

Understanding the Combined Effects of Environmental Chemical and Non-Chemical Stressors: Atherosclerosis as a Model

April 3-4, 2018

NIEHS Building 101, Rodbell Auditorium
111 TW Alexander Drive, Research Triangle Park, North Carolina

DAY ONE – Tuesday, April 3, 2018

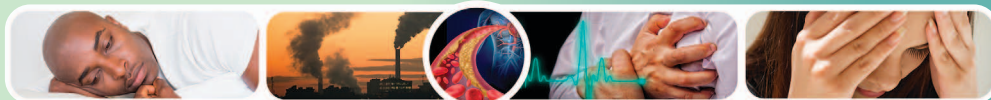
- 7:30 a.m. Registration**
- 8:30 a.m. Opening Remarks/Goals of Workshop/Housekeeping Items**
Danielle Carlin, Ph.D., National Institute of Environmental Health Sciences (NIEHS)
- 8:45 a.m. Opening Remarks**
Linda Birnbaum, Ph.D., NIEHS
- 8:55 a.m. Opening Remarks**
David Goff, M.D., Ph.D., National Heart, Lung, and Blood Institute (NHLBI)

Session One: Environmental Chemical Stressors and Atherosclerosis | Moderator: Bill Suk, Ph.D., NIEHS

- 9:05 a.m. Overview of Atherosclerosis and Chemical Stressors**
Wayne Cascio, M.D., U.S. Environmental Protection Agency (EPA)
- 9:25 a.m. Metals and Cardiovascular Disease: Epidemiologic Evidence, Potential Mechanisms, and Opportunities for Prevention**
Ana Navas-Acien, M.D., Ph.D., Columbia University
- 9:45 a.m. Air Pollution and Animal Models of Atherosclerosis**
Jesus Araujo, M.D., Ph.D., University of California, Los Angeles (UCLA)
- 10:05 a.m. Defining Mechanisms of Arsenic-Enhanced Atherosclerosis in Mouse Models**
Koren Mann, Ph.D., McGill University
- 10:25 a.m. Break**

Session Two: Non-Chemical Stressors and Atherosclerosis | Moderator: Catherine Stoney, Ph.D., NHLBI

- 10:40 a.m. Lifestyle Effects on Atherosclerosis**
Filip Swirski, Ph.D., Massachusetts General Hospital
- 11:00 a.m. Atherosclerosis and Non-Chemical Stressors**
Zahi Fayad, Ph.D., Icahn School of Medicine at Mount Sinai
- 11:20 a.m. Novel Biomarkers for Risk Prediction in Coronary Artery Disease**
Arshed Quyyumi, M.D., Emory University
- 11:40 a.m. Dietary Mitigation of Psychosocial Stress Effects on Health in Female Primates**
Carol Shively, Ph.D., Wake Forest University
- Noon LUNCH** (NIEHS Cafeteria)



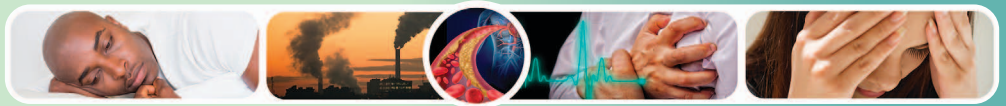
Session Three: Modifying Factors of Atherosclerosis | Moderator: Michelle Olive, Ph.D., NHLBI

- 1:00 p.m.** **Spatiotemporal Trends of Heart Disease**
Michele Casper, Ph.D., Centers for Disease Control and Prevention (CDC)
- 1:20 p.m.** **Genetic/Epigenetic Susceptibility in Atherosclerosis: Importance in Considerations of Chemical and Non-Chemical Stressors**
Cavin Ward-Caviness, Ph.D., EPA
- 1:40 p.m.** **The Interaction of Psychological Stress and Metal Exposures: Effects on Children's Cardiovascular Functioning and Subclinical Cardiovascular Disease**
Brooks Gump, Ph.D., Syracuse University
- 2:00 p.m.** **Interactions Between Chemical Stressors and Diet**
Michael Petriello, Ph.D., University of Kentucky
- 2:20 p.m.** **The Social and Physical Context of Health Behaviors Associated With Atherosclerosis: Parks and Physical Activity**
Deborah Cohen, M.D., RAND Corporation
- 2:40 p.m.** Break

Session Four: Chemical and Non-Chemical Stressors in Atherosclerosis: Can They Be Studied Together?

Moderator: Janice Allen, Ph.D., NIEHS

- 2:55 p.m.** **Air Pollution, Psychosocial Stress, and Subclinical Atherosclerosis: Can We Identify Vulnerable Populations?**
Anjum Hajat, Ph.D., University of Washington
- 3:15 p.m.** **Non-Chemical Stressors as Vulnerabilities for Cardiovascular Disease**
Karina Davidson, Ph.D., Columbia University
- 3:35 p.m.** **Using Adverse Outcome Pathways to Document the Collective Causes of Atherosclerosis**
Stephen Edwards, Ph.D., RTI International
- 3:55 p.m.** **The Current State of Cumulative Risk Assessment**
Glenn Rice, Ph.D., EPA
- 4:15 p.m.** **Group Discussion/Address Additional Questions**
- 5:00 p.m.** **Meeting Adjourned;** Shuttle Takes Participants Back to Hotel
- 6:30 p.m.** **Group Dinner** at Mez Contemporary Mexican Restaurant
5410 Page Road, Durham, North Carolina



DAY TWO – Wednesday, April 4, 2018

7:30 a.m. Registration

8:30 a.m. Opening Remarks/Goals of Workshop/Synthesis of Day 1/ Housekeeping Items
Michelle Olive, Ph.D., NHLBI

8:45 a.m. Environmental Factors in Atherosclerosis: Lessons From Research on Ambient Air Pollutants
Joel Kaufman, M.D., University of Washington

9:05 a.m. Break

9:20 a.m. Breakout Session One: Determining Knowledge Gaps and Future Directions for Research

Breakout Group One: Rodbell A

Moderators: Danielle Carlin, Ph.D., NIEHS, and Jesus Araujo, M.D., Ph.D., UCLA

Breakout Group Two: Rodbell B

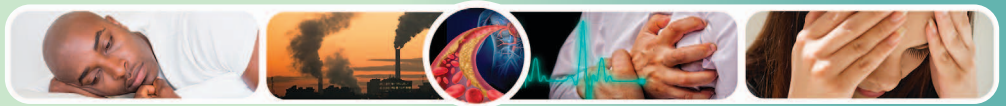
Moderators: Michelle Olive, Ph.D., NHLBI, and Koren Mann, Ph.D., McGill University

Breakout Group Three: Rodbell C

Moderators: Catherine Stoney, Ph.D., NHLBI, and Carol Shively, Ph.D., Wake Forest University

Breakout Session One: Please Address the Following Questions:

- 1) Which environmental chemicals are known to affect key biological mechanisms/pathways leading to atherosclerosis, and which key biological mechanisms/pathways are affected by these chemicals?
- 2) Which non-chemical stressors are known to affect key biological mechanisms/pathways leading to atherosclerosis, and which key biological mechanisms/pathways are affected by these non-chemical stressors?
- 3) Which key biological mechanisms/pathways of atherosclerosis are known to be affected by the combined exposures of chemical and non-chemical stressors?
- 4) What are the qualitative and quantitative (i.e., dose-response) impacts of exposure to the combination of chemical and non-chemical stressors and technical challenges in quantitative assessment of these exposures or impacts?
- 5) What are the types of scientific data (e.g., mechanistic, epidemiological) needed to address underlying knowledge gaps of chemical and non-chemical stressors leading to atherosclerosis?
- 6) What are the new technologies and innovative research approaches that could be leveraged to address these underlying knowledge gaps?



10:30 a.m. Breakout Session Two: Developing an Adverse Outcome Pathway

Breakout Group One: Rodbell A

Moderators: Stephen Edwards, Ph.D., RTI, and Daniel Conklin, Ph.D., University of Louisville

Breakout Group Two: Rodbell B

Moderators: Andrew Rooney, Ph.D., NIEHS, and Karina Davidson, Ph.D., Columbia University

Breakout Group Three: Rodbell C

Moderators: Glenn Rice, Ph.D., EPA, and Changcheng Zhou, Ph.D., University of Kentucky

Breakout Session Two: Please Address the Following Questions:

- 1) What are the biological measurements (e.g., blood pressure, c-reactive protein, cholesterol) that should be used to follow the progression of perturbations associated with chemical and non-chemical stressors to atherosclerosis?
- 2) What are the biological events corresponding to these measurements (i.e., key events)?
- 3) How are these key events causally related (i.e., key event relationships)?
- 4) How would you illustrate the adverse outcome pathway (see attached PowerPoint template)?
- 5) What evidence supports the key event relationships? Components of evidence include biological plausibility and empirical support (i.e., temporal concordance and response/response concordance).
- 6) What additional information is needed (i.e., knowledge gaps) to increase confidence in the existing key event relationships or to complete a pathway?
- 7) What basic, clinical, and epidemiological tools are needed to monitor the pathways?

11:30 a.m. LUNCH (NIEHS Cafeteria)

12:30 p.m. **Breakout Session Two: Developing an Adverse Outcome Pathway (continued)**

1:15 p.m. Break

1:30 p.m. **Report Back to Audience**

Moderator: Cynthia Rider, Ph.D., NIEHS

Breakout Group One (20 minutes)

Breakout Group Two (20 minutes)

Breakout Group Three (20 minutes)

2:30 p.m. **Open Discussion With Audience**

3:00 p.m. **Closing Remarks and Next Steps**

Danielle Carlin, Ph.D., NIEHS, and Michelle Olive, Ph.D., NHLBI

3:30 p.m. **Meeting Adjourned**