BIOGRAPHICAL SKETCH

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NAME: Good, Miranda Elizabeth

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

POSITION TITLE: Assistant Professor of Medicine

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 Arizona, Tucson, AZ	BS	05/2009	Physiology
University of Arizona, Tucson, AZ	PhD	09/2014	Physiological Sciences
University of Virginia, Charlottesville, VA	Post-doc	12/2019	Cardiovascular Physiology

A. Personal Statement

I am a new assistant professor and investigator in the Molecular Cardiology Research Institute (MCRI) at Tufts Medical Center. As a post-doctoral fellow at the University of Virginia Robert M. Berne Cardiovascular Research Center in Dr. Brant Isakson's Lab, I was awarded a K99/R00 grant from the NHLBI in 2018. This grant was broadly focused on cerebral ischemia, with a focus on the role of Pannexin1 (Panx1; an ATP release channel) in the cerebral vasculature. I transitioned to the R00 phase and started my lab in the MCRI in January 2020. My lab takes an interdisciplinary approach encompassing fundamental molecular and cellular biology, *in vivo* state-of-the-art imaging technologies, and *in vivo* pathophysiological models to further our long-term research goal to understand how blood flow regulation and inflammation contribute to the etiology of neurological diseases and to identify novel targets, such as endothelial Panx1, for therapeutic intervention.

We have recently found that endothelial Panx1 regulates cerebral arterial myogenic tone, and thus cerebral blood flow, and venous inflammation (Good et al, 2018, *JCI Insight*), which are dysregulated in ischemic stroke (R00 grant). This work has found that increased Panx1 expression, specifically in endothelial cells, is detrimental to ischemic stroke outcome, resulting in increased vasoconstriction, reduced recovery of cerebral blood flow and exacerbated inflammatory response specifically in female mice (manuscript in preparation). Furthermore, we have identified a vital role for endothelial Panx1 in contributing to the breakdown of the peripheral vascular barrier in response to sepsis (Maier-Begandt, et al 2021, *Sci Signal*). Increased mortality from ischemic stroke is observed in Alzheimer's Disease patients, possibly due to preexisting cerebral vascular dysfunction; therefore, we have begun investigating the detrimental role of cerebral endothelial Panx1 in ischemic stroke outcome in Alzheimer's Disease (R21 Grant). Overall, our studies have revealed important roles for endothelial cell Panx1 in regulating neurological diseases.

Ongoing funded projects that I would like to highlight include:
R00-HL143165 NHLBI
Good (PI)
04/01/2020-03/31/2024 (1 yr no cost extension)
Title: Vascular Pannexin 1 in Ischemic Stroke

R21-AG075796 NIA
Good (PI)
08/01/2022-07/31/2024
Role: Principal Investigator
Title: Endothelial Pannexin1 in Alzheimer's Disease

Publications that I would like to highlight include:

a. **Good ME**, Eucker SA, Li J, Bacon HM, Lang SM, Butcher JT, Johnson TJ, Gaykema RP, Patel MK, Zuo Z, Isakson BE. (2018). Endothelial cell Pannexin1 modulates severity of ischemic stroke by regulating cerebral inflammation and myogenic tone. *JCI Insight*. 3(6). PMID: 29563335. PMCID: PMC5926909.
   - Editor's Pick for *JCI This Month*, April 2018 (https://www.jci.org/this-month/2018/4)

b. **Good ME***, Chiu YH*, Poon IKH*, Medina C, Butcher JT, Mendu SK, DeLalio LJ, Lohman AW, Leitinger N, Barrett E, Lorenz UM, Desai BN, Jaffe IZ, Bayliss DA, Isakson BE#, Ravichandran KS#. (2018). Pannexin 1 channels as an unexpected new target of the anti-hypertensive drug spironolactone. *Circ Res.* 122(4): 606-615. PMID: 29237722. PMCID: PMC5815904.
   - * Co-First Authors; # Co-Corresponding Authors.

