

Nature Medicine: An immune cell subtype plays an ‘unexpected’ role in protecting against atherosclerosis

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Marginal B cells, a subtype of immune cells, appear to protect against atherosclerosis. The findings are published in *Nature Medicine* by a team including researchers from the *Centro Nacional de Investigaciones Cardiovasculares Carlos III* (CNIC) and Cambridge University (United Kingdom). In this first study to examine the role of this specific B cell subtype, the research team not only shows that marginal B cells protect against atherosclerosis but also describes the mechanism through which they enact this protective function.

Atherosclerosis is the leading cause of death in developed countries. “Atherosclerosis is the accumulation of cholesterol in the arteries due to poor diet, genetic predisposition, and other risk factors,” explains first author Meritxell Nus, of Cambridge University. Over time, “these cholesterol plaques can rupture and trigger a heart attack.”

B cells are one of the most important cell types involved in the immune response. In mice, marginal B cells are found exclusively in the spleen, but in humans they are also located in the blood, explains José Luis de la Pompa, researcher at the CNIC and the *Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares* (CIBERCV), and one of the authors on this study led by Ziad Mallat of Cambridge University. The possible role of B cells in atherosclerosis was controversial for many years, until research revealed the importance of distinguishing between different B cell subtypes with distinct functions.

“Marginal B cells express high levels of a protein called Pdl1 on their cell surface, and these levels are increased by a cholesterol-rich diet,” explains Meritxell Nus, who carried out part of her research at the CNIC. “Pdl1 binds another protein, PD1, on the surface of a T lymphocyte subtype called follicular regulatory T cells. This interaction limits the T cells’ mobility, impeding their ability to reduce cholesterol plaques.” Dr. Nus adds that Pdl1 expression on marginal B cells is also important in other fields, such as cancer, and many current antitumor therapies include Pdl1-blocking drugs.

The *Nature Medicine* study also shows that marginal B cells are required for the full differentiation of follicular regulatory T cells. According to Nus, “This is an important finding because until now workers in the field of immunology did not suspect any relation between these cell types, which occur in different locations.”

In summary, this study reveals a previously unsuspected role of marginal B cells in the control of atherosclerosis, and also identifies a Pdl1-dependent mechanism through which these cells’ innate immune properties prevent an excessive adaptive immune response. According to the research team, these results could have important implications for our understanding of how environmental factors such diet impact the appearance or progression of immune-mediated diseases.

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[Nus, M., Sage, A. P., Lu, Y., Masters, L., Lam, B. Y. H., Newland, S., . . . Mallat, Z. \(2017\). Marginal zone B cells control the response of follicular helper T cells to a high-cholesterol diet. *Nature Medicine*. doi:10.1038/nm.4315](https://doi.org/10.1038/nm.4315)

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