BIOGRAPHICAL SKETCH

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NAME: Keller, Amy Celeste

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

POSITION TITLE: Assistant Professor

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
University of Colorado Boulder	B.A.	5/1998	Biology, Russian
City University of New York, Graduate Center	Ph.D.	2/2011	Biology-Plant Sciences
Colorado State University (Postdoctoral Researcher)		7/2011	Medicinal Plants
University of Colorado Denver (Postdoctoral Researcher)		6/2017	Diabetes/Vascular Physiology/Botanical Therapies

A. Personal Statement

I am an assistant professor with a scientific background in cardiovascular physiology along with medicinal plant research and phytochemistry. I intend to take the *investigation of herbal supplements, nutritional components, and plant mixtures and compounds forward by researching their bioactivity in the context of chronic disease*. My research addresses the alleviation of cardiovascular risk in those suffering from diabetes. I pursued a postdoctoral fellowship in the laboratory of Dr. Jane Reusch to acquire training in biomedical research techniques and cellular and molecular biology using animal models of disease. I have investigated the integrated role of endothelial nitric oxide synthase (eNOS) and mitochondria in vascular health and have applied medicinal plants and bioactive compounds toward supporting these cellular lynchpins. Recent work has described the potential for natural products to reinforce glucose homeostasis in concert with physiological vascular reactivity, in part by support eNOS activity and thus mitochondrial function. As part of my plan for a career dedicated to serving those with diabetes, I have continued the *investigation of cellular signaling and redox homeostasis in the diabetic vasculature, with an emphasis on plant compounds and natural products as potential modulators of specific cellular homeostasis*.

Ongoing and recently completed projects that I would like to highlight include:

Veteran's Affairs Merit
Keller (PI)
Delineating mechanisms of impaired vasoreactivity in thermoneutrality
July 2023-June 2027

SCORE Pilot Award:
Keller (Co-PI with Dr. Kimberley Bruce)
The interaction between sex hormones and brain metabolism: implications for increased Alzheimer's Disease risk in women
October 2023-September 2024

Citations:

1. **Keller AC**, Hull SE, Hanan E, Johnston A, Knaub LA, Chun JH, Walker L, Nozik-Grayck E, Reusch JEB. (–)-Epicatechin Modulates Mitochondrial Redox in Vascular Cell Models of Oxidative Stress. Oxid Med Cell Longev. Volume 2020, Article ID 6392629, doi.org/10.1155/2020/6392629.
2. **Keller AC**, Knaub LA, Scalzo RL, Hull SE, Johnston AE, Walker LA, Reusch JEB. Sepiapterin Improves Vascular Reactivity and Insulin-Stimulated Glucose in Wistar Rats. Oxid Med Cell Longev. 2018;2018:7363485. doi: 10.1155/2018/7363485. eCollection 2018.
3. **Keller AC**, Knaub LA, McClatchey PM, Connon CA, Bouchard R, Miller MW, Geary KE, Walker LA, Klemm DJ, Reusch JE. Differential Mitochondrial Adaptation in Primary Vascular Smooth Muscle Cells from a Diabetic Rat Model. Oxid Med Cell Longev. 2016;2016:8524267. doi: 10.1155/2016/8524267. Epub 2016 Jan 11.
4. **Keller AC**, Ma J, Kavalier A, He K, Brillantes AM, Kennelly EJ. Saponins from the traditional medicinal plant *Momordica charantia* stimulate insulin secretion in vitro. Phytomedicine. 2011 Dec 15;19(1):32-7. doi: 10.1016/j.phymed.2011.06.019. Epub 2011 Nov 30.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023-present	Chair, Subcommittee on Research Safety, RMR VA Medical Center
2023	Co-organizer, NORC Retreat 2023
2023-present	Co-Chair, Social Media Committee, American Society of Pharmacognosy
2023-present	Assistance to the RMR VA Medical Center Research Day
2023	CCTSI Translational Pilot Award Reviewer
2023	University of Sharjah, United Arab Emirates, Ad-Hoc Grant Reviewer
2022	No Co-Pay Radio Presentation, Botanical for Health Support
2020	Student abstract reviewer for David J. Slatkin Symposium, Chicago State University
2019-present	Secretary, American Society of Pharmacognosy
2019-present	Co-Organizer, Molecular Metabolism Journal Club (Nutrition Obesity Research Center)
2019-2020	Logo Design Committee, American Society of Pharmacognosy
2018-present	Co-organizer, RMR VA Medical Center Research Days
2018-present	Organizer, RMR VA Research Seminar Series
2018-present	What's Blooming Boulder Blog and Twitter. Mission: sharing botanical knowledge with the lay public
2017-Present	Research Scientist, Denver VA. Mentors: Drs. Jane Reusch, Kerrie Moreau, and Paul MacLean
2017-Present	Assistant Professor, Division of Endocrinology, Metabolism, & Diabetes, University of Colorado School of Medicine
2017-present	Bad Ass Lady Scientists (BALS) Twitter. Mission: promoting science conducted by women
2014- 2018	Co-Organizer, Junior Faculty MeetUp (This is a career-oriented gathering featuring guest speakers and advisement on transitioning from postdoctoral positions to junior faculty)
2013-2017	Member (Scientist), VA Research Institutional Animal Care and Use Committee (IACUC) Committee
2011-2017	Postdoctoral Fellow, Division of Endocrinology, Metabolism, & Diabetes, Department of Medicine, University of Colorado Denver, Aurora, Colorado
2011-2011	Research Scientist, Flint Animal Cancer Center, Colorado State University, Fort Collins, Colorado
2011-2017	Writer, American Botanical Council, Austin, Texas
2008-2011	Student Representative, Plant Science Advisory Committee, Graduate Center, City University of New York
2007-2009	President, Ethnobiology Club, Graduate Center, City University of New York
2006-2017	Writer/Reporter, American Society of Pharmacognosy, New York, New York
2005-2008	Co-Coordinator, Red Shed Community Garden, Brooklyn, New York
2003-2007	Adjunct Lecturer, Department of Biology, Lehman College, City University of New York, New York