c. Maier-Begandt D, Comstra HS, Molina SA, Krüger N, Ruddiman CA, Chen YL, Chen X, Biwer LA, Johnstone SR, Lohman AW, **Good ME**, DeLalio LJ, Hong K, Bacon HM, Yan Z, Sonkusare SK, Koval M, Isakson BE. (2021). A venous-specific purinergic signaling cascade initiated by Pannexin 1 regulates TNFα-induced increases in endothelial permeability. *Sci Signal*. 14(672): eaba2940. PMID: 33653920. PMCID: PMC8011850.

d. **Good ME***, Young AP, Wolpe AG, Ma M, Hall PJ, Duffy CK, Aronovitz MJ, Martin GL, Blanton RM, Leitinger N, Johnstone SR, Wolf MJ, Isakson BE. (2021). Endothelial pannexin 1 regulates cardiac response to myocardial infarction. *Circ Res*. 128(8): 1211-13. PMID: 33641341. PMCID: PMC8049979.
   - * Corresponding Author.

B. Positions, Scientific Appointments, and Honors

Positions and Employment:

2023–present	Graduate Biomedical Sciences Member, Neuroscience Program, Tufts University
2022–present	Graduate Biomedical Sciences Member, Pharmacology Program, Tufts University
2021–present	Secretary, Microcirculation Society (2-year position)
2020–present	Investigator, Molecular Cardiology Research Institute, Tufts Medical Center, Boston, MA
2020–present	Assistant Professor of Medicine, Tufts University School of Medicine, Boston, MA
2017–present	Member, International Society of Neuroimmunology (ISNI)
2015–present	Member, Microcirculatory Society (MCS)
2015–present	Member, North American Vascular Biology Organization (NAVBO)
2014 – 2019	Postdoctoral Fellow, Robert M. Berne Cardiovascular Research Center, University of Virginia, Charlottesville, VA
2014–present	Member, American Physiological Society
2013–present	Member, American Heart Association
2009 – 2014	Graduate Student Researcher, Department of Physiological Sciences, University of Arizona, Tucson, AZ
2007 – 2009	Undergraduate Student Researcher, Department of Physiology, University of Arizona, Tucson, AZ

Academic and Professional Honors:

2023	Early Career Investigator Travel Award, European Society for Microcirculation and The Microcirculatory Society, Aarhus, Denmark
2022	Early Career Researcher Presenter at the UC Davis Cardiovascular Symposium, UC Davis, Davis, CA
2021	Top 10 finalist for the Charleston Conference on Alzheimer's Disease New Vision Grant
2021	Nominated and voted in as Secretary of the Microcirculatory Society (reelected for second term)
2019	Cardiovascular Section Outstanding Postdoctoral Trainee Award Finalist, Second Place, Experimental Biology, Orlando, FL
2018	Pappenheimer Postdoctoral Travel Award, Microcirculatory Society Annual Meeting, Experimental Biology, San Diego, CA
2018	Microcirculatory Society Travel Award for Vascular Biology 2018, Newport, RI
2017	Pappenheimer Postdoctoral Travel Award, MCS Annual Meeting, Experimental Biology, Chicago, IL
2017	Selected for Oral Presentation at the International Gap Junction Conference, Glasgow, UK
2017	Best Poster Award at the International Gap Junction Conference, Glasgow, UK
2016	NAVBO Travel Award, International Vascular Biology Meeting, Boston, MA
2016	Selected for an Oral Presentation at the International Pannexin Conference, Charlottesville VA

2015 Selected for Oral Presentation, International Gap Junction Conference, Valparaiso, Chile
2014 Herbert E. Carter Travel Award, University of Arizona
2014 Selected for Oral Presentation, Experimental Biology Annual Meeting, San Diego, CA
2013 Graduate and Professional Student Council Travel Grant Award, University of Arizona
2009 Graduated summa cum-laude, University of Arizona
2009 Selected for Oral Presentation, International Gap Junction Conference, Sedona, AZ

