Manipulating calcium accumulation in blood vessels may provide a new way to treat heart disease

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Hardening of the arteries, or atherosclerosis, is the primary cause of heart disease. It is caused by calcium accumulation in the blood vessels, which leads to arteries becoming narrow and stiff, obstructing blood flow and leading to heart complications. Although many risk factors for atherosclerosis have been identified, the cause is not known and there is currently no way to reverse it once it sets in. In a new study published 9th April in the open access journal *PLOS Biology*, researchers have characterized the cells responsible for driving this calcium build-up in vessel walls.

The process of calcium accumulation in blood vessels resembles bone formation and involves maintaining a balance between bone-forming cells called osteoblasts and bone-destroying cells called osteoclasts. In the new study, Hyo-Soo Kim and colleagues characterize the origin of a population of vascular calcifying progenitor cells, and the potential of these cells to differentiate into different cell types.

"We show that vascular calcifying progenitor cells in the artery have the potential to become either osteoblasts or osteoclasts," said Dr Kim of Seoul National University. "And a certain chemical can push these cells towards becoming osteoclasts, which leads to the softening of the blood vessels."

The researchers sorted cells from the aortas of mice into two groups. Both groups originated from bone marrow and expressed a cell surface protein, called Sca-1, but only one group expressed another cell surface protein called PDGFR?. They found that the cells which only expressed Sca-1 could become either osteoblasts or osteoclasts, whereas the cells which expressed both Sca-1 and PDGFR? were committed to an osteoblastic lineage.

The team then treated the cells with a protein called PPAR?, which is known to promote the formation of osteoclasts and inhibit the formation of osteoblasts. When treated with PPAR?, only Sca-1 expressed cells preferentially differentiated into osteoclast-like cells. Furthermore, in vivo study demonstrated that, while bidirectional cells that were injected into mouse models of atherosclerosis increased the severity of calcium build-up in arteries, cells that were then treated with a drug activating PPAR? markedly decreased this effect and even reversed the calcification.

"These findings suggest that a subtype of calcifying progenitor cells offer a new therapeutic target for the prevention of calcification," said Dr Kim. "This opens up the possibility of new drug development to inhibit the hardening of the arteries, and thereby reduce the risk of heart disease."

More information: Cho H-J, Cho H-J, Lee H-J, Song M-K, Seo J-Y, et al. (2013) Vascular Calcifying Progenitor Cells Possess Bidirectional Differentiation Potentials. PLoS Biol 11(4): e1001534. doi:10.1371/journal.pbio.1001534

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