

AbsolutePro fractured only under bending, but significantly abraded the wall under both bending and compression, with less effect under torsion (15/21). SmartControl fractured under all three deformations and produced significant abrasion due to strut penetration (15/21). SmartFlex also fractured under all three deformations and produced significant abrasion due to strut penetration (19/21). Larger oversizing resulted in greater interaction between the stents and the tube and, in general, worse abrasion, although the results were device and deformation-specific.

**Conclusions:** This study presents a new method for assessing peripheral stent abrasiveness under limb flexion-induced deformations, which can guide current device selection and future stent developments.

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## 22-VIRC-470-AHA-VD

### Genetic Ablation of CCDC92 Protects against Vascular Inflammation and Atherosclerosis

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**Background:** Genome-wide association studies have uncovered specific genetic variants of the coiled-coil domain containing 92 (CCDC92) gene that are associated with coronary artery disease and type 2 diabetes. However, the biological function of CCDC92 in cardiovascular disease remains unclear. This study aims to investigate the impact of CCDC92 on atherosclerosis, a leading cause of cardiovascular disease, and dissect underlying mechanisms.

**Methods:** To investigate the effects of CCDC92 on atherosclerosis development in vivo, we used *Ccdc92* knockout (KO) mice and littermate wild-type mice (in an *ApoE* KO background) fed a high-cholesterol diet for 18 weeks. To provide a comprehensive characterization of cellular identity within the atherosclerotic lesion, we applied single-cell sequencing to the whole atherosclerotic aorta from *Ccdc92* KO/*ApoE* KO and littermate control mice on high-cholesterol diet for 12 weeks.

**Results:** *Ccdc92* KO significantly reduced atherosclerotic plaque by sixty percent compared with littermate control mice measured by en face analysis of atherosclerotic lesions in the aortic tree after Oil Red O staining ( $n = 11-12/\text{group}$ ;  $P < .001$ ). The single-cell sequencing analysis identified 12 cell subpopulations in the atherosclerotic aorta. Cell-specific gene set enrichment analysis further indicated that *Ccdc92* deficiency had protective effects on multiple vascular cell subpopulations. Specifically, in subpopulations of endothelial cells (ECs), CCDC92 regulates cell inflammation and fatty acid metabolism. Using human coronary artery ECs and mouse aortic EC from *Ccdc92* KO and wild-type mice, we demonstrated that deletion of CCDC92 significantly inhibited proinflammatory adhesion molecules and cytokines induced by tumor necrosis factor- $\alpha$ . Interestingly, adenovirus-mediated CCDC92 overexpression increased lipid droplet accumulation (to an average of four-fold increase) in human coronary artery ECs exposed to oleic acid overload.

**Conclusions:** Our findings revealed the proatherogenic effects of CCDC92 in vivo and demonstrated a critical role of CCDC92 in EC dysfunction during atherosclerosis development. These data address an important new mechanism associated with atherosclerosis and provide a potential new target for atherosclerotic disease.

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## 22-VIRC-508-AHA-VD

### African American Women with Cyp3a4/5 Polymorphisms Have Increased Statin Intolerance

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**Background:** Approximately 3 million Americans have ill managed lipidemia due to statin intolerance (SI) or statin-associated myopathy (SAM). Atorvastatin and simvastatin are the most prescribed statins, which are transported into the liver by SLCO1B1 and metabolized by cytochrome P450 (CYP) 3A4 and 3A5. CYP3A4\*22 and CYP3A5\*3 are two polymorphisms known to decrease their activity; thus, increasing the systemic daily exposure (area under the curve) and serum concentration of unmetabolized statin. In Caucasian populations the prevalence (5%-7% CYP3A4\*22 and 90% CYP3A5\*3) and effect of these polymorphisms is well characterized but not in African American populations. We hypothesize that the prevalence of SI and SAM are correlated with CYP3A4/5 polymorphisms in African American populations.

**Methods:** After institutional review board approval, saliva samples were collected from patients currently prescribed atorvastatin or simvastatin at The Ohio State University Medical for genotyping. SLCO1B1 status was assessed to control for its confounding effect. Participants with polymorphic results were contacted to complete 8 blood draws over 13 hours for pharmacokinetic analysis. Electronic medical records were used to collect demographic information, medical histories, risk factors, and concomitant medications.

**Results:** A preliminary analysis of 502 participants (395 African American, 104 Caucasian, and 3 others) shows racially different polymorphic prevalence. Reduced activity of CYP3A4 was present in 5.8% Caucasians versus 0.51% African Americans. Notably, CYP3A5\*3 is inactive in 73% and reduced in 20.3% of Caucasians compared with 41.7% and 40.7% respectively in African Americans. A statistically significant increase in SI in African American women vs Caucasian women ( $P = .0032$ ) was observed. In combined analysis, atorvastatin has a reduced odds of intolerance compared with simvastatin (odds ratio [OR], 0.463;  $P < .05$ ). However, the odds of SAM is higher in patients with no history of cardiovascular disease (OR, 6.137;  $P < .01$ ) and those with chronic kidney disease (OR, 1.269;  $P < .05$ ).

**Conclusions:** Considering that CYP3A5 is fully active in 18.5% of the African American population compared with 6.8% Caucasian, the characterization of this metabolic enzyme is of clinical significance in minority populations to better manage lipidemia, assess the safety profile of current therapeutic doses, and reduce SAM.

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## 22-VIRC-525-AHA-VD

### Mangiferin Conjugated Gold Nanoparticles Protect against the Development of Abdominal Aortic Aneurysm in an *ApoE*<sup>-/-</sup> Mouse Model

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**Background:** There are no drugs to prevent the growth of abdominal aortic aneurysm (AAA), responsible for approximately 200,000 deaths in the world each year. There is a growing interest in natural anti-inflammatory compounds using nanotechnology-based drug-delivery. Mangiferin (MGF) is one such phytochemical isolated from *Mangifera indica*. Conjugation of MGF on gold nanoparticles (MGF-AuNPs) enhances bioavailability, through cellular penetration, presenting new opportunities toward the design of innovative nanomedicine agents. Recently, we have demonstrated the unique applications of MGF-AuNPs as an immunomodulatory therapeutic agent in the treatment of metastatic breast and prostate cancers. Here, we investigated whether MGF-AuNPs prevent the development of AAA.

**Methods:** *ApoE*<sup>-/-</sup> mice were subjected to angiotensin (AngII; 1  $\mu\text{g}/\text{min}/\text{kg}$ )-induced AAA. MGF-AuNPs (approximately 7 mg/30 g mouse) or starch (S)-AuNPs were administered daily, a week before AngII and continued for 28 days ( $n = 6-12$  per group).

**Results:** The incidences of AAA were significantly attenuated with MGF-AuNPs than AngII group ( $P < .001$ ), associated with a decrease in maximal intra-luminal diameter ( $P < .001$ ), pulse wave velocity ( $P < .001$ ), distensibility ( $P < .05$ ), and radial strain ( $P < .05$ ). Degradation of elastin ( $P < .001$ ), proinflammatory cytokines ( $P < .01$ ), and apoptotic cell death ( $P < .01$ ) were significantly reduced in the aortae of MGF-AuNPs-treated *ApoE*<sup>-/-</sup> mice than the AngII