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ANTI-APOLIPOPROTEIN A-1 IGG IN PATIENTS WITH MYOCARDIAL INFARCTION PROMOTES INFLAMMATION THROUGH TLR2/CD14 COMPLEX.

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Introduction: Toll-like receptors (TLRs) mediated vascular inflammation, inducible by- amongst other factors- auto-antibodies, is increasingly recognized as a potential mediator of cardiovascular disease. We investigated whether anti-apolipoprotein A-1 (ApoA-1) IgG were associated with a pro-inflammatory cytokine profile in myocardial infarction (MI) patients, and whether anti-ApoA-1 IgG elicited a pro-inflammatory response by activating TLRs.
Méthode: As surrogate markers of atherosclerotic plaque vulnerability, interleukin (IL)-6, tumor necrosis factor (TNF)-α, matrix-metalloproteinase (MMP)-9 and MMP-3 levels were assessed on 221 consecutive MI patients. Using human monocyte-derived macrophages (HMDMs) we investigated i) the anti-ApoA-1 IgG interaction with TLRs using proximity ligation assay (PLA), and ii) anti-ApoA-1 IgG-dependent IL-6/TNF-α production. TLR involvement was further confirmed using HEK293-Blue TLR-2/-4 cells and by computational docking simulations.
Résultat: In MI patients, anti-ApoA-1 IgG positivity was associated with higher levels of IL-6, TNF-α, MMP-9, but lower MMP-3 levels. In in vitro experiments, anti-ApoA-1 antibodies bound to HDMDs in a TLR2-dependent manner, resulting in nuclear translocation of NFκB and a significant increase in TNF-α and IL-6 production. Subsequent functional studies highlighted the importance of CD14 as co-receptor in the anti-ApoA-1 IgG-TLR2- induced cytokine production. Additional bioinformatic studies identified structural homologies between TLR2 and ApoA-1, which may explain the observed cross-reactivity between antibodies against these two molecules.
Conclusion: Anti-apoA-1 IgG positivity in MI is associated with a high-risk cytokine profile. These auto-antibodies promote inflammation by stimulating the TLR2/CD14 receptor complex, probably because of molecular mimicry, which may contribute to atherosclerosis-related complications in patients.