2000-2003 Research Assistant, Department of Pathology, Albert Einstein College of Medicine, New York, New York
1998-1999 Laboratory Technician, Quest Diagnostics, Inc., Denver, Colorado

Honors

2021: CU Anschutz Department of Medicine Research Day 2021 Abstract Award
2018: Ludeman Family Center for Women's Health Research Best Poster Award
2016: American Society of Pharmacognosy Travel Award for Active Members
2014: Colorado Nutrition Obesity Research Center (NORC) Pilot Award "Restoration of vascular contractility and mitochondrial function by NOS recoupling" (NIH- P30DK048520)
2011: National Institutes of Health Heart, Lung, and Blood Postdoctoral Training Fellowship Award "Adaptation to Hypoxia Postdoctoral Training Fellowship Award" (NIH-1P01HL14985)
2011: Phytochemical Society of North America Postdoctoral Poster Award
2010: American Society of Pharmacognosy Student Poster Award
2006: City University of New York: University Fellowship
2004-2006: City University of New York: Plant Research Fellowship
2003-2005: City University of New York Science Fellowship
1997: University of Colorado, Boulder: Study Abroad Travel Grant
1996: University of Colorado, Boulder: Biospheric and Atmospheric Research Training Grant

C. Contributions to Science

1. During my graduate work and beyond, I focused on supporting the use of botanical traditional medicine by connecting medicinal plants to measurable bioactivity. My research involved the traditional medicine of the Dominican Republic used for diabetes, particularly bitter melon (*Momordica charantia*). I verified previous reports of hypoglycemic activity of the ethanol extract and saponin compounds unique to this plant and provided new evidence about their insulin secretagogue activity. According to my in vitro experiments, this bioactivity was likely due to structure differences of different *M. charantia* compounds. This work is being continued with bioavailability assays in vitro and potential clinical trials. I briefly researched fermented tea (*Camellia sinensis*) and compared global compound profiles with non-fermented tea using metabolomics. I found significant differences in certain compounds, as well as differences in bioactivity of the two teas. This strongly suggests a large role of fermentation in compound content and bioactivity of a beverage consumed worldwide. In summary, I have applied myriad techniques to verify the efficacy of medicinal and food plants.

a. **Keller AC**, He K, Brillantes AB, Kennelly EJ. A characterized saponin-rich fraction of Momordica charantia shows antidiabetic activity in C57BLK/6 mice fed a high fat diet. Phytomedicine Plus. 2021 November; 1(4).
b. Wu SB, Yue GG, To MH, **Keller AC**, Lau CB, Kennelly EJ. Transport in Caco-2 cell monolayers of antidiabetic cucurbitane triterpenoids from *Momordica charantia* fruits. Planta Med. 2014 Jul;80(11):907-11. doi: 10.1055/s-0034-1382837. Epub 2014 Aug 12.
c. **Keller AC**, Weir TL, Broeckling CD, Ryan EP. Antibacterial activity and phytochemical profile of fermented *Camellia sinensis* (fuzhuan tea). Food Research International (Ottawa, Ont.). 2013 October; 53(2):945-949
d. **Keller AC**, Ma J, Kavalier A, He K, Brillantes AM, Kennelly EJ. Saponins from the traditional medicinal plant *Momordica charantia* stimulate insulin secretion in vitro. Phytomedicine. 2011 Dec 15;19(1):32-7. doi: 10.1016/j.phymed.2011.06.019. Epub 2011 Nov 30.

2. During my graduate work, I became interested in treatments and mechanisms of action for diabetes. I began a postdoctoral fellowship in the laboratory of Dr. Jane Reusch, a diabetes physician scientist, in 2011. I helped to show disrupted mitochondrial response to exercise in diabetic models, as well as verify the role of nitric oxide synthase (NOS) upstream of mitochondrial function in diabetic vasculature both in vitro and in vivo. As NOS may help to repair mitochondrial function in diabetes, we attempted to target this enzyme with saxagliptin, a pharmaceutical used to indirectly stimulate NOS activity. We showed that saxagliptin recovered exercise response in an in vivo model of insulin resistance. We also treated rats with the NOS co-factor sepiapterin on vasoreactivity in rats and found that it significantly improved vasodilation. The body of work below illustrates the potential of mitochondria and NOS as therapeutic targets in diabetic physiology.

a. **Keller AC**, Knaub LA, Scalzo RL, Hull SE, Johnston AE, Walker LA, Reusch JEB. Sepiapterin Improves Vascular Reactivity and Insulin-Stimulated Glucose in Wistar Rats. Oxid Med Cell Longev. 2018;2018:7363485. doi: 10.1155/2018/7363485. eCollection 2018.
b. **Keller AC**, Knaub LA, Miller MW, Birdsey N, Klemm DJ, Reusch JE. Saxagliptin restores vascular mitochondrial exercise response in the Goto-Kakizaki rat. J Cardiovasc Pharmacol. 2015 Feb;65(2):137-47. doi: 10.1097/FJC.0000000000000170.
c. Miller MW, Knaub LA, Olivera-Fragoso LF, **Keller AC**, Balasubramaniam V, Watson PA, Reusch JE. Nitric oxide regulates vascular adaptive mitochondrial dynamics. Am J Physiol Heart Circ Physiol. 2013 Jun 15;304(12):H1624-33. doi: 10.1152/ajpheart.00987.2012. Epub 2013 Apr 12.
d. Knaub LA, McCune S, Chicco AJ, Miller M, Moore RL, Birdsey N, Lloyd MI, Villarreal J, **Keller AC**, Watson PA, Reusch JE. Impaired response to exercise intervention in the vasculature in metabolic syndrome. Diab Vasc Dis Res. 2013 May;10(3):222-38. doi: 10.1177/1479164112459664. Epub 2012 Nov 16.

3. Based on our work above, we began investigations of nutrient stress on NOS and mitochondrial activity, and how to characterize this response as well as mitigate resultant cellular damage. The publications below describe cell and animal experiments of well-defined, disrupted vascular and mitochondrial function in response to metabolic insults, as well as successful pharmaceutical support of NOS activity in vivo. Reported results from this line of inquiry set a strong foundation of pursuing the restoration of vascular NOS and mitochondrial homeostasis as a therapeutic target. Through my career development award at the VA, I currently research the botanical compound (–)-epicatechin, a known vasodilator, for its ability to restore NOS and mitochondrial function, thereby restoring vascular responsiveness in diabetes. My ongoing work reflects my stated goal of integrating botanicals in the treatment of vascular dysfunction in diabetes.

a. Chun JH, Henckel MM, Knaub LA, Hull SE, Pott GB, Walker LA, Reusch JE, **Keller AC**. (-)-Epicatechin Improves Vasoreactivity and Mitochondrial Respiration in Thermoneutral-Housed Wistar Rat Vasculature. Nutrients. 2022 Mar 5;14(5). doi: 10.3390/nu14051097. PubMed PMID: 35268072; PubMed Central PMCID: PMC8912787.
b. Chun JH, Henckel MM, Knaub LA, Hull SE, Pott GB, Ramirez DG, Reusch JE, **Keller AC**. (-)-Epicatechin Reverses Glucose Intolerance in Rats Housed at Thermoneutrality. Planta Med. 2022 Aug;88(9-10):735-744. doi: 10.1055/a-1843-9855. Epub 2022 Jul 1. PubMed PMID: 35777366; PubMed Central PMCID: PMC9343939.
c. **Keller AC**, Hull SE, Hanan E, Johnston A, Knaub LA, Chun JH, Walker L, Nozik-Grayck E, Reusch JEB. (–)-Epicatechin Modulates Mitochondrial Redox in Vascular Cell Models of Oxidative Stress. Oxid Med Cell Longev. Volume 2020, Article ID 6392629, doi.org/10.1155/2020/6392629.
d. **Keller AC**, Knaub LA, McClatchey PM, Connon CA, Bouchard R, Miller MW, Geary KE, Walker LA, Klemm DJ, Reusch JE. Differential Mitochondrial Adaptation in Primary Vascular Smooth Muscle Cells from a Diabetic Rat Model. Oxid Med Cell Longev. 2016;2016:8524267. doi: 10.1155/2016/8524267. Epub 2016 Jan

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1hawjzMPlmaQY/bibliography/public/