Published in final edited form as:

Sci Transl Med. 2018 July 25; 10(451): . doi:10.1126/scitranslmed.aau7379.

The lymphatic border patrol outwits inflammatory cells in myocardial infarction

Gaetano Santulli

Department of Medicine, Albert Einstein College of Medicine, Montefiore University Hospital, New York, NY 10461, USA. Department of Advanced Biomedical Sciences, “Federico II” University of Naples, Naples 80131, Italy

Abstract

Lymphangiogenesis modulates inflammation by clearing immune cells in the infarcted heart in a lymphatic vessel endothelial hyaluronan receptor 1 (LYVE-1)–dependent process to ameliorate cardiac dysfunction.

The lymphatic vascular network plays a fundamental role in cardiac fluid regulation: It collects and drains lymph to mediastinal lymph nodes, preventing accumulation of leukocytes, macromolecules, and excessive interstitial fluid. The exact role of the lymphatic system in cardiac injury has not been fully established.

Using ligation of the left anterior descending coronary artery to obtain myocardial infarction (MI) in mice, Vieira and collaborators elegantly demonstrated that stimulation of the growth of lymphatic vessels—a process known as lymphangiogenesis—markedly improved myocardial function after cardiac ischemia. Lymphangiogenesis induced an active clearance of immune cells within the injured heart, eventually leading to the resolution of the inflammatory response, thereby reducing cardiac fibrosis and pathological remodeling. Mechanistically, the lymphatic vessel endothelial hyaluronan receptor 1 (LYVE-1), a protein essential in leukocyte docking, was identified as a key player in these processes. *Lyve1* knockout mice exhibited lower clearance of immune cells after MI compared with wild-type littermates; moreover, *Lyve1* ablation triggered a progressive deterioration of myocardial function, accompanied by collagen deposition and scarring, in absence of any lymphatic vessel defects at baseline.

These findings elucidate the functional role of the cardiac lymphatic system after MI. Although the study mainly focused on the regulation of the innate immune response, it is possible that lymphangiogenesis could also regulate the programming of naïve T cells and macrophage polarization. These preclinical results have translational potential, providing the basis for novel therapeutic strategies aimed at enhancing lymphangiogenesis in patients with ischemic heart disease.

Highlighted Article

I. J. M. Vieira, S. Norman, C. Villa del Campo, T. J. Cahill, D. N. Barnette, M. Gunadasa-Rohling, L. A. Johnson, D. R. Greaves, C. A. Carr, D. G. Jackson, P. R. Riley, The cardiac lymphatic system stimulates resolution of inflammation following myocardial infarction. *J. Clin. Invest.* 10.1172/JCI97192 (2018).

Acknowledgments

GS is supported by the NIH: R00DK107895

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript