IgG1 anti-PC reduces CVD risk in SLE patients by efficiently clearing apoptotic cells

Thiagarajan D, Frostegård A and **Frostegård J**
Karolinska Institutet, Sweden

Background: Dual role of natural IgM antibodies against both phosphorylcholine (PC) and Malondialdehyde (MDA) in assisting the clearance of apoptotic cells and reducing atherosclerotic plaques size has been suggested previously. In this study we aim to understand the role of IgG1, IgG2 in Cardiovascular outcomes in SLE and their functions in in-vitro conditions.

Methods: We used a unique SLE- Vascular Impact Cohort (SLEVIC), which consisted of 116 SLE-patients from Karolinska University Hospital Huddinge and 110 matched controls. The levels of IgG1s and IgG2 was measured by ELISA. For functional studies, we used fully human monoclonal antibodies. Primary human macrophages were cultured with MCSF. Apoptosis was induced in TAMRA labelled Jurkat T-cells by CD95 ligand and incubated with anti-PC IgGs or isotype control IgG1 (1µg/mL), one hour prior to phagocytosis. Anti-PC antibody labelled apoptotic Jurkat cells were fed to mature M2 macrophages for 60-80 mins and the cells were formalin-fixed for microscopic examination. Phagocytosis was assessed by number of macrophages up-taking TAMRA labelled Jurkat cells to the total number of macrophages in the given area.

Results: IgG1 Anti-PC and IgG2 Anti-MDA were negatively associated with atherosclerosis IgG1 Anti-PC was negatively associated with CVD, SLEDAI and SLICC Simultaneously, the IgG1 anti-PC clones D05, improved phagocytosis efficiency from 25% (both macrophages and isotype control) to and 53%(p=0,007) followed by E01, 37%(p=0,05) and A01,28% (p=NS) where, the anti-PC IgG1s bind to phosphorylcholine exposed on apoptotic cells and facilitate the uptake by macrophage though Fc gamma receptor.

Conclusion: The impaired clearance of apoptotic cells and increased OxLDL uptake are hallmark in both SLE and development of necrotic core in atherosclerotic plaques respectively. This study evidently show that anti-PC IgG1 is not only lower in atherosclerotic patients but exogenous addition of anti-PC IgG1s efficiently improves the apoptotic cell uptake thereby making a possible therapeutic candidate for SLE patients in future.

divya.thiagarajan@ki.se

Notes: