graduate Student Association Symposium, Harley-Davidson Museum, Milwaukee, WI.

Molecular Genetics of Bacteria and Phages Meeting 2016, University of Wisconsin, Madison, WI. Poster: “NR Supplementation in Risperidone-treated Mice Alters the Gut Microbiome to Prevent Risperidone-related Dysbiosis”.

Graduate Student Judge in the 6th Annual Fall Undergraduate Research Symposium, The University of Iowa, Iowa City, IA.

Post-Baccalaureate Education Program (PREP) Research Day, Case Western Reserve University, Cleveland, OH. Oral: “The role of the exoU genomic island in the
pathogenesis of *Pseudomonas aeruginosa* 19660 keratitis”.

05/2015  Post-Baccalaureate Education Program (PREP) Symposium, Case Western Reserve University, Cleveland, OH. Poster: “The role of the *exoU* genomic island in the pathogenesis of *Pseudomonas aeruginosa* 19660 keratitis”

11/2014  Annual Biomedical Research Conference for Minority Students (ABRCMS), San Antonio, TX. Poster: “The role of the *exoU* genomic island in the pathogenesis of *Pseudomonas aeruginosa* 19660 keratitis”

10/2014  The Association of Underrepresented Minority Fellows National Symposium, Case Western Reserve University, Cleveland, OH.

11/2013  Annual Biomedical Research Conference for Minority Students (ABRCMS), Nashville, TN. Poster: “Post-translational Modifications on Histones”

08/2013  Summer Undergraduate Course Creating Excellence in Scientific Study (Success) Poster Session, The Ohio State University, Columbus, OH. “Post-translational Modifications on Histones”

08/2013  Summer Undergraduate Course Creating Excellence in Scientific Study (Success), Oral Session, The Ohio State University, Columbus, OH. “Post-translational Modifications on Histones”

05/2013  American Society of Microbiology General Meeting in Denver, CO. Poster: “Distribution of Vancomycin Resistant Enterococci in isolates from River, Beach, Clinical, Human Fecal and Animal Fecal isolates”

05/2013  3rd Undergraduate Research Symposium, University of Puerto Rico, Mayaguez, PR. Oral: “Distribution of Vancomycin Resistant Enterococci in isolates from River, Beach, Clinical, Human Fecal and Animal Fecal isolates”

02/2013  North East Alliance (NEA) Poster Presentation, University of Puerto Rico, Mayaguez, PR. Poster: “Distribution of Vancomycin Resistant Enterococci in isolates from River, Beach, Clinical and Human Fecal isolates”

11/2012  Annual Biomedical Research Conference for Minority Students (ABRCMS), San Jose, CA. Poster: “The oxysterol responsive nuclear receptor LXRα binds to fatty acid derivatives”

08/2012  Short-Term Training Program to Increase Diversity in Health-Related Research (STREAMS), Wright State University, Dayton, OH. Poster: “The oxysterol responsive nuclear receptor LXRα binds to fatty acid derivatives”

**PUBLICATIONS**


**COURSES**

2015, Fall, University of Iowa, Prokaryotic Biology Module I
2015, Fall, University of Iowa, Graduate Microbial Genetics
2015, Fall, University of Iowa, Graduate Student Research Seminar
2016, Spring, University of Iowa, Pathogenic Bacteriology
2016, Spring, University of Iowa, Bacterial Diversity
2016, Spring, University of Iowa, Graduate Student Research Seminar
2016, Fall, University of Iowa, Prokaryotic Biology Module II
2016, Fall, University of Iowa, Bioinformatics
2016, Fall, University of Iowa, Conduct in Research I
2016, Fall, University of Iowa, Graduate Student Research Seminar
2017, Spring, MIMG25236, Cellular Microbiology
2017, Spring, MIMG25295, Reading and Research
2017, Summer, MIMG25295, Reading and Research
2017, Fall, MIMG25260, Mucosal Pathogenesis
2017, Fall, MIMG25295, Reading and Research
2018, Spring, BIOE10222 Ethics & Integrity in Science
2018, Spring, MIMG25269, Advanced Bacterial Physiology
2018, Spring, MIMG25295, Reading and Research
2018, Spring, MIMG25300, Seminar
2018, Summer, MIMG25295, Reading and Research
2018, Fall, BIOS04224, Biostatistical Computing
2018, Fall, MIIM25295, Reading and Research
2018, Fall, MIIM25300, Seminar
2019, Spring, BIOE10444, Research Ethics Discussion Series
2019, Spring, MIIM25295, Reading and Research
2019, Summer, MIIM25295, Reading and Research
2019, Fall, MIIM25295, Reading and Research
2020, Spring, MIIM25295, Reading and Research
2020, Summer, MIIM25295, Reading and Research
2020, Fall, MIIM25295, Reading and Research
2021, Spring, MIIM25399, Doctoral Dissertation