BIOGRAPHICAL SKETCH

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NAME: Ng, Hooi Hooi

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

POSITION TITLE: American Heart Association Postdoctoral Fellow

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
RMIT University, Australia	BBiomedSc	12/2011	Biomedicine
RMIT University, Australia	BBiomedSc (Hons)	12/2012	Vascular Physiology
The University of Melbourne, Australia	PhD	03/2017	Vascular Physiology
Florida International University, USA	Postdoctoral	Present	Cardiovascular

A. Personal Statement

My research interest centers around identifying novel therapeutic targets for cardiovascular diseases, with an emphasis on the regulation of vascular function. One of my primary research interests is on investigating novel therapeutic interventions for diabetes-related vascular complications. Vascular lesions are a common pathological process in diabetic patients, and contribute to the increase in morbidity and mortality of diabetes-related complications. The ultimate goal of my research is to identify novel therapeutic targets and treatment strategies to improve overall cardiovascular health outcomes in patients. My undergraduate Honours work identified key signaling targets of a gasotransmitter, hydrogen sulfide, in the vasculature under oxidative stress conditions. I followed this area of research during my PhD to examine the role of a naturally occurring peptide hormone, relaxin, in diseased blood vessels. During my graduate research, I unraveled the therapeutic potential of relaxin to ameliorate diabetes-induced vascular dysfunction, and contributed to the landmark discovery of relaxin-prostaglandin interactions in the vasculature under both health and disease conditions. I have since established a strong record of research in delineating the mechanisms of relaxin action in the vascular system, as shown through a track record of publications.

My postdoctoral research builds upon this record, where I am currently studying the fundamental mechanisms that lead to vascular calcification, and test the therapeutic effects of a small molecule compound that targets the relaxin receptor in animal models of chronic kidney disease and atherosclerosis. The presence of hydroxyapatite crystals in cardiovascular tissues is now accepted as the most significant predictor of coronary artery disease and heart failure. Despite increasing incidence of chronic disease-related vascular complications and massive healthcare costs related to cardiovascular calcification, effective therapeutic strategies remain elusive. Currently, there are no approved pharmacotherapies for the treatment of vascular calcification, in part due to the delayed onset of symptoms once a detectable calcification has occurred. The goal of my postdoctoral research is to address this significant knowledge gap and provide important insights related to the therapeutic potential of relaxin receptor agonists for the treatment of cardiovascular calcification, particularly in the context of chronic kidney disease and atherosclerosis.

I have had the opportunity to work in a unique environment with interdisciplinary expertise in vascular biology and biomedical engineering. My experience in interdisciplinary research allows me to cultivate new conceptual and technical training in cardiovascular research. During my postdoctoral career, I have attracted over $150,000 in competitive funding, which provided me the opportunity to generate solid preliminary data for future application of "pathway to independence" type grants to launch my independent academic career in cardiovascular research.

B. Positions and Honors

Positions and Employment

2017-2018 Postdoctoral Associate, Department of Human & Molecular Genetics, Herbert Wertheim College of Medicine, Florida International University, USA

2017-2019 Honorary Fellow, School of BioSciences, Faculty of Science, The University of Melbourne, Australia

2019- American Heart Association Postdoctoral Fellow, Department of Biomedical Engineering, Department of Human & Molecular Genetics, Florida International University, USA

Professional Memberships, Service and Other Experience

2012-2013 Student Member, Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT)

2013-2016 Student Member, Australian Vascular Biology Society (AVBS)

2014-2015 Student Member, Australian Society for Medical Research (ASMR)

2016-2019 Student Member, Australian Physiological Society (AuPS)

2017- Affiliate Member, National Postdoctoral Association (NPA)

2017- Early Career Member, American Heart Association (AHA)

2018-2019 At Large Introductory Member, Graduate Women in Science (GWIS)

2019- Trainee Member, North American Vascular Biology Organization (NAVBO)

2016- Ad-hoc journal reviewer for Cellular Physiology and Biochemistry, Biomolecules, Antioxidants, International Journal of Molecular Sciences, Nutrients, Frontiers in Pharmacology, Journal of Diabetes Research, Journal of Molecular Histology, Prostaglandins, Leukotrienes & Essential Fatty Acids, ACS Pharmacology & Translational Science

2017 Abstract reviewer for ASMR student symposium

2017- Abstract reviewer for Annual Biomedical Research Conference for Minority Students (ABRCMS)

2017-2018 Oral presentations judge for MARC U*STAR & NIGMS RISE graduate student symposium at Florida International University

2018 Invited early career small grant reviewer for Diabetes UK

2019 Poster presentations judge for Graduate Student Appreciation Week Scholarly Forum at Florida International University

2019 Oral presentation moderator for McNair Scholars Research Conference at Florida International University

2014-2015 Sub-Committee Member (administration coordinator), 6th ASMR student symposium

2017-2018 Sub-Committee Member (travel & childcare awards), 16th NPA annual conference

2018 Session co-chair "Circulatory and Vascular Actions" 8th International Conference on Relaxin & Related Peptides, Cabo San Lucas, Mexico

2018-2019 Sub-Committee co-chair (travel & childcare awards), 17th NPA annual conference

2019 Panelist "The Future of Cardiovascular Research and Medicine", 2nd Annual Miami Heart Day Symposium, Florida International University

Honors and Awards

2010	Top student in Biochemistry and Molecular Biology, RMIT University
2012	ASCEPT Travel Award
2012	Vice-Chancellor's List Award, RMIT University
2013-2016	Melbourne International Research Scholarship, The University of Melbourne
2013-2016	Melbourne International Fee Remission Scholarship, The University of Melbourne
2015	British Journal of Pharmacology Young Investigator Travel Award
2015	F H Drummond Travel Award, The University of Melbourne
2016	AuPS Travel Award
2016-2017	Albert Shimmins Postgraduate Writing-Up Award, The University of Melbourne
2018	B & J Steinetz Memorial Travel Award
2019	Postdoctoral Fellowship, AHA

C. Contributions to Science

1. Vasoprotective Actions of Hydrogen Sulfide (H_2S) in Diabetes

Recent evidence has emerged revealing the role of H_2S in many physiological and pathophysiological processes, and extensive efforts have been made to uncover the benefit of H_2S in a wide range of diseases. My undergraduate Honours work provided the first evidence that H_2S is an antioxidant in intact blood vessels, and served as a 'proof-of-principle' evidence for future *in vivo* studies in animal models where there is increased oxidative stress. This finding subsequently led to the investigation of the therapeutic potential of H_2S in diabetes. My research demonstrated that chronic treatment with a fast-releasing H_2S donor, NaHS, reversed diabetes-induced vascular dysfunction in the mouse aorta. This was associated with a reduction in NADPH-dependent superoxide production and restoration of nitric oxide efficacy. These data showed the specific protective effects of NaHS on the vasculature in diabetes, and provided further evidence of the potential role of NaHS to regulate vascular tone under diseased conditions. The data gained from my research confirmed the antioxidant effects of H_2S and laid the foundation for the understanding of the molecular mechanisms and physiological outcomes of H_2S in diabetes.

1. **Ng HH**, Yildiz GS, Ku JM, Miller AA, Woodman OL, Hart JL. Chronic NaHS treatment decreases oxidative stress and improves endothelial function in diabetic mice. *Diab Vasc Dis Res.* 2017; 14: 246-253.
2. Al-Magableh MR, Kemp-Harper BK, **Ng HH**, Miller AA, Hart JL. Hydrogen sulfide protects endothelial nitric oxide function under conditions of acute oxidative stress in vitro. *Naunyn Schmiedebergs Arch Pharmacol.* 2014; 387: 67-74.
3. Streeter E, **Ng HH**, Hart JL. Hydrogen sulfide as a vasculoprotective factor. *Med Gas Res.* 2013; 3: 9.

2. Vasoprotective Actions of Relaxin in Diabetes

My PhD work first demonstrated the vasoactive role of endogenous relaxin in males and that relaxin deficiency increased superoxide production which was at least in part attributed to the reduction in nitric oxide efficacy in the mouse aorta. These findings laid the foundation to study the effects of the recombinant form of relaxin-2 to ameliorate hyperglycemia-induced vascular dysfunction. Cardiovascular complications are the major cause of mortality in patients with diabetes, whereby a dysfunctional endothelium precedes the morphological changes in the progression of diabetes. Although there are multiple therapies to control diabetes, the ultimate goal of these therapies is to lower blood glucose levels for as long as possible after diagnosis. Some of these glucose-lowering drugs, however, fail to prevent the onset of cardiovascular complications, despite their favorable effects on glycemic control. My research demonstrated that relaxin treatment reversed diabetes-mediated endothelial dysfunction in the large and resistance blood vessels of diabetic mice. This was attributed to an increase in nitric oxide-mediated relaxation, normalization of vasoconstrictor prostanoids, and suppression of angiotensin II-evoked contraction. Additionally, relaxin attenuated diabetes-induced

cardiomyocyte hypertrophy and apoptosis in the left ventricle. These mechanistic studies in diabetic mice contributed significantly to the relaxin field and provided a promising treatment strategy to target the relaxin receptor as an intervention to mitigate diabetes-related vascular complications.

1. **Ng HH**, Leo CH, Parry LJ, Ritchie RH. Relaxin as a therapeutic target for the cardiovascular complications of diabetes. *Front Pharmacol.* 2018; 9: 501.
2. **Ng HH**, Leo CH, Prakoso D, Qin CX, Ritchie RH, Parry LJ. Serelaxin treatment reverses vascular dysfunction and left ventricular hypertrophy in a mouse model of Type 1 diabetes. *Sci Rep.* 2017; 7: 39604.
3. **Ng HH,** Leo CH, Parry LJ. Serelaxin (recombinant human relaxin-2) prevents high glucose-induced endothelial dysfunction by ameliorating prostacyclin production in the mouse aorta. *Pharmacol Res.* 2016; 107: 220-228.
4. **Ng HH,** Jelinic M, Parry LJ, Leo CH. Increased superoxide production and altered nitric oxide-mediated relaxation in the aorta of young but not old male relaxin-deficient mice. *Am J Physiol Heart Circ Physiol.* 2015; 309: H285-96.

3. Relaxin Receptor as a Therapeutic Target for Fibrosis and Vascular Calcification

A plethora of studies has identified relaxin as a potent anti-fibrotic agent in various animal models of fibrosis. There are, however, several drawbacks for relaxin to be used therapeutically for chronic diseases due to its pharmacokinetics and high cost to produce the recombinant peptide. Discovery of a potent and selective agonist of the relaxin receptor, ML290, provides an alternative to the endogenous ligand. My initial work demonstrated that ML290 treatment effectively suppressed TGF-β1-induced myofibroblast activation on a hepatic stellate cell line, and significantly attenuated aberrant extracellular matrix remodeling in the kidneys of a mouse model of acute kidney injury. My current work focuses on the potential of ML290 to mitigate vascular calcification in chronic kidney disease and atherosclerosis mouse models. The presence of calcium mineral in cardiovascular tissues is now accepted as the most significant predictor of coronary artery disease and heart failure. Despite increasing incidence of calcification-related cardiovascular diseases, effective therapeutic strategies remain elusive. My research demonstrated the potent action of ML290 to mitigate vascular calcification *in vitro*, by reversing osteogenic phenotype in the smooth muscle cells. My goals for these projects are to demonstrate therapeutic efficacies of ML290 to attenuate vascular calcification, and delineate the pathological processes that initiated calcification in these mouse models. These studies will lead to the discovery of clinically-viable therapies for the treatment of vascular calcification that can benefit the rapidly increasing patient population.

1. **Ng HH**, Medina D, Bakhshian Nik A, Hutcheson JD. Cellular contraction is required for hyperglycemia-induced vascular calcification. *Circulation.* 2019; 140: A16072-A16072.
2. **Ng HH**, Shen M, Samuel CS, Schlossmann J, Bennett RG. Relaxin and extracellular matrix remodeling: Mechanisms and signaling pathways. *Mol Cell Endocrinol.* 2019; 487: 59-65.
3. **Ng HH**, Esteban-Lopez M, Agoulnik AI. Targeting the relaxin/insulin-like family peptide receptor 1 and 2 with small molecule compounds. *Mol Cell Endocrinol.* 2019; 487: 40-44.
4. Kaftanovskaya EM, **Ng HH**, Soula M, Rivas B, Myhr CB, Ho BA, Cervantes B, Shupe TD, Devarasetty M, Hu X, Xu X, Patnaik S, Wilson KJ, Barnaeva E, Ferrer M, Southall NT, Marugan JJ, Bishop CE, Agoulnik IU, Agoulnik AI. Therapeutic effects of a small molecule agonist of the relaxin receptor ML290 in liver fibrosis. *FASEB J.* 2019; 33: 12435-12446.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/hooi%20hooi.ng.1/bibliography/public/

D. Research Support

Ongoing

Florida International University Foundation
Herbert Wertheim College of Medicine Pilot Grant **Ng H.H. (PI)** 06/01/2020-05/31/2021
"Small molecule agonist of the human relaxin receptor for treatment of vascular calcification"
To investigate the preventative and therapeutic potentials of a relaxin receptor agonist to limit the progression of chronic kidney disease-mediated medial calcification.

19POST34380255
AHA Association Wide Postdoctoral Fellowship **Ng H.H. (PI)** 01/01/2019-12/31/2020
"Targeting relaxin receptor for the treatment of diabetes-induced cardiovascular calcification"
To investigate the therapeutic potentials of a relaxin receptor agonist, ML290, to mitigate hyperglycemia-induced vascular calcification *in vitro* and *in vivo*.