C. Contributions to Science

1) **Endothelial cell Pannexin1 regulation of vascular function**: The major focus of my recent research has been identifying the role of endothelial cell Pannexin1 in regulating vascular function following injury. I have focused on the roles of vascular Pannexin1 during ischemia/reperfusion injuries. We are continuing to understand the mechanism by which Pannexin1 regulates vascular tone and inflammation. Endothelial cell Panx1 has emerged as a novel target in tumor necrosis factor alpha (TNFα)-driven endothelial permeability and ischemia/reperfusion injuries in multiple organs, including brain, lung and heart. In the brain, I have found that deletion of endothelial Pannexin1 reduces pressure-induced vasoconstriction in cerebral arteries and reduces post-ischemic stroke infiltration of leukocytes and infarct size. These data suggest endothelial Pannexin1 regulates post-ischemic stroke injury through both an arterial and venous-dependent mechanism, which could provide novel therapeutic targets. This work is the basis for my funded K99/R00 NHLBI grant. We have also identified vital inflammatory-mediated roles for EC Panx1 in ischemic injury in the heart and lungs. The implications of these findings are twofold: 1) endothelial Panx1 provides a pharmacological target for ischemic injuries throughout the body and further work is needed to understand the arterial vs venous roles of endothelial Panx1 and 2) endothelial Panx1 may also contribute to the etiology of neurological disorders associated with vascular dysfunction, such as Alzheimer's Disease and Vascular Induced-Dementia.

Peer-reviewed Publications

a. **Good ME***, Young AP, Wolpe AG, Ma M, Hall PJ, Duffy CK, Aronovitz MJ, Martin GL, Blanton RM, Leitinger N, Johnstone SR, Wolf MJ, Isakson BE. (2021). Endothelial pannexin 1 regulates cardiac response to myocardial infarction. *Circ Res*. 128(8): 1211-13. PMID: 33641341. PMCID: PMC8049979.
    1. * Corresponding Author.
b. Maier-Begandt D, Comstra HS, Molina SA, Krüger N, Ruddiman CA, Chen YL, Chen X, Biwer LA, Johnstone SR, Lohman AW, **Good ME**, DeLalio LJ, Hong K, Bacon HM, Yan Z, Sonkusare SK, Koval M, Isakson BE. (2021). A venous-specific purinergic signaling cascade initiated by Pannexin 1 regulates TNFα-induced increases in endothelial permeability. *Sci Signal*. 14(672): eaba2940. PMID: 33653920. PMCID: PMC8011850.
c. **Good ME**, Eucker SA, Li J, Bacon HM, Lang SM, Butcher JT, Johnson TJ, Gaykema RP, Patel MK, Zuo Z, Isakson BE. (2018). Endothelial cell Pannexin1 modulates severity of ischemic stroke by regulating cerebral inflammation and myogenic tone. *JCI Insight*. 3(6). PMID: 29563335. PMCID: PMC5926909.
    1. Editor's Pick for *JCI This Month*, April 2018 (https://www.jci.org/this-month/2018/4)
d. Sharma AK, Charles EJ, Zhao Y, Narahari AK, Baderdinni PK, **Good ME**, Lorenz UM, Kron IL, Bayliss DA, Ravichandran KS, Isakson BE, Laubach VE. (2018) Pannexin1 channels on endothelial cells mediate vascular inflammation during lung ischemia-reperfusion injury. A*m J Physiol Lung Cell Mol Phys*. 315(2): L301-L312. PMID: 29745255. PMCID: PMC29745255.

2) Smooth muscle cell Pannexin1 regulation of vascular function: I have done substantial work in identifying the role of Pannexin1 in regulating to hypertension. We have found that smooth muscle cell Pannexin1, not endothelial cell Pannexin1, contributes to regulation of peripheral blood pressure. In smooth muscle cells, Pannexin1 is activated downstream of α-adrenergic receptor activation, which results in src-mediated phosphorylation of Pannexin1 and activation of vasoconstrictive mechanisms. Interestingly, Pannexin1-caveolin 1 interaction, which localizes Pannexin1 to the membrane for activation downstream of the α-adrenergic receptor, is necessary for Pannexin1 to contribute to regulation of peripheral blood pressure. Using our novel human Pannexin1 overexpressing mice crossed with a smooth muscle cell cre, we find that expression level of smooth muscle Pannexin1 regulates sympathetic nerve-driven vasoconstriction. In collaboration with the Pannexin Interest Group at the University of Virginia, we identified

spironolactone, which is currently used as an anti- hypertensive, as a potent novel inhibitor of Pannexin1.

Peer-reviewed Publications

a. Dunaway LS, Billaud M, Macal E, **Good ME**, Medina CB, Lorenz U, Ravichandran K, Koval M, Isakson BE. (2023). Amount of Pannexin 1 in Smooth Muscle Cells Regulates Sympathetic Nerve-Induced Vasoconstriction. *Hypertension*. 80(2): 416-25. PMID: 36448464. PMCID: PMC9851955.
b. DeLalio LJ, Billaud M, Ruddiman CA, Johnstone SR, Butcher JT, Wolpe AG, Jin X, Keller TCS 4th, Keller AS, Rivière T, **Good ME**, Best AK, Lohman AW, Swayne LA, Penuela S, Thompson RJ, Lampe PD, Yeager M, Isakson BE. (2019). Constitutive SRC-mediated phosphorylation of pannexin 1 at tyrosine 198 occurs at the plasma membrane. *J Biol Chem.* 294(17): 6940-6956. PMID: 30814251. PMCID: PMC6497939.
c. **Good ME***, Chiu YH*, Poon IKH*, Medina C, Butcher JT, Mendu SK, DeLalio LJ, Lohman AW, Leitinger N, Barrett E, Lorenz UM, Desai BN, Jaffe IZ, Bayliss DA, Isakson BE#, Ravichandran KS#. (2018). Pannexin 1 channels as an unexpected new target of the anti-hypertensive drug spironolactone. *Circ Res.* 122(4): 606-615. PMID: 29237722. PMCID: PMC5815904.
    1. * Co-First Authors; # Co-Corresponding Authors.
    2. Editorial: Huke S. (2018). Pannexin Channel Inhibition: An Evolving Target to Lower Blood Pressure? *Circ Res*. 122(4): 543-545. PMID: 29449359.
d. DeLalio LJ, Keller AS, Chen J, Boyce AKJ, Artamonov M, Askew-Page HR, Keller TCS 4th, Johnstone SR, Weaver RB, **Good ME**, Murphy S, Best AK, Mintz EL, Penuela S, Greenwood I, Machado RF, Somlyo AV, Swayne LA, Minshall R, Isakson BE. (2018) Interaction between Pannxein 1 and Caveolin-1 in smooth muscle can regulate blood pressure. *Arter Thromb Vasc Biol*. 38(9): 2065-2078. PMID: 30026274. PMCID: PMC6202122.

3) **Regulation of vascular function**: During my post-doctoral work, I collaborated on projects focused on the regulation of the microvasculature. In particular, my contributions included my expertise in vasoreactivity using both animal and human vessels and radiotelemetry blood pressure analysis in mice. These projects have resulted in a number of novel findings (including but not limited to): 1) eNOS in endothelial cells and red blood cells differentially regulate blood pressure; 2) circulating extracellular vesicles regulate vascular function in normotension, which is impaired in hypertension; and 3) endothelial Fto, a gene associated with obesity, is a regulator in the development of obesity-induced hypertension and vasoconstriction. 4) non-endoplasmic reticulum-based calreticulin, which traditionally sequesters calcium in the endoplasmic reticulum, regulates the endothelial cell feedback mechanism following alpha adrenergic mediated vasoconstriction;

