

## Highlights From Vascular Discovery: From Genes to Medicine Scientific Sessions 2018

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Personalized medicine was the theme for the newly renamed conference Vascular Discovery: From Genes to Medicine Scientific Sessions 2018. The goal of the conference was to address the current complex landscape of cardiovascular disease, with a push to reduce stroke and cardiovascular disease by 20% by the year 2020. With 550 abstracts accepted and >830 attendees from 23 countries, the formerly named ATVB/PVD [arteriosclerosis, thrombosis, and vascular biology/peripheral vascular disease] Scientific Sessions, held in San Francisco, encompassed a diverse range of topics including functional genomics, vascular dysfunction and inflammation, thrombosis, and cell biology. The central idea was that we are moving toward translating the science of vascular medicine to cutting-edge technologies and therapeutics with the aim of treating the individual patient—using precision or personalized medicine.

### Precision Medicine

This year's meeting kicked off with a session focused on precision medicine, an emerging area in which scientists and physicians are defining new strategies to customize treatments for patients with cardiovascular disease. Dr Dan Roden from Vanderbilt University opened the session by providing a view of precision medicine from the clinic. An area of discussion was phenome-wide association studies, through which one can analyze many phenotypes of a single genetic variant and link to cardiovascular outcomes. A follow-up to

this talk considered personalized medical care in a discussion of pharmacogenomics. Dr Paul Gurbel from Ivona Heart and Vascular Institute discussed how a specific human single nucleotide polymorphism in *CYP 2C19* affects drug responsiveness to clopidogrel, a P2Y<sub>12</sub> antagonist. At a molecular level, Dr Joseph Wu from Stanford University discussed the concept of precision medicine in a dish using induced pluripotent stem cells. The idea was that cells isolated from patient blood with cardiovascular disease can be reprogrammed into cells of interest to define the mechanism causing disease and to identify new strategies for therapeutic interventions. Finally, Dr Kiran Musumuru from the University of Pennsylvania led an interactive session in which the audience voted on a definition of *precision medicine*. The winning definition was "A clinical and scientific strategy to optimize patient care by individualizing diagnosis, treatment, and prognosis, facilitated by ongoing advances in molecular and clinical diagnostics." With the growing availability of genetic testing, patients are becoming more empowered to partake in their own healthcare decisions. Precision medicine will likely help guide future decisions for better health care for individuals with cardiovascular disease.

### No Longer "Junk" RNA

Given this growing ability to detect genetic differences, many presentations at this year's meeting considered the use of deep sequencing and identification of the role of what

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All abstracts published in conjunction with the American Heart Association's "Vascular Discovery: From Genes to Medicine Scientific Sessions 2018" can be found online here: [http://atvb.ahajournals.org/sites/default/files/additional-assets/pdfs/ucm\\_501107.pdf](http://atvb.ahajournals.org/sites/default/files/additional-assets/pdfs/ucm_501107.pdf).

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*J Am Heart Assoc.* 2018;7:e009470. DOI: 10.1161/JAHA.118.009470.

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was once considered “junk” RNA. Dr Stephanie Dimmeler from the Institute of Cardiovascular Regeneration in Frankfurt, Germany, presented the Keynote Lecture on “RNA Control in Vascular Biology: Implications for Atherosclerosis and Neovascularization.” She highlighted the use of non-coding RNAs as potential targets in atherosclerosis, starting with microRNA miR-92a in the regulation of angiogenesis and endothelial cells before demonstrating that the long noncoding RNA MALAT1 (metastasis associated lung adenocarcinoma transcript 1) regulates endothelial proliferation and that a reduction in this long noncoding RNA augments atherosclerosis. Many other presentations throughout the meeting also discussed the emergence of these new markers as significant indicators of disease. Notably, the winner of the Irvine Page Award, Dr Elizabeth Tarling of the University of California, Los Angeles, and the winner of the Daniel Steinberg Early Career Award, Dr Mireille Ouimet of Ottawa Heart Institute, also demonstrated the role of microRNAs in atherosclerosis. Dr Tarling discussed miR-144’s role in the regression of atherosclerosis and, specifically, differences in gender, and Dr Ouimet presented on macrophage autophagy and the involvement of miR-33. In addition, Dr Muredach Reilly of Columbia University introduced the role of long intergenic noncoding RNAs in modulating macrophage inflammatory and metabolic functions that affect complex cardiometabolic disease. Knowledge about the involvement of noncoding RNAs in cardiovascular disease is rapidly increasing and will provide a road map for interrogation of biological systems to predict potential treatment strategies.

## The Aging Cell

A number of presentations addressed the concept of the aging blood vessel and the role of senescence and calcification in this process. Dr Catherine Shanahan of Kings College London described the role of programmed cell death and apoptosis in chronic kidney disease patients receiving dialysis and the associated vascular calcification that occurs. In addition, she presented data on the interaction of aging and vascular cell phenotype, addressing the *nuclear lamina*, or network of filament proteins, that is part of the cell nucleus. The aging vascular smooth muscle cell accumulates prelamin A, which leads to DNA damage and triggers the osteogenic phenotype switch, leading the vascular calcification. Dr Delphine Gomez of the University of Pittsburgh also addressed the epigenetic control of smooth muscle cells and how histone markers can maintain lineage memory. Abstract presentations also discussed senescence in other cells of the atherosclerotic plaque, such as macrophages and foam cells. Dr Elena Aikawa from Harvard Medical School, Brigham and Women’s Hospital, presented advances she and

her team have made in the understanding of matrix vesicles, which are critical precursors of microcalcification. In her *Journal of Clinical Investigations* article,<sup>1</sup> the colocalization of the protein sortilin with caveolin 1 and tissue-nonspecific alkaline phosphatase was identified. Emerging evidence suggests a significant role of sortilin in the pathogenesis of vascular and metabolic diseases and atherosclerosis through arterial wall inflammation and calcification. These discussions raised the following questions: Would future therapies that block activation of sortilin prevent inflammation and thus prevent vascular calcification? If we were able to reverse the senescent properties of these cell types, would we be able to reverse vascular calcification and aging?

## Gut Microbes and Inflammation

A definite highlight of the meeting was the presentation by Dr Stan Hazen from the Cleveland Clinic Lerner Research Institute on the involvement of gut microbes as therapeutic targets for cardiovascular disease. Dr Hazen presented new data from his laboratory showing that a new small molecule inhibitor targeting the gut microbiome attenuates the onset of cardiovascular disease in experimental animal models. This major advance in the field continues to highlight the symbiotic relationship and consequences of diet, gut microbes, and risk of cardiovascular disease.

## CANTOS and Beyond

The release of CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcome Study) in September 2017<sup>2</sup> was the basis of the Distinguished Lecture, an excellent presentation by Paul Ridker from Brigham and Women’s Hospital to wrap up what was a very successful meeting. He highlighted the need to address the residual inflammatory risk in atherosclerosis in addition to lipid lowering. CANTOS has significantly advanced the inflammatory hypothesis of coronary artery disease.

## Conclusions

In summary, the ATVB conference, Vascular Discovery: From Genes to Medicine Scientific Sessions 2018, was highly stimulating and successful. Special thanks to Drs Steve Lenz, Nancy Webb, and Lars Maegdefessel; Alan Daugherty; the ATVB Early Career Committee; the Program Committee; the Women’s Leadership Committee; the Council on Peripheral Vascular Disease and the Council on Genomic and Precision Medicine for all the dedication and hard work to make this year’s sessions a success.

## Disclosures

None.

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**Key Words:** atherosclerosis • ATVB (arteriosclerosis, thrombosis, and vascular biology) • meeting highlights • thrombosis • vascular biology