Effects of Pro-Resolving Lipid Mediators on Nitric Oxide and Prostacyclin Pathways in Human Endothelial Cells

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Introduction and Aim: Inflammation plays a central role in the development and progression of atherosclerosis. Pro- resolving lipