Correspondence

CD1 Expression and the Nature of CD1-Expressing Cells in Human Atherosclerotic Plaques

To the Editor-in-Chief:

In a recent issue of *The American Journal of Pathology*, Melián et al reported that CD1 molecules are expressed in human atherosclerotic plaques.¹ CD1 molecules are antigen-presenting molecules in the same sense as the classical MHC class I and II molecules.² The observations of Melián et al¹ that all four types of CD1 molecules, namely, CD1a, CD1b, CD1c, and CD1d are expressed and coexpressed in atherosclerotic plaques are important.

Melián et al reported that all four CD1 molecules were expressed in atherosclerotic lesions, but none of these were expressed in the normal nondiseased arterial wall.¹ The latter conclusion disagrees with our findings, namely, that CD1a is expressed in the nondiseased arterial intima.^{3,4} We observed that CD1a is expressed by S-100-positive dendritic cells, which were disseminated throughout the subendothelial layer of the normal arterial intima, although there were more dendritic cells in the areas predisposed to atherosclerosis than in the areas resistant to atherosclerosis.⁴

Melián et al reported that in atherosclerotic plaques, CD1a expression is restricted to foam cells.¹ We disagree, because in our studies, CD1a was mainly expressed in plaques by cells which coexpressed S-100 proteins as well as Lag-antigen and actin-bundling protein p55, both of which are specific markers of dendritic cells.⁵ In our studies, most vascular dendritic cells did not transform into foam cells,^{3,5} although a few accumulated excess lipids and transformed into foam cells.⁶ These foam cells of dendritic cell origin are distinct, as they contain cisterns of the tubulovesicular system and Birbeck granule-like structures typical of dendritic cells.⁶

Because CD1 molecules were displayed by CD68-positive foam cells, Melián et al concluded that CD1 expression related to foam cells of macrophage origin.¹ We differ, considering that these foam cells represent foam cells of dendritic cell origin. The hematopoietic development of dendritic cells may allow for several precursor pathways, some closely linked to monocytes.⁷ Dendritic cells may display leukocyte and macrophage markers including CD14 and CD68.⁷ Using a double immunostaining technique, we demonstrated an association of CD68 with both CD1a and S-100 around the atheromatous core in human atherosclerotic plaques,⁸ but it was not clear to us that CD1a and CD68 were coexpressed by dendritic cells alone or that the close apposition of these antigens reflected a close apposition of dendritic cells and macrophages.⁸ Ultrastructural in-

vestigations demonstrated direct contacts between dendritic cells and macrophages.³ Although CD68 expression by some dendritic cells in the atherosclerotic intima cannot be excluded, it is certain that the vast majority of CD68-positive foam cells are negative for CD1a.^{3,8}

Yuri V. Bobryshev
Reginald S. A. Lord

University of New South Wales
Sydney, Australia

References

1. Melián A, Geng YJ, Sukhova GK, Libby P, Porcelli SA: CD1 expression in human atherosclerosis. *Am J Pathol* 1999, 155:775–789
2. Porcelli SA: The CD1 family: a third lineage of antigen-presenting molecules. *Adv Immunol* 1995, 59:1–98
3. Bobryshev YV, Lord RSA: Langhans cells of human arterial intima: uniform by stellate appearance but different by nature. *Tissue Cell* 1996, 28:177–194
4. Lord RSA, Bobryshev YV: Clustering of dendritic cells in athero-prone areas of the aorta. *Atherosclerosis* 1999, 146:197–198
5. Bobryshev YV, Lord RSA: 55-kD actin-bundling protein (p55) is a specific marker for identifying vascular dendritic cells. *J Histochem Cytochem* 1999, 47:1481–1486
6. Bobryshev YV, Watanabe T: Subset of vascular dendritic cells transforming into foam cells in human atherosclerotic lesions. *Cardiovasc Pathol* 1997, 6:321–331
7. Hart DNJ: Dendritic cells: unique leukocyte populations which control the primary immune response. *Blood* 1997, 90:3245–3287
8. Bobryshev YV, Lord RSA: Mapping of vascular dendritic cells in atherosclerotic arteries suggests their involvement in local immune-inflammatory reactions. *Cardiovasc Res* 1998, 37:799–810

Author's Reply:

In the article by Melián et al¹ we report the expression of CD1 molecules in atherosclerotic plaques. As shown in Figure 1 of the article,¹ staining for CD1 molecules occurred predominately in atherosclerotic plaques and by comparison was not readily detectable in normal, nondiseased tissue. We do not disagree with the point made by Drs. Bobryshev and Lord that CD1a-positive dendritic cells may reside in normal arterial walls, as supported by their studies. Our failure to detect these cells in the normal artery samples that we studied may reflect the relatively small numbers of these cells in such samples, as well as differences in the particular antibodies or staining techniques used in our studies compared to those of Bobryshev and Lord. In any case, the up-regulation of CD1 expression in atherosclerotic lesions compared to normal arterial tissue shown in our study remains striking. In terms of the question of the cell type(s) expressing CD1 molecules in atheroma, we consistently observed staining with antibodies directed against all four of the