



# Atherosclerosis: Lessons Learned and Concepts Challenged

February 4–8, 2018 | Sagebrush Inn & Suites | Taos, New Mexico | USA

## Scientific Organizers:

**Laura F. Michael**, Eli Lilly and Company, USA

**Gerard Pasterkamp**, University Medical Center Utrecht, Netherlands

**Sekar Kathiresan**, Massachusetts General Hospital, USA

*Atherosclerosis is a chronic, systemic disease process whereby fatty deposits, inflammation and fibrosis accumulate in arterial vessel walls. Organ systems, including heart, brain, kidneys, as well as extremities, can be damaged, leading to atherosclerosis-driven clinical outcomes. According to the American Heart Association, 15.5 million Americans have coronary heart disease, of which 7.6 million experienced myocardial infarction. These statistics are reflective of global incidence. Treatment of atherosclerosis often begins with robust cholesterol-lowering treatments, yet many patients continue to experience cardiovascular events. Recent attempts to provide cardiovascular protection to such patients have included anti-inflammatory and HDL-raising therapeutic approaches that have yielded little benefit. Building knowledge of atherosclerosis disease etiology, defining unique attributes of patient differences as simple as sex or genetic inheritance, and using technology to identify patients with early disease is foundational for the scientific community to develop urgently needed therapeutics. The current concept of acute coronary syndrome (“the vulnerable plaque”) and widely applied animal models are debated because clinical presentation, underlying pathology and pathogenetic mechanisms are subject to change due to improved medical treatment. The goals of this meeting are to: 1) Challenge current dogma of atherosclerosis etiology and explore intra-organ cross-talk that may underlie disease evolution; 2) Consider emerging risk factors and their origins as intervention targets; and 3) Explore cutting-edge technologies to discover new therapeutic targets and approaches for drug development. By bringing together scientists from preclinical to clinical settings and from industry to academic institutions, this conference will nurture discussions to translate breakthrough discoveries into therapeutics.*

## Session Topics:

- The Natural History of Atherosclerotic Disease
  - Lipoprotein Risk Factors
  - Diabetes, Obesity and Atherosclerosis
  - The Inflammation Hypothesis
  - The Milieu Extérieur
  - Crosstalk Among Organs
  - Models and Biomarkers for Atherosclerotic Disease
  - Emerging Fields of Research
- plus three workshops*

**Scholarship Application & Discounted Abstract Deadline: October 5, 2017**

**Abstract Deadline: November 7, 2017**

**Discounted Registration Deadline: December 7, 2017**



Note: Scholarships are available for graduate students and postdoctoral fellows and are awarded based on the abstract submitted. Submitting an abstract is an excellent opportunity to gain exposure for your work. Abstracts submitted by the abstract deadline will also be considered for short talks on the program.

Meeting Hashtag: #KSathero

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# KEYSTONE SYMPOSIA

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### SUNDAY, FEBRUARY 4

#### Arrival and Registration

### MONDAY, FEBRUARY 5

#### The Natural History of Atherosclerotic Disease

\***Daniel J. Rader**, University of Pennsylvania, USA

**Peter Libby**, Brigham and Women's Hospital, USA  
*Requiem for the Vulnerable Plaque, Challenging Current Concepts*

**Sekar Kathiresan**, Massachusetts General Hospital, USA  
*Inherited Basis for Myocardial Infarction*

**Gerard Pasterkamp**, University Medical Center Utrecht, Netherlands  
*Geno-Phenotyping of the Vulnerable Plaque and Patient*

**Philippe Boucher**, University of Strasbourg, France  
*Short Talk: Wnt5a Decreases mTORC1/SREBP2 Activity and Promotes Endosomal Cholesterol Trafficking to the ER in Mice and in Human Vascular Smooth Muscle Cells*

**Sumeet A. Khetarpal**, University of Pennsylvania, USA  
*Short Talk: A Human APOC3 Missense Variant and Monoclonal Antibody Accelerate apoC-III Clearance and Lower Triglyceride-rich Lipoprotein Levels*

#### Workshop 1

\***Ira G. Schulman**, University of Virginia Health System, USA

**Liam Brunham**, University of British Columbia, Canada  
*Genetic Regulation of HDL Cholesterol Levels during Sepsis*

**Ruchi Gupta**, MedImmune/AstraZeneca, USA  
*LOX-1: The Cause of and Solution to Inflammation and Lipid Accumulation in Atherosclerosis*

**Anna Kerstin Emy Hultgardh**, Lund University, Sweden  
*IL-22 Deficiency Reduces Formation of Advanced Atherosclerotic Carotid Plaques in ApoE-Deficient Mice*

**Ashok Kumar Kumawat**, Orebro University, Sweden  
*Targeting IL-6/IL17A in Vascular Inflammation using Affibody Molecules*

**Mulugeta Melkie Zegeye**, Orebro University, Sweden  
*Activation of JAK/STAT3 and PI3K Pathways Are Crucial for MCP-1 Induction by IL6 Trans-Signaling in Human Endothelial Cells*

**Sean Allen**, Northwestern University, USA  
*Targeted Inhibition of NF- $\kappa$ B in Mouse Models of Atherosclerosis Results in Sex-Dependent Immunomodulation*

**Anna Mathew**, University of Michigan, USA  
*Myeloperoxidase-Derived Oxidants Damage Artery Wall Proteins in an Animal Model of Chronic Kidney Disease-Accelerated Atherosclerosis*

#### Lipoprotein Risk Factors

\***Laura F. Michael**, Eli Lilly and Company, USA

**Kiran Musunuru**, University of Pennsylvania, USA  
*Therapeutic Genome Editing as a Cure for Atherosclerosis*

**Anne Tybjærg-Hansen**, Copenhagen University Hospital, Denmark  
*Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease: New Insights from Epidemiology, Genetics, and Biology*

**Daniel J. Rader**, University of Pennsylvania, USA  
*Functionalizing HDL Cholesterol*

#### Poster Session 1

### TUESDAY, FEBRUARY 6

#### Diabetes, Obesity and Atherosclerosis

\***Siddhartha Jaiswal**, Stanford University, USA

**J. Mark Brown**, Cleveland Clinic, USA  
*Selective Small Molecule Inhibition of Gut Microbial Enzymes for the Treatment of Cardiometabolic Disorders*

**Joerg Heeren**, , Germany  
*Protective Role of Brown Adipose in Atherosclerosis Development*

**Laura F. Michael**, Eli Lilly and Company, USA  
*Diabetes and Atherosclerosis: Anti-Diabetic Agents that Improve Cardiovascular Outcomes*

**Robert C. Bauer**, Columbia University, USA  
*Short Talk: Adipose Knockout of Tribbles-1, a GWAS Locus for Coronary Artery Disease, Reduces Plasma Lipids and Increases Circulating Adiponectin*

**Brian Parks**, University of Wisconsin-Madison, USA  
*Journal of Lipid Research Junior Investigator Award: Short Talk: Leveraging Mouse Liver Co-Expression Networks and Human Lipid GWAS Data to Identify and Validate Cholesterol Metabolism Genes*

#### The Inflammation Hypothesis

\***Katey Rayner**, University of Ottawa, Canada

**Ziad Mallat**, University of Cambridge, UK  
*Immune Modulation in Atherosclerosis*

**Jan Nilsson**, Lund University, Sweden  
*Autoimmunity, Injury and Repair as Potential Targets for Intervention in Atherosclerosis*

**Paul M. Ridker**, Brigham and Women's Hospital, Harvard Medical School, USA  
*Anti-inflammatory Therapies for Chronic Atherosclerosis*

#### Poster Session 2

### WEDNESDAY, FEBRUARY 7

#### The Milieu Exterior

\***Gerard Pasterkamp**, University Medical Center Utrecht, Netherlands

**Salim Yusuf**, McMaster University, Canada  
*How Can We Reduce Premature CVD Globally in a Generation?*

**Sudha B. Biddinger**, Boston Children's Hospital, Harvard Medical School, USA  
*Beyond Hyperglycemia: Novel Mediators of Diabetes-Associated Cardiovascular Disease*

**Seppo Yla-Herttuala**, University of Eastern Finland, Finland  
*Epigenetics, VEGFs and Noncoding RNAs in Atherosclerosis and Angiogenesis*

**Robert E. Gerszten**, Beth Israel Deaconess Medical Center, USA  
*Translating Exercise into Reduced Atherosclerosis Burden*

**Brian Bennett**, US Department of Agriculture, USA  
*Short Talk: Genetic and MicroRNA Association with the Cardiometabolic Disease Risk Factor TMAO*

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**Michael C. Petriello**, University of Kentucky, USA  
*Short Talk: Serum Levels of Dioxin-Like Pollutants Are Positively Associated with the Cardiometabolic Disease Risk Biomarker Trimethylamine-N-oxide in Leaner Individuals*

### Workshop 2

\***Dominique P.V. de Kleijn**, University Medical Center Utrecht, Netherlands

**Camilla Gustafsen**, Aarhus University, Denmark  
*Heparan Sulfate Proteoglycans Present PCSK9 to the LDL Receptor*

**Fan E. Mo**, National Cheng Kung University, Taiwan  
*CCN1 and Its Receptor Integrin alpha6beta1 Instigate a Vicious Circle to Accelerate Disturbed Flow-Induced Atherosclerosis*

**Andrew J. Morris**, University of Kentucky, USA  
*Functional Validation of PPAP2B Gene Variants as Determinants of Coronary Artery Disease Risk*

**Edward R. O'Brien**, University of Calgary, Canada  
*Natural Antibodies to HSP27 Are Novel Biomarkers for Cardiovascular Health: HSP27 Immunization Attenuates PCSK9 Transcription and Atherogenesis*

**Ira G. Schulman**, University of Virginia Health System, USA  
*Regulation of HDL Function and Inflammation by Liver X Receptors*

**Tapan Shah**, Rutgers New Jersey Medical School, USA  
*Sex Specific Differences in Post-Transcriptional Gene Regulation of BMP2 in Cardiovascular Calcification*

**Vincent J. Venditto**, University of Kentucky, USA  
*Anti-ApoA-I Antibody Profiles Predict Cardiovascular Disease Outcomes in Patients and in a Mouse Model of Atherosclerosis*

**Hong Yang**, Meharry Medical College, USA  
*Upregulation of ABCA1 Transcription and Inhibition of ABCA1 Protein Degradation by VLDLR/apoER2 Pathway*

### Crosstalk Among Organs

\***Jan Nilsson**, Lund University, Sweden

**Viktoria Gusarova**, Regeneron Pharmaceuticals, USA  
*ANGPTL3 Blockade as a Therapeutic Approach for Treatment of Dyslipidemia and Atherosclerosis*

**Lilach O. Lerman**, Mayo Clinic, USA  
*New Concepts in Atherosclerotic Renovascular Disease: Current Status*

**Joachim Herz**, University of Texas Southwestern Medical Center, USA  
*Multitasking Therapeutics: What Brain Development, Alzheimer's Disease and Atherosclerosis Have in Common*

**Johan Lars Markus Björkegren**, Icahn School of Medicine at Mount Sinai, USA  
*Cardiometabolic Risk Loci Share Downstream Cis- and Trans-Gene Regulation Across Tissues and Diseases*

### Poster Session 3

## THURSDAY, FEBRUARY 8

### Keynote Address

\***Sekar Kathiresan**, Massachusetts General Hospital, USA

**Jesper Gromada**, Regeneron Pharmaceuticals, USA  
*PCSK9 and ANGPTL3 Inhibitors: A New Era of Lipid-Lowering Therapies*

### Models and Biomarkers for Atherosclerotic Disease

\***Viktoria Gusarova**, Regeneron Pharmaceuticals, USA

**Jacob Fog Bentzon**, Centro Nacional de Investigaciones Cardiovasculares, Spain  
*Gene-Modified Minipigs: Applications in Atherosclerosis Imaging*

**Lesca Miriam Holdt**, University Hospital, LMU Munich, Germany  
*Circular RNA in Atherosclerosis*

**Katey Rayner**, University of Ottawa, Canada  
*New Inflammatory Drivers and Biomarkers of Atherosclerosis*

**Kelsey E. Jarrett**, Baylor College of Medicine, USA  
*Short Talk: Somatic Genome Editing of Ldlr with AAV-CRISPR Is a Rapid Method for Atherosclerosis Investigation*

### Workshop 3

\***Thomas Beyer**, Eli Lilly and Company, USA

**Maria Ines Azambuja**, Universidade Federal do Rio Grande do Sul, Brazil

*The Information that We Need to Advance Knowledge on Atherogenesis Exists and It Is Stored as Levels and Trends of Mortality over the Last Century: Influenza is the Key to Retrieve It*

**Dominique P.V. de Kleijn**, University Medical Center Utrecht, Netherlands  
*Diagnosis of Atherosclerotic Coronary Heart Disease using Plasma Extracellular Vesicle Proteins*

**Trine Pagh Ludvigsen**, Novo Nordisk A/S, Denmark  
*Effect of Statin Treatment Compared to Dietary Cessation on Aortic Plaque Size and Inflammation in a Diet-Induced Atherosclerotic Göttingen Minipig Model*

**Ananthi Rajamoorthi**, St. Louis University School of Medicine, USA  
*Therapeutic Silencing of CIDEA/Fsp27 Is Atheroprotective in Ldlr-/- Mice*

**Divya Sagar**, MedImmune, USA  
*Soluble LOX-1: A Potential Biomarker for SLE and Cardiovascular Comorbidity*

**James Wingrove**, CardioDx, USA  
*The Added Value of a Multi-Omics Approach for the Evaluation of Patients with Suspected Obstructive Coronary Artery Disease*

**Jifeng Zhang**, University of Michigan, USA  
*Attenuated Atherosclerosis in Human Apolipoprotein A-II knockin Rabbits*

### Emerging Fields of Research

\***Sekar Kathiresan**, Massachusetts General Hospital, USA

**Marlys L. Koschinsky**, Western University, Canada  
*Lipoprotein(a): Ready for Prime Time?*

**Hester den Ruijter**, University Medical Center, Utrecht, Netherlands  
*Sex Differences in Cardiovascular Disease*

**Siddhartha Jaiswal**, Stanford University, USA  
*Clonal Hematopoiesis in Aging and Atherosclerotic Cardiovascular Disease*

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers)

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**FRIDAY, FEBRUARY 9**

**Departure**