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Anti-TNF: Possibilities of Rising Anti-Phosphorylcholine Antibodies

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Abstract : The role of the human immune system is essential in cardiovascular diseases and atherosclerosis. Activated cells in atherosclerosis produce abundant amounts of cytokines, but the exact mechanisms involved in the effects of these inflammatory cytokines are not clear in atherosclerosis. In a large clinical cohort, we have previously determined that antibodies against phosphorylcholine (anti-PC) are negatively and independently associated with both development of atherosclerosis and also a low risk of cardiovascular disease. Further, we reported that rheumatoid arthritis patients who were non-responders to TNF-inhibitors, where those with low anti-PC levels. Upon anti-TNF treatment, anti-PC levels increased. We, therefore, hypothesised that proinflammatory cytokines such as TNF could play a role in anti-PC regulation. Peripheral blood mononuclear cells (PBMC) were cultured with or without TNF and anti-TNF. The cell supernatants were collected after six days for ELISA measurements. In separate experiments, cells were cultured for 24 hours in both polystyrene plates and ELISPOT plates under a similar condition for ELISA and ELISPOT assays respectively. Total RNA was extracted after 6 hours of cell culture to perform RT-qPCR. Cell viability was confirmed by trypan blue staining and MTT assays. ELISA measurements detected less than 40% of anti-PC in TNF-treated cells, in comparison to control cells, whereas anti-PC production was recovered by anti-TNF treatment. ELISPOT assays showed that TNF suppresses anti-PC production by inhibiting anti-PC producing B-cells. In addition, RT-qPCR and ELISA showed that TNF also has effects also on B-cell activation as BAFF expression was inhibited by TNF treatment. Atherosclerosis is a major cause of cardiovascular diseases, but anti-PC is a protection marker for atherosclerosis development. Our findings show that TNF is a negative regulator of anti-PC production. Immune modulation and rising of anti-PC could be of major significance for the patients.

Keywords : anti-PC, Anti-TNF, atherosclerosis, cardiovascular diseases, phosphorylecholine
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