Mitochondrial regulator DRP1 promotes vascular calcification, report Rogers et al.

Blood vessel calcification is associated with adverse hemodynamics and cardiovascular conditions. Once believed to be a passive process of aging, it is now known that calcification involves the active differentiation of smooth muscle cells (SMCs) and valve interstitial cells (VICs) into bone-like cells (osteoblasts). Many of the biological processes related to vessel calcification—such as cell differentiation, apoptosis, and calcium homeostasis—involve mitochondrial dynamics, and it has been shown that mutations to the mitochondrial regulator dynamin-related protein 1 (DRP1) are associated with calcification of heart tissue in mice. Rogers and colleagues have examined the potential link between DRP1 and calcification in humans. They found that in human carotid artery plaques and in calcified valve tissue—from patients undergoing aortic valve replacements—DRP1 staining was elevated in regions of calcium deposition. Furthermore, DRP1 levels were also high in cultures of human SMCs and VICs undergoing osteoblast differentiation, and inhibition of DRP1 attenuated calcification. The findings suggest that human DRP1 promotes vascular calcification and that this condition may be prevented or attenuated by therapeutic inhibition of DRP1.

Haddad et al identify the necrosis sensor DNGR1 as a potential therapeutic target in atherosclerosis.

The accumulation of apoptotic cells and necrotic debris within atherosclerotic plaques is associated with both chronic inflammation and an increased risk of plaque rupture. But how the insufficient clearance of dead cells leads to inflammation in atherosclerosis is not well understood. Haddad and colleagues hypothesized that the dendritic cell NK lectin group receptor-1 (DNGR1), which is known to recognize molecules released from dying cells, might be involved in this process. To investigate this possibility, the team examined atherosclerosis-prone mice that lacked DNGR1—either fully or specifically in bone marrow cells—and showed that these animals had reduced plaque sizes and slower atherosclerosis progression. DNGR1 deletion also led to a dramatic decrease in the number of macrophages and slower atherosclerosis progression. They obtained similar results by depleting either CD36 or Nox2 (the enzyme responsible for ROS production) specifically from perivascular macrophages. These results confirm the involvement of CD36 and Nox2 in Apβ driven neurovascular dysfunction, identify perivascular macrophages as the cellular mediators, and suggest that therapeutic manipulations of these cells may ameliorate brain dysfunction in AD patients.
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