

Autonomic Neural Mechanisms of Cardiopulmonary Regulation

September 2-3, 2020

Virtual Workshop, Zoom meeting

Workshop Goals: The intent of this workshop is to bring together experts in the basic and clinical sciences in addition to individuals familiar with the associated technologies to identify gap areas to help guide future research efforts and foster multi-disciplinary collaborations. The working group will:

- Critically evaluate the current state of knowledge of the roles that the ANS plays in regulation of cardiopulmonary function in health and in pathophysiology of arrhythmias, heart failure and breathing disorders.
- Identify approaches to further developing predictive markers of ANS dysfunction and to precisely target these neural mechanisms with antiarrhythmic, heart failure, pulmonary and sleep disorders therapies, including novel approaches to both subclinical and clinical heart failure and arrhythmia prevention.
- Identify opportunities related to non-pharmacological neuromodulation and device-based therapies.
- Provide a concise, prioritized list of research opportunities based on identified gaps in the field and public health impact.

Organizers: *NHLBI, Division of Cardiovascular Sciences (DCVS):* Olga Tjurmina, PhD, George Sopko, MD MPH, Ravi Balijepalli, PhD
NHLBI, Division of Lung Diseases (DLD): Josh Fessel, MD PhD; Aaron Laposky, PhD; Mike Twery, PhD
NIH, Office of the Director (OD), Office of Strategic Coordination (OSC), Common Fund SPARC Program: Gene Civillico, PhD; Felicia Qashu, PhD; Kristina Faulk

Co-Chairs: Kalyanam Shivkumar, MD PhD, *UCLA*, Reena Mehra, MD, *Cleveland Clinic-CWRU*

Agenda

Wednesday, September 2, 2020

Overviews and Workshop Goals

- 9:00 am* Welcome from NLHBI/OSC Leadership
David Goff, MD, PhD, Director, DCVS, NHLBI, NIH
- 9:10 am Introduction and Charge to Group
Olga Tjurmina, PhD, Program Director, HFAB, DCVS, NHLBI, NIH
- 9:20 am NHLBI Portfolio Review of Autonomic Neural Mechanisms in Cardiopulmonary Research
Olga Tjurmina, PhD, Program Director, HFAB, DCVS, NHLBI, NIH
- 9:30 am State of Science - Autonomic Neural Mechanisms in Cardiopulmonary Research: Challenges and Opportunities
Kalyanam Shivkumar, MD PhD, UCLA
- 9:50 am Overview of Major Gaps in Diagnosis and Treatment of ANS Related Complications in Heart Failure, Arrhythmias and Pulmonary Diseases.
Reena Mehra, MD, Cleveland Clinic-CWRU

10:10 am BREAK

Session 1: Fundamental Mechanisms of Neural Signaling in Development and Progression of Cardiopulmonary Diseases

Moderator: *Beth Habecker, PhD, Oregon HSU*

10:20 am Spinal Cardiac and Pulmonary Afferent/Efferent Reflexes
Irving Zucker, PhD, University of Nebraska

10:30 am Vagal Cardiopulmonary Afferent/Efferent Reflexes
Thomas Taylor-Clark, PhD, University of South Florida

10:40 am Peripheral Neuro-Inflammation in Arrhythmias and Heart Failure
Olujimi Ajijola, MD, PhD, UCLA

10:50 am Sex and Race Differences in Autonomic Neural System Physiology and Pathophysiology
Colleen Clancy, PhD, UC Davis

11:00 am Q&A for Speakers and Discussion
Brief summary by Moderator

11:30 am LUNCH

Session 2: Autonomic Neural System (ANS) Related Pathophysiology of Heart Failure

Moderator: *Peng-Sheng Chen, MD, Cedars-Sinai Medical Center*

12:30 pm Neural Remodeling in Heart Failure: Molecular and Translational Perspectives
Beth Habecker, PhD, Oregon HSU

12:40 pm Pathophysiology of Baroreceptor Reflex and Cardiac Control in Heart Failure
Mark W. Chapleau, PhD, University of Iowa

12:50 pm Stress, Catecholamines, and Acute Cardiac Pathophysiology
David Goldstein, MD PhD, CNP, DIR, NINDS, NIH

1:00 pm Device Based Neuromodulation and Neurotherapeutics in Heart Failure
Michael Gold, MD, Medical University of South Carolina

1:15 pm Q&A for Speakers and Discussion
Brief summary by Moderator

Session 3: Neuro-Electrophysiologic Contributions to Atrial Arrhythmias

Moderator: *Colleen Clancy, PhD, UC Davis*

1:45 pm Autonomic Regulation of Cardiomyocyte Electrophysiology
Thomas Hund, PhD, Ohio State University

1:55 pm Autonomic Remodeling and Neuroplasticity in Atrial Fibrillation
Rishi Arora, MD, Northwestern University

2:05 pm Glial Cells Role as New Biomarkers and Novel Therapeutic Targets in Atrial Electrophysiology
Chris Meyer, MD, MA, University of Düsseldorf, Germany

2:15 pm Sleep apnea and Neural Mechanisms in Atrial Tachyarrhythmia
Virend Somers, MD, PhD, Mayo Clinic

2:25 pm Neuromodulation and Neurotherapeutics in Atrial Fibrillation
Stavros Stavrakis, MD, PhD, University of Oklahoma

2:40 pm Q&A for Speakers and Discussion
Brief summary by Moderator

3:10 pm BREAK

Session 4: Neuro-Electrophysiologic Aspects of Ventricular Arrhythmias
Moderator: *Chris Meyer, MD, MA, University of Düsseldorf, Germany*

3:20 pm Autonomic Control of Ventricular Electrophysiology
Crystal Ripplinger, PhD, UC Davis

3:30 pm Assessment of Autonomic Nervous System Function in Ventricular Arrhythmia and Sex and Race Differences
Peng-Sheng Chen, MD, Cedars-Sinai Medical Center

3:40 pm Circadian Variations of Ventricular Tachyarrhythmias and Sudden Cardiac Death
Brian Delisle, PhD, University of Kentucky

3:50 pm Autonomic Neuromodulation and Neurotherapeutics for Ventricular Arrhythmia and Prevention of Sudden Cardiac Death
Robert Harvey, PhD, University of Nevada

4:05 pm Q&A for Speakers and Discussion
Brief summary by Moderator

4:35 pm Wrap-up of Day 1
Kalyanam Shivkumar, UCLA, Reena Mehra, Cleveland Clinic-CWRU

4:45 pm Adjourn

Thursday, September 3, 2020

9:00 am Recap and Charge for the Day
Kalyanam Shivkumar, UCLA, Reena Mehra, Cleveland Clinic-CWRU

9:15 am Summary of the SPARC Program and Data Resource Center Portal
Gene Civillico, PhD, Program Leader, SPARC Program, DPCPSI, OSC, OD, NIH

Session 5: Autonomic Nervous System Alterations in Cardiopulmonary Related Sleep Disorders

Moderator: Susan Redline, MD, MPH, Brigham and Women's, Harvard

- 9:30 am Wake and Sleep State Dependent Cardiopulmonary Autonomic Neural Mechanisms
Richard Verrier, PhD, Beth Israel Deaconess Med Center, Harvard
- 9:40 am Sleep and Circadian Patterning and Autonomic Neural Biomarkers from
Electrocardiographic Signal Processing and Monitoring Technologies
Jeffrey Goldberger, MD, MBA, University of Miami
- 9:50 am Central Autonomic Control Circuits: Substrates for Neuromodulation by Upper Airway
Afferent Systems
Donald Bolser, PhD, University of Florida
- 10:05 am Sleep Disordered Breathing Endophenotypes and Autonomic Nervous System Control
in Cardiac Arrhythmia and Heart Failure
Susan Redline, MD, MPH, Brigham and Women's, Harvard
- 10:15 am Q&A for Speakers and Discussion
Brief summary by Moderator
- 10:45 am BREAK**
- Session 6: Neurophysiologic Mechanisms in Pulmonary Diseases and Interaction with
Cardiac Function**
Moderator: Thomas Taylor-Clark, PhD, University of South Florida
- 10:55 am Autonomic Neural Mechanisms and Neurotherapeutics in Right Ventricular
Dysfunction and Pulmonary Hypertension
Louis Handoko, MD, PhD, VU University Medical Center, Amsterdam, Netherlands
- 11:05 am Neural Mechanisms Underlying Airway Narrowing and Hyperresponsiveness in
Asthma
Bradley Udem, PhD, Hopkins University
- 11:15 am Lessons Learned from Autonomic Cardiopulmonary Denervation/Alterations in Heart
Transplantation
Marc Simon, MD, University of Pittsburgh
- 11:25 am Neural Ablation/Modulation and Targeted Lung Denervation and Cardiopulmonary
Interactions
James Hummel, MD, Yale University
- 11:35 am Q&A for Speakers and Discussion
Brief summary by Moderator
- 12:05 pm BREAK**
- 12:15 pm **Breakout Sessions** (closed sessions)
Two panel discussion groups collaborate and discuss to come up with the identified
gaps in knowledge and a list of preliminary key research opportunities.

- 1:15 pm Working LUNCH & Continue with Breakout Sessions**
- 2:00 pm Summary from the Workshop: Research Gaps and Opportunities**
Shivkumar, UCLA, Mehra, Cleveland Clinic-CWRU
The breakout group leaders present their lists, all participants discuss and prioritize a final list of knowledge gaps and opportunities.
- 3:50 pm Post-Workshop Activities and Closing Remarks**
NHLBI and OD Organizers
- 4:00 pm Adjourn**

* All times are ET