A new look at heart disease

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Scientists at the Interfaculty Institute of Biochemistry (IFIB) have collaborated with colleagues from the Department of Pharmacy and the Department of Dermatology of the University of Tübingen to identify a long-overlooked function of vascular smooth muscle cells in atherosclerosis.

Atherosclerosis, the buildup of plaques in the arteries, leads to myocardial infarction and stroke and is the major cause of death in the Western world. It is a chronic inflammatory disease of the arteries arising from interactions of modified lipoproteins and various cell types including monocyte-derived macrophages from the blood and smooth muscle cells (SMCs) in the vessel wall. "It is unclear, however, how each particular cell type contributes to the development of an atherosclerotic lesion," says Professor Robert Feil, senior author of the study. "One highly controversial issue is the contribution of vascular SMCs to plaque growth."

The IFIB researchers performed lineage tracing experiments in mice, in which they have genetically labeled mature SMCs in the vessel wall of young mice before the onset of the disease and then monitored their fate in older atherosclerotic animals. "Surprisingly, we found that SMCs in the arterial wall can undergo clonal expansion during disease progression and convert into macrophage-like cells that have lost the classical SMC marker, ?-smooth muscle actin," says Dr. Susanne Feil, the first author of the publication. "It seems that certain atherosclerotic lesions contain even more SMC-derived macrophages than traditional monocyte-derived macrophages."

These findings indicate that previous studies based on immunostaining of plaque cells for smooth muscle and macrophage markers have vastly underestimated the role of SMCs and overestimated the role of monocyte-derived macrophages in atherosclerosis. Robert Feil notes that the results in the mouse model might also translate to humans. "Targeting SMC-to-macrophage transdifferentiation could be a novel therapeutic strategy to treat atherosclerotic heart disease and perhaps many other diseases with a smooth muscle component."

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