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# Journal club

## TRAFFICKING PATTERNS OF MONONUCLEAR PHAGOCYTES

My passion for how mononuclear phagocytes get out of tissues began when I was a Ph.D. student. A study by Ross Gerrity, published in 1981, which hinted at macrophage trafficking out of atherosclerotic plaques, particularly inspired my thesis and postdoctoral work. This area of research was to become the focus of my own laboratory for its first decade.

The study by Gerrity presented electron micrographs from pig atherosclerotic plaques that clearly showed lipid-rich macrophages wedged between intact arterial endothelial cells. These could not be incoming cells from the blood stream, as blood monocytes did not carry so much lipid. Thus, the paper suggested that lipid-loaded macrophages (foam cells) may crawl out of atherosclerotic plaques. Inspired by this study, I dedicated my efforts to investigating whether monocytes, or the dendritic cells (DCs) and macrophages they become, might re-enter the bloodstream from tissues, possibly not only clearing cholesterol from plaques but also facilitating pathogen spread.

> “everything I was doing was in preparation for the unaddressed question of macrophage trafficking in atherosclerosis”

I decided that the pathological state of atherosclerosis was not the place to start on this question. To understand the normal behaviour of monocytes, I carried out postdoctoral work with Bill Muller and Ralph Steinman, studying how monocytes could gain the capacity to emigrate out of tissues. I learned that they did so by becoming DCs, which readily entered the lymph. So, the quest to understand monocyte biology led me to focus on monocytes becoming DCs that migrate to lymph nodes. It was through this effort that I acquired a passion for studying the lymphatic vasculature.

Despite not working on atherosclerosis for more than 10 years after I read the work of Gerrity, I felt internally that everything I was doing was in preparation for the unaddressed question of macrophage trafficking in atherosclerosis. Within a year of starting my own laboratory in 2000, the US National Institutes of Health put out a ‘Request For Applications’ on ‘Immunity and Atherosclerosis’ and we received funding to study whether foam cells can leave atherosclerotic plaques and reverse disease.

We ultimately concluded that macrophages probably do not crawl out of plaques. Instead, we believe that Gerrity observed the cytoplasmic extensions of phagocytes passing through the endothelium of the artery to sample blood contents, without resulting in the phagocyte leaving the plaque (see Further reading). Nonetheless, I believe that Gerrity’s paper was pivotal in getting me, and the field in general, to consider the mechanisms involved in macrophage accumulation during inflammation.

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The author declares no competing interests.

**ORIGINAL ARTICLE** Gerrity, R. G. The role of the monocyte in atherogenesis: II. Migration of foam cells from atherosclerotic lesions. *Am. J. Pathol.* **103**, 191–200 (1981)
**FURTHER READING** Choi, J. H. *et al.* Identification of antigen-presenting dendritic cells in mouse aorta and cardiac valves. *J. Exp. Med.* **206**, 497–505 (2009)