Peer-reviewed Publications

a. Leo F, Suvorava T, Heuser SK, Li J, LoBue A, Barbarino F, Piragine E, Schneckmann R, Hutzler B, **Good ME**, Fernandez BO, Vornholz L, Rogers S, Doctor A, Grandoch M, Stegbauer J, Weitzberg E, Feelisch M, Lundberg JO, Isakson BE, Kelm M, Cortese-Krott MM. (2021). Red Blood Cell and Endothelial eNOS Independently Regulate Circulating Nitric Oxide Metabolites and Blood Pressure. *Circulation*. 144(11):870:89. PMID: 34229449. PMCID: PMC8529898.
b. **Good ME**, Musante L, La Salvia S, Howell NL, Carey RM, Le TH, Isakson BE, Erdbrügger U. (2020). Circulating extracellular vesicles in normotension restrain vasodilation in resistance arteries. *Hypertension*. 75(1):218-228. PMID: 31760883. PMCID: PMC7158164.
    1. Editorial: Bagher, P Extracellular Vesicles: How a Circulating Biomarker Can Double As a Regulator of Blood Pressure. *Hypertension*. 2020; 75(1):40-43. doi: 10.1161/ HYPERTENSIONAHA.119.13549. Epub 2019 Nov 25. PMID: 31760887
c. Krüger N, Biwer LA, **Good ME**, Ruddiman CA, Wolpe AG, DeLalio LJ, Murphy S, Macal EH Jr, Ragolia L, Serbulea V, Best AK, Leitinger N, Harris TE, Sonkusare SK, Gödecke A, Isakson BE. (2020). Loss of endothelial Fto antagonizes obesity-induced metabolic and vascular dysfunction. *Circ Res*. 126(2): 232-242. PMID: 31801409. PMCID: PMC7007767.
d. Biwer LA, **Good ME**, Hong K, Patel RK, Michalak M, Agrawa lN, Looft-Wilson R, Sonkusare SK, Isakson BE. (2018). Non-endoplasmic reticulum based calreticulin can coordinate heterocellular calcium signaling and vascular function. *Arterioscler Thromb Vascu Biol*. 38(1): 120-130. PMID: 29122814.

PMCID: PMC5746467.

4) **Connexin-dependent regulation of proliferation**: My undergraduate and graduate contributions were focused on the channel properties of Cx37 and the role of Cx40 in post-ischemic vascular remodeling. Cx37 is found to be growth suppressive in endothelial cells and I found that a functional Cx37 channel is necessary for Cx37-depednent growth suppression; hemichannel function was not sufficient for Cx37- dependent growth suppression. In addition, I found that a different connexin isoform, Cx40, plays an important role in regulating the inflammatory response following an ischemic insult independent of gender. This work on Cx40 is currently in preparation for submission.

Peer-reviewed Publications

a. Begandt D*, **Good ME***, Keller AS, DeLalio LJ, Rowley C, Isakson BE, Figueroa, XF. (2017). Pannexin channel and connexin hemichannel expression in vascular function and inflammation. *BMC Cell Biology*. 18(Suppl1):2. PMID: 28124621 PMCID: PMC5267334.
    1. * authors contributed equally
b. **Good ME**, Ek Vitorin JF, Burt JM. (2014). Stuctural determinants and proliferative consequences of connexin 37 hemichannel function in insulinoma cells. *J Biol Chem*. 289(44): 30379-86. PMCID: PMC4215222.
c. **Good ME**, Ek Vitorin JF, Burt JM. (2012). Extracellular loop cysteine mutant of Cx37 fails to suppress proliferation of rat insulinoma cells. *J Membr Biol*. 245(7): 369-80. PMCID: PMC3527626.
d. **Good ME**, Nelson TK, Simon AM, Burt JM. (2011). A functional channel is necessary for growth suppression by Cx37. *J Cell Science*. 124: 2448-56. PMCID: PMC3124374 PMCID: PMC3124374.

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1Ls1r6mm6l9QO/bibliography/public/