MicroRNA-29 in Aortic Aneurysm Formation (p 1115)

Boon et al find that blocking a particular microRNA prevents aortic aneurysm.

As we age, our blood vessels become weaker and more prone to aneurysms. Indeed, abdominal aortic aneurysm is a problem that affects approximately 9% of elderly men. Growth and development of normal blood vessel is regulated by, among other things, microRNAs (miRs), so Boon et al wondered whether miRs might also play a role in vessel aging and pathology. The team examined the aortas of old and young mice and found that 18 miRs were differentially expressed. However, only one of these, miR-29, controlled mRNA expression. miR-29 was upregulated not only in aging aortas, but also in mouse models of aortic aneurysm and in human aneurysm biopsies. miR-29 had previously been shown to repress the expression of extracellular matrix proteins in the heart after infarction, thereby reducing fibrosis and scarring. These same ECM miRNAs were the targets for miR-29 in aging aortas, but in this case the team showed that the result was vessel weakening. Inhibiting miR-29 prevented the downregulation of ECM proteins and, more importantly, the formation of aneurysms in aged mice. Localized inhibition of miR-29 at the site of an aortic aneurysm might therefore be a way to aid repair, strengthen the vessel wall, and prevent future aneurysms.

Hypoxia and Macrophage Lipid Content (p 1141)

Mice are good models for studying hypoxia in atherosclerosis, say Parathath et al.

The cores of human atherosclerotic plaques are often far enough from the passing blood flow that they are deprived of an oxygen supply. This hypoxic environment is associated with the activation of a transcription factor called hypoxia inducible factor (HIF-1), which regulates genes involved in apoptosis, metabolism, inflammation, and other processes relevant to atherosclerosis. Whether hypoxia and HIF-1 are actually involved in atherogenesis, however, is not known. Mouse models of atherosclerosis were considered irrelevant for studying the role of hypoxia in atherogenesis because it was thought that due to the small size of mouse plaques oxygen could still reach the cores. Parathath et al now show that, in fact, mouse plaques do express HIF-1 as well as its transcriptional targets. The team also showed that mouse macrophages had altered lipid metabolism under hypoxic conditions, with increased sterol content and decreased cholesterol efflux – changes that would likely worsen atherosclerosis. Blocking the activity of HIF-1 prevented these hypoxia effects, indicating the transcription factor was directly responsible. The findings of Parathath et al suggest that hypoxia has a negative impact on atherogenesis and that mice would be useful for studying the damaging effect of hypoxia and for finding ways to combat it.

Linking Exercise Capacity With Mortality (p 1162)

A genetic proclivity for exercise is linked to longevity, report Koch et al.

That exercise decreases the risk for cardiovascular disease is well-known, but Koch et al now show that you can be born with this benefit. Well, at least rats can. The researchers selectively bred rats over 14 or so generations until they had populations of low capacity runners (LCRs) and high capacity runners (HCRs), as determined by treadmill testing. Then, they compared oxygen uptake, myocardial function, endurance performance, and body mass in adult and aged rats from the 2 groups. As the rats progressed from adulthood to old age, the HCRs had sustained activity levels, energy expenditure, and lean body mass. They also had lower blood pressure, improved cardiomyocyte function – assessed by contractility, morphology and intracellular calcium handling – and longer lifespans. The finding that longevity is linked with a genetic propensity for exercise does not mean that those of us who are naturally less active will not reap the same benefits from exercise. Rather, the research suggests that the LCR and HCR model rats will be excellent tools for studying the biological pathways that link aerobic activity with healthy aging and longevity – work likely to benefit everybody.

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