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Low levels of natural antibodies against phosphorylcholine—a novel concept in autoimmunity

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Background: Atherosclerosis is a chronic inflammatory disease process, which leads to cardiovascular disease (CVD) which is increased in rheumatic diseases, especially in systemic lupus erythematosus (SLE). IgM antibodies to phosphorylcholine (anti-PC) constitute a significant part of the circulating IgM pool. We reported that anti-PC is a protection marker for atherosclerosis and CVD, and applies also to rheumatic and autoimmune diseases.

Material & Methods: We use a combination of *ex vivo* studies and cohort studies. Dendritic cells (DC) and T cells from patients with SLE, and from atherosclerotic plaques, are studied, and anti-PC is determined by ELISA.

Results: Having low levels of anti-PC (below tertile or quartile) was associated with SLE, with CVD and atherosclerosis in SLE, and with being a non-responder to biologics in rheumatoid arthritis. Anti-PC promoted polarization of T cells from SLE patients into T regulatory cells, and from a lower level than among controls, T regs normalized in SLE patients after anti-PC exposure. Other potential underlying mechanisms include an anti-inflammatory property (inhibition of pro-inflammatory lipids which are raised in SLE); inhibition of uptake of oxidized LDL in macrophages; increased clearance by phagocytosis of dead cells. Anti-PC levels were very high in New Guinea among people living a traditional “stone age” life, and where rheumatic diseases and chronic inflammatory conditions are virtually unknown and also anti-PC was associated with some infectious agents there.

Conclusion: Low anti-PC could contribute to development of autoimmune and rheumatic disease, in addition to atherosclerosis and CVD. One underlying cause could be lack of exposure to some microorganisms. These findings could have therapeutic implications, including immunization to raise anti-PC levels.

Biography

Johan Frostegård is a Professor of Medicine since 2003 and Senior Consultant in Internal Medicine and in Rheumatology. His research is focused on Autoimmunity and Atherosclerosis, where his research group has for the first time identified a novel protection marker, natural antibodies against phosphorylcholine (anti-PC) and also mechanisms which could provide a cause as to how anti-PC could protect against both autoimmunity and atherosclerosis. He led a European Union research consortium, CVDIMMUNE, where some of the concepts developed were presented.

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