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Understating of Vascular Calcification: the Role of Stem/Progenitor Cells

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Vascular disorders, such as atherosclerosis and calcification, present a significant clinical challenge. Intimal and medial calcifications are the two major forms of calcification that can be distinguished pathologically and exist in different clinical settings. Intimal calcification is usually associated with the atherosclerotic milieu, occurs under the injured endothelium, and is mediated by atherosclerosis-associated lipids and cytokines. In contrast, medial calcification is involved with accumulation of minerals in the smooth muscle layer and is associated with metabolic disorders such as chronic kidney disease and diabetes. Here, I have focused on atherosclerotic intimal calcification.

Recent studies have revealed that cellular components and their dynamics play a pivotal role in vascular disease, representing potential therapeutic targets for the treatment, or even reversal, of disease processes. We have recently identified vascular calcifying progenitor cells in arterial tissue, mainly the adventitia, using the cell surface markers stem cell antigen-1 (Sca-1) and platelet-derived growth factor receptor alpha (PDGFRα). These cells were derived from the bone marrow (BM) and homed to inflamed atherosclerotic lesions. These BM-derived vessel-infiltrated calcifying progenitor cells were of two types: (1) Sca-1+/PDGFRα+ cells possessing a unipotent osteoblastic (OB) differentiation potential and (2) Sca-1+/PDGFRα- cells exhibiting bipotent (OB/osteoclastic (OC) differentiation (bidirectional) properties. We demonstrated that bipotent Sca-1+/PDGFRα- cells could be used to reduce vascular calcification by inducing them to differentiate into OC-like cells upon peroxisome proliferator-activated receptor γ (PPARγ) activation.

The concept of OB/OC bipotent progenitor cells, especially in adults, is against the traditional concept. Therefore, we have attempted to determine whether mesodermal progenitor cells (MPCs) exist in adults. We demonstrate MPCs (Lin-CD29+Sca-1+/PDGFRα- cells) are present in the adult BM. Lin-CD29+Sca-1+/PDGFRα- cells have bidirectional (OB/OC) and hematopoietic potential, and are ancestors of Sca-1+/PDGFRα+ cells. MPCs mobilize into peripheral blood and infiltrate the artery under the influence of atherosclerosis-related cytokines. In contrast, Lin-CD29+Sca-1+/PDGFRα+ cells have unidirectional (osteoblastic differentiation) potential and are not affected by the atherosclerotic milieu.

This new concept provides valuable insights into the pathophysiology of atherosclerosis and vascular calcification, and may enable the identification of novel therapies for the treatment of vascular diseases.