AMPKα1 and Atherosclerotic Calcification (p 422)

Cai et al show that AMPK prompts Runx2 degradation to prevent atherosclerotic calcification.

Calcification of atherosclerotic lesions is a major predictor of plaque rupture and adverse cardiovascular outcomes in patients. A key process in atherosclerotic calcification is the differentiation of vascular smooth muscle cells (VSMCs) toward an osteogenic (bone-like) fate. The process of calcification in VSMCs is regulated by the transcription factor Runx2, and recent work has shown that the enzyme adenosine monophosphate activated kinase (AMPK)—better known for its role in cellular energy homeostasis—suppresses Runx2 expression in VSMCs. However, the mechanism by which AMPK2 exerts this effect is not known. Cai et al have now shown that deletion of AMPKα1—the version of the enzyme expressed in VSMCs—increases arterial Runx2 expression and calcification in mice. Activation of AMPKα1 in VSMCs, on the other hand, prompted Runx2 sumoylation—a modification that can tag proteins for destruction. Indeed, AMPKα1 activation reduced Runx2 stability. The team went on to show that AMPKα1 phosphorylates PIA1, the enzyme responsible for Runx2 sumoylation and inhibition of this phosphorylation prevented AMPKα1-induced Runx2 sumoylation. Hence, atherosclerotic calcification could be potentially prevented by targeting AMPKα1 activation or PIA1 phosphorylation.

Swiss-AMI 12 Months (p 481)

Sürder et al present the 12-month follow-up results to the Swiss-AMI clinical trial.

The SWiss multicenter Intracoronary Stem cell Study for Acute Myocardial Infarction (SWISS-AMI) trial began in 2006 with the aim of assessing the benefit of autologous bone marrow progenitor cell transfer to patients who had suffered heart attacks. Two hundred patients were enrolled and divided into 3 groups: one given intracoronary infusions of their own bone marrow mononuclear cells roughly 1 week after myocardial infarction (early group), one given the cells at 3 to 4 weeks (late group), and one acting as a control. An initial analysis of the patients (4 months after the procedure) found no benefit in left ventricular ejection fraction—as assessed by cardiac magnetic resonance imaging (CMR). Now Sürder and colleagues report that, even after 1 year, there is no significant benefit of autologous bone marrow progenitor cell transfer to patients who had suffered heart attacks. Nevertheless, the lack of clinical benefit seen in the SWISS-AMI trial—more than a decade after the first clinical trial began in 2006 with the aim of assessing the benefit of autologous bone marrow progenitor cell transfer to patients who had suffered heart attacks—remains unclear whether decreased levels of adiponectin are a cause of cardiovascular disease. Borges and colleagues performed a Mendelian randomization study to examine whether such a causal relationship existed. From genome-wide association studies, they identified genetic variants linked to adiponectin levels (from the ADIPOgen consortium) and to coronary artery disease risk (from the CARDIOGRAM and CARDIOGRAMplusC4D consortia), and found there was no consistent evidence that a genetic predisposition for elevated levels of adiponectin is associated with coronary artery disease risk (from the CARDIOGRAM and CARDIOGRAMplusC4D consortia), and found there was no consistent evidence that a genetic predisposition for elevated levels of adiponectin is associated with coronary artery disease risk. Borges and colleagues performed a Mendelian randomization study to examine whether such a causal relationship existed. From genome-wide association studies, they identified genetic variants linked to adiponectin levels (from the ADIPOgen consortium) and to coronary artery disease risk (from the CARDIOGRAM and CARDIOGRAMplusC4D consortia), and found there was no consistent evidence that a genetic predisposition for elevated levels of adiponectin is associated with coronary artery disease risk.

Adiponectin and Coronary Heart Disease Risk (p 491)

Low adiponectin levels do not increase the risk for coronary heart disease, report Borges et al.

Adiponectin is a small protein produced and secreted by mature adipocytes, and its production is inversely correlated with obesity, as circulating levels of adiponectin decrease with an increase in the body mass index (BMI). Therefore, low levels of adiponectin are generally associated with known cardiovascular risk factors, such as insulin resistance and dyslipidemia, but it remains unclear whether decreased levels of adiponectin are an effective strategy for preventing heart disease. Based on these results, the authors suggest that therapies aimed at boosting circulating levels of adiponectin might not be an effective strategy for preventing heart disease.