IN BRIEF

ATHEROSCLEROSIS

SMC switch to fibromyocytes is atheroprotective

The current paradigm is that smooth muscle cells (SMCs) can adopt various phenotypes in atherosclerotic lesions, including a pro-inflammatory macrophage-like phenotype that might promote plaque rupture. A new study using single-cell RNA sequencing now shows that rather than assuming multiple phenotypes, SMCs transform almost exclusively into fibroblast-like cells (termed fibromyocytes) in atherosclerotic lesions in vivo in both humans and mice. This fibromyocyte phenotype is promoted by the expression of *TCF21*, a gene that has been causally associated with coronary artery disease (CAD). SMC-specific *Tcf21* deletion in *Apoe*$^{-/-}$ mice markedly reduced SMC transition to fibromyocytes, leading to thinner fibrous caps. *TCF21*-expressing fibromyocytes were also present in human atherosclerotic lesions, and lower *TCF21* levels in SMCs were associated with a higher risk of CAD. "These data suggest that both TCF21 expression and SMC phenotypic modulation are beneficial during the disease process," conclude the authors.

ORIGINAL ARTICLE Wirka, R. C. et al. Atheroprotective roles of smooth muscle cell phenotypic modulation and the *TCF21* disease gene as revealed by single-cell analysis. *Nat. Med.* https://doi.org/10.1038/s41591-019-0512-5 (2019)

ATRIAL FIBRILLATION

AI can help to diagnose AF during sinus rhythm

Combining artificial intelligence (AI) with a standard electrocardiogram (ECG) acquired during normal sinus rhythm enables the point-of-care identification of individuals with atrial fibrillation (AF). Researchers have developed and validated an AI-enabled ECG that uses a trained neural network to detect the ECG signature of AF in a standard 10-s, 12-lead ECG recorded during sinus rhythm. A single AI-enabled ECG identified AF with an area under the curve of 0.87 (95% CI 0.86–0.88), a sensitivity of 79.0% (95% CI 77.5–80.4%), a specificity of 79.5% (95% CI 79.0–79.9%), an F_1 score of 39.2% (95% CI 38.1–40.3%) and an overall accuracy of 79.4% (95% CI 79.0–79.9%). Performance improved with the inclusion of all ECGs acquired during the first month of each patient's window of interest (from the start of the study for those without AF and from 31 days before the first recorded AF ECG for patients with AF).

ORIGINAL ARTICLE Attia, Z. I. et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. *Lancet* https://doi.org/10.1016/S0140-6736(19)31721-0 (2019)

PREVENTION

Effect of statin discontinuation in elderly people

Among people aged 75 years who have been taking statins for the primary prevention of cardiovascular disease (CVD), statin discontinuation is associated with a 33% increased risk of admission to hospital for cardiovascular events. This finding comes from an observational study that included individuals from the French national health-care system who had turned 75 years of age in 2012–2014, had no history of CVD and had been adherent to statin therapy for ≥2 years. Statin discontinuation was defined as three consecutive months without exposure. Of the 120,173 people included in the analysis, 14.3% discontinued statins and 4.5% were admitted to hospital for a cardiovascular event during the 2.4 years of follow-up (HR 1.33, 95% CI 1.18–1.50). The association was stronger for coronary events than for cerebrovascular events (increased risk 46% versus 26%).

ORIGINAL ARTICLE Giral, P. et al. Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in France. *Eur. Heart J.* https://doi.org/10.1093/eurheartj/ehz458 (2019)

HYPERTENSION

Systolic and diastolic hypertension independently predict CVD risk

The decision-making process in the management of hypertension has been complicated by changes in the thresholds for the definition of hypertension in the 2017 ACC/AHA guidelines, which reduced the blood-pressure target for high-risk patients to <130/80 mmHg but retained the <140/90 mmHg target for other patients. In addition, the relationship between systolic and diastolic hypertension and the risk of cardiovascular disease (CVD) is unclear, and some risk estimation tools do not include diastolic blood pressure for the determination of CVD risk. A new study now shows that although systolic hypertension has a larger effect on cardiovascular outcomes, both systolic and diastolic hypertension can independently contribute to the risk of adverse cardiovascular events. Moreover, this relationship is not altered by the threshold used for the definition of hypertension.

In this prospective study, Flint and colleagues analysed blood pressure data from 1.3 million adults in a general outpatient population of Northern California, USA, obtained in routine clinical practice using an oscillometric blood-pressure cuff. The prevalence of hypertension was 18.9% for the threshold of ≥140/90 mmHg and 43.5% for the threshold of ≥130/80 mmHg. Both systolic and diastolic hypertension independently predicted adverse cardiovascular outcomes (a composite of myocardial infarction, ischaemic stroke or haemorrhagic stroke) over a period of 8 years. A continuous burden of systolic hypertension (≥140 mmHg) was associated with a hazard ratio (HR) per unit increase in z score of 1.18 (95% CI 1.17–1.18), and a continuous burden of diastolic hypertension (≥90 mmHg) was associated with a HR per unit increase in z score of 1.06 (95% CI 1.06–1.07).

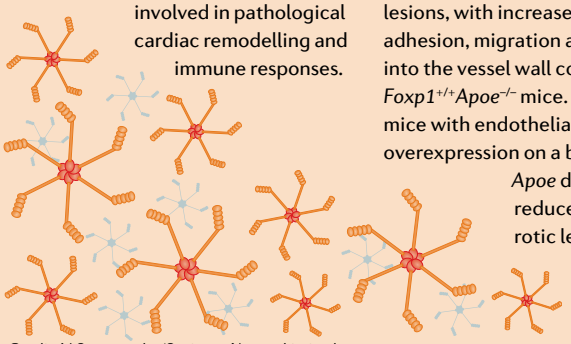
ATHEROSCLEROSIS

FOXP1 suppresses the endothelial NLRP3 inflammasome

Forkhead box protein P1 (FOXP1) is a transcription factor that downregulates activation of the endothelial NLRP3 inflammasome and suppresses vascular inflammation, protecting against atherosclerosis. Simvastatin can upregulate FOXP1 expression, thus revealing a novel anti-atherogenic effect of this drug.

FOXP1 is highly expressed in the cardiovascular system and is involved in pathological cardiac remodelling and immune responses. Given that the expression of FOXP1 was significantly reduced in endothelial cells from atherosclerotic lesions in *Apoe*$^{-/-}$ mice fed a high-fat diet and those from human atherosclerotic coronary arteries, Yuzhen Zhang and colleagues investigated the role of endothelial FOXP1 in atherogenesis.

Endothelial-specific *Foxp1*$^{-/-}$ mice crossed with *Apoe*$^{-/-}$ mice had significantly enlarged aortic atherosclerotic lesions, with increased monocyte adhesion, migration and infiltration into the vessel wall compared with *Foxp1*$^{+/+}$*Apoe*$^{-/-}$ mice. By contrast, mice with endothelial-specific *Foxp1* overexpression on a background of *Apoe* deletion had reduced atherosclerotic lesion formation. FOXP1 was found to suppress genes encoding inflammasome



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