Imaging Proliferation in Atherosclerosis (p 835)

Ye et al employ a cancer imaging method to monitor macrophage proliferation in atherosclerosis.

In early stages of atherosclerosis, monocytes from the bone marrow and spleen travel to fatty plaques on blood vessel walls where they accumulate and develop into macrophages. During later stages of the disease, however, these macrophages proliferate locally. Thus, regardless of location—whether bone marrow, spleen or plaques—monocyte and macrophage proliferation is a driving force of atherosclerotic lesion formation. Currently, there is no available method for monitoring proliferation at these sites in patients, yet this information would be of great diagnostic and prognostic value. For a possible solution, Ye and colleagues have now turned to the field of cancer imaging where bone marrow, spleen or plaques—monocyte and macrophage proliferation is a driving force of atherosclerotic lesion formation. Currently, there is no available method for monitoring proliferation at these sites in patients, yet this information would be of great diagnostic and prognostic value. For a possible solution, Ye and colleagues have now turned to the field of cancer imaging where a radioactive thymidine analog (18F-FLT) that accumulates in proliferating cells, is being employed as a promising technique for imaging tumor growth. The team asked whether

18F-FLT PET might also reveal proliferating inflammatory cells in atherosclerosis. Indeed, they found that 18F-FLT PET did accumulate in the bone marrow, spleen and plaques of atherosclerotic mice, as well as the plaques of rabbits and humans with atherosclerosis. The use of this existing imaging method would facilitate not only the monitoring of atherosclerotic lesion formation, but also the evaluation of novel therapies.

Myeloid Suppressor Cells and Hypertension (p 858)

Myeloid-derived suppressor cells reduce inflammation and blood pressure in mouse models of hypertension, report Shah et al.

High blood pressure puts a person at increased risk of suffering a heart attack, heart failure, or stroke. The kidneys, nervous system and vascular injuries have all been implicated in promoting or exacerbating hypertension, but recently an additional culprit has been identified: inflammation. Activation of T cells has been linked to hypertensive pathology, but less is known about the roles of other immune cells such as myeloid-derived suppressor cells (MDSCs). These cells are known to suppress T cell activation and reduce excessive inflammation. Shah and colleagues investigated MDSCs in mouse models of hypertension and found that the number of these cells increased as the hypertension persisted. They showed that both in vitro and in vivo, MDSCs isolated from hypertensive mice suppressed T cell proliferation. They also found that the cells generated high levels of hydrogen peroxide, which was necessary for suppressing T cell activity. Furthermore, depleting MDSCs from hypertensive mice increased the animals’ blood pressures and inflammation, while transfer of exogenous MDSCs to hypertensive mice had the opposite effect. The findings suggest that modulation of MDSCs might be a novel strategy for treatments aimed at tackling hypertension refractory to current therapy.

miR-206 Mediates Hypertrophy and Survival (p 891)

Yang et al uncover the cellular mechanisms behind YAP-induced hypertrophy.

Yes-associated protein (YAP) is an important promoter of proliferation, hypertrophy and survival in cardiomyocytes, particularly after myocardial infarction and ischemia/reperfusion injury. But the downstream effectors of YAP remain largely unknown. Because several previous studies have shown that microRNAs (miRs) influence cell growth, proliferation and survival, Yang and colleagues investigated whether miRs might be the sought-after YAP effectors. To examine the role of miRs, they screened a large number of these molecules in neonatal rat cardiomyocytes and found that three miRs were upregulated in response to YAP overexpression. However, only one of these—miR-206—affected cardiomyocyte size and survival in a manner similar to that of YAP itself. Indeed transgenic mice with a cardiac-specific overexpression of miR-206 exhibited cardiac hypertrophy. Furthermore, downregulation of miR-206 prevented YAP-induced cell survival and hypertrophy in cultured cardiomyocytes. The team went on to show that miR-206 suppresses expression of a transcription factor called FoxP1. And, that inhibiting FoxP1 could recapitulate the hypertrophy and increased cardiomyocyte survival seen with YAP overexpression. These findings suggest that the YAP-miR206-FoxP1 pathway could be a valuable target for modulating the processes that control cell growth and survival in heart disease.
In This Issue
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Circ Res. 2015;117:825
doi: 10.1161/RES.0000000000000079

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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