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Phosphorylcholine and antibodies against it in atherosclerosis and CVD: novel protection marker and potential for immunization against atherosclerosis

Johan Frostegård
Karolinska Institutet, Stockholm, Sweden

Statement of the Problem: Atherosclerosis and cardiovascular disease (CVD) represents together a major cause of morbidity and mortality, even though both prevention and treatment. Atherosclerosis is characterized by accumulation of dead cells, oxidized low density lipoprotein (OxLDL), activated immune competent cells and ensuing calcification. Phosphorylcholine (PC) is a small epitope, which is immunogenic when expressed, which occurs on both dead cells and OxLDL. PC plays an important role in OxLDL-induced immune activation. PC is also exposed on nematodes, helminths, parasites and some bacteria. Antibodies against PC (anti-PC) are present in all humans we studied and constitute around 5-10% of IgM.

Results: We combinate experimental and clinical/epidemiological approaches. We reported 2006 that anti-PC is associated with protection against atherosclerosis development. After this, we published many studies, reporting that IgM and IgG1 (but less IgG2) anti-PC are protection markers, and low levels are risk markers, independent of and similar or higher as established ones as hypertension, smoking, diabetes and hyperlipidemia. These associations have been largely confirmed and extended by other researchers. Underlying mechanisms of anti-PC-effects include anti-inflammatory, immunomodulatory, and inhibition of uptake of OxLDL in the artery wall. Immunization with PC ameliorates atherosclerosis and mouse models. Brown bears, in spite of uremia, immobility and very high blood cholesterol. We recently reported that IgM and IgG1 anti-PC gets very high during fall and at hibernation, and suggested this may be a natural immunization against atherosclerosis. Individuals from Papua, New Guinea in the early 90s, who have no signs of CVD, have very high levels of anti-PC. We proposed a development of the Hygiene/ Old Friends hypothesis: low anti-PC levels may be caused by lack of PC-exposing microorganisms.

Conclusion: Anti-PC is a protection marker for atherosclerosis and CVD. Immunization with PC, raising IgM and IgG1 be developed into a human vaccine.

Biography

Johan Frostegård, born 2 October 1959, is Professor of Medicine at Karolinska Institutet and also senior consultant, being specialist in both Internal Medicine and in Rheumatology . JF has published about 180 scientific peer reviewed papers.

The research area is focused on immunology, inflammation and atherosclerosis/CVD, with special emphasis on autoimmunity and rheumatology. Anti-PC and PC (together with OxLDL) have been a major interest for long time, but also other novel aspects have been studied, including Annexin A5 as a potential anti-inflammatory compound in this context and also immunological properties of statins and PCSK9. JF is active as inventor, and is co-founder of biotech companies, including Annexin Pharma ceuticals. JF is also active as a writer.

johan.frostegard@ki.se