MicroRNA-181b Inhibits Atherogenesis (p 32)

MicroRNA-181b inhibits vascular inflammation and atherosclerosis in mice, report Sun et al.

Atherosclerosis is a chronic inflammatory vascular disease that is in part driven by the activation of the transcription factor NF-kB. In vascular endothelial cells, oxidized low-density lipoproteins, angiotensin II and other pro-atherogenic factors activate NF-kB. These factors promote the transfer of NF-kB from the cytoplasm to the nucleus where it increases the transcription of pro-inflammatory genes. Recently, miR-181b was found to repress importin-α3, the protein responsible for transferring NF-kB to the nucleus. But whether this miR could actually suppress atherosclerosis was unknown. This prompted Sun and colleagues to inject atherosclerosis-prone mice with a version of miR-181b. They found that miR-181b reduced NF-kB activity as well as the expression of importin-α in the aortic arches of the mice. Importantly, atherosclerotic lesion formation was also reduced, and the lesions contained fewer macrophages and T cells. Interestingly, the team also found that patients with coronary artery disease had reduced levels of miR-181b in their blood. Taken together, these results indicate that increasing miR-181b levels in patients could be a potential therapy for diminishing atherogenesis.

Lasting Effects of AAV1/SERCA2a in Heart Failure (p 101)

A gene therapy trial for heart failure patients shows promising long-term results, say Zsebo et al.

A non-fatal heart attack often leads to progressive tissue damage that results in heart failure. Indeed, despite recent advances, heart failure remains a leading cause of death worldwide. An important factor that contributes to the condition is reduction in the calcium pumping activity of sarcoplasmic reticulum ATPase, or SERCA2a. Previous studies have shown that boosting SERCA2a activity improves cardiac function in animal models of heart failure. Based on these findings, a gene therapy trial was initiated in which the SERCA2a gene was delivered to the coronary arteries of 39 heart failure patients. Twelve months later, patients who received the gene had lower rates of cardiac events including worsening heart failure, myocardial infarction, heart transplant and death compared with those who received the placebo. Zsebo and colleagues now report that, after three years, these patients still showed low rates of cardiac events, and still expressed the transgene in their heart tissue. And because there were no safety concerns with the treatment, these findings suggest that a single dose of SERCA2a gene therapy could have positive long-lasting effects in heart failure patients. Researchers can therefore be somewhat optimistic about the large-scale international trial of the treatment that is currently underway.

Stress-Induced Microparticle Release (p 109)

Levels of circulating microparticles rise in response to cardiac stress, report Augustine et al.

Microparticles are small—0.1 to 1µm diameter—vesicles released from the surfaces of cells, and are thought to participate in a large variety of physiological processes including cell-to-cell communication and waste disposal. Certain subtypes of these vesicles—identified by the expression of cell-of-origin surface markers—are known to be abundant in the blood of patients with cardiovascular disease. However, similar increases can also be observed in healthy people after strenuous exercise. Thus, Augustine and colleagues measured microparticle levels in the blood of patients following an exercise-free, drug-induced cardiac stress test called a dobutamine stress echocardiogram (DSE). Of the 119 patients referred for DSE, 25 had a positive result indicating ischemic heart disease. The remaining 94 patients had negative DSE results. Interestingly, both negative and positive DSE patients had comparable baseline levels of microparticles prior to the stress test, but afterwards only those patients with a negative DSE result showed an increase in circulating microparticles, which returned to baseline approximately an hour later. The authors propose that this rise and fall in microparticles is a normal physiological response to stress and might even be protective against vascular disease. If so, procedures to boost and then clear microparticles may be useful disease prevention strategies.