PUBLIC DEFENSE
OF DOCTORAL DISSERTATION
TRANSLATIONAL BIOLOGY,
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GRADUATE PROGRAM

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"EFFECTS OF PERFUSATE COMPOSITION (NA+ AND CA2+) ON CARDIAC ELECTRICAL AND MECHANICAL FUNCTION IN THE ISOLATED LANGENDORFF-PERFUSED HEART"

RYAN KING

POELZING LAB
FRALIN BIOMEDICAL RESEARCH INSTITUTE AT VTC

TRANSLATIONAL BIOLOGY, MEDICINE, AND HEALTH GRADUATE PROGRAM

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CONTACT THE TRANSLATIONAL BIOLOGY, MEDICINE, AND HEALTH GRADUATE PROGRAM:

MICHELLE THEUS, PH.D.
Co-Director, TBMH
Associate Professor,
Biomedical Sciences and Pathobiology
(540) 231-0909
mtheus@vt.edu

STEVEN POELZING, PH.D.
Co-Director, TBMH
Associate Professor,
Fralin Biomedical Research Institute
(540) 526.2108
poelzing@vtc.vt.edu

TBMH.VT.EDU

RYAN KING

- *HOMETOWN:* Gastonia, NC
- *UNDERGRADUATE DEGREE:*
  Biology
  UNC- Chapel Hill
- *MENTOR:* Steven Poelzing, Ph.D.
- *COMMITTEE MEMBERS:*
  Rob Gourdie, Ph.D.
  Rob Grange, Ph.D.
  Sarah Henrickson Parker, Ph.D.
- *EX OFFICIO COMMITTEE MEMBERS:*
  Michael J. Friedlander, Ph.D.
  Michelle Theus, Ph.D.
  Steven Poelzing, Ph.D.
- *HONORS:*
  - Michael J Quillen Leadership Award
  - Ruth L. Kirschstein Predoctoral (F31) Fellowship
  - Honorable Mention, NSF Graduate Research Fellows Program
- *SERVICE:*
  - HS&T Student Services Committee
  - RGSA Executive Chair
  - Virginia Tech Order of the Gavel
  - Virginia Tech Board of Visitors (Graduate Representative)

PRESENTATIONS

King DR, Entz II M, Blair G, Crandell I, Hanlon AL, Lin J, Hoeker GS, Poelzing S. Increased Extracellular Sodium and Calcium Modify the Extracellular Potassium and Cardiac Conduction Velocity Relationship in a Langendorff-Perfused Guinea Pig Heart. American Heart Association 2020 Scientific Sessions. ePoster.

Wu X, Hoeker GS, **King DR**, Gourdie R, Weinberg SH, Poelzing S. Increased Extracellular Sodium and Intercellular Cleft Separation Synergistically Prolong Repolarization in the Long-QT Syndrome Type 3. American Heart Association 2020 Scientific Sessions. ePoster.

Padget R, **King DR**, North MD, Tanenbaum MN, Calhoun PJ, Hoeker GS, Poelzing S, Smyth JW. Cardiotropic Adenovirus Increases Arrhythmia Susceptibility During Acute Infection. American Heart Association Basic Cardiovascular Sciences Scientific Sessions, July 2020. Poster.

ABSTRACT

In recent years, scientific rigor and reproducibility has garnered increased attention in both the scientific and public media. In several recent reports, the high attrition rate observed in clinical trials has been attributed to irreproducibility at the preclinical level. Preclinical cardiology is no exception to this rule. In our systematic review of the ex vivo Langendorff-perfused heart, we found methods reporting to be sparse at best, specifically as it pertains to documenting the ex vivo perfusate compositions employed in the Langendorff heart. Previously, our lab has demonstrated that variation in perfusate compositions can unmask disease states in genetically modified animals. In this dissertation, we exploit this concept with a therapeutic end-point in mind. We show that perfusate variation, specifically sodium and calcium elevations, can attenuate conduction slowing associated with severe hyperkalemia. Likewise, elevating sodium is capable of sustaining intrinsic rhythm where hearts would otherwise go asystolic. In doing so, elevated sodium prevents repolarization prolongation in these hearts. Together, these studies would suggest that elevating extracellular sodium, and calcium, should be considered as therapeutic targets in the context of conduction defects. However, when considering the heart's primary role as a pump, we found that elevating sodium depresses cardiac mechanical function. This is both in a healthy and post-ischemic setting. In short, we show that electrolyte variation may influence both cardiac electrophysiology and contraction; however, an improvement in one does not guarantee an improvement in both. Maintaining proper cardiac physiological function is a complex process that is tightly regulated by the ionic makeup of the extracellular environment and in order to improve insights from preclinical studies at the clinical level it is paramount that we, as researchers, properly document employed methodologies as they pertain to perfusate composition.

PUBLICATIONS

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George SA, Hoeker G, Calhoun PJ, Entz II M, Raisch TB, **King DR**, Kahn M, Baker C, Smyth JW, Nielsen MS, Poelzing S. Modulation electrophysiology during metabolic ischemia with perfusate sodium and calcium in guinea pigs. *American Journal of Physiology- Heart and Circulatory Physiology*. 2019;316(4):H849-H861. PMID: 30707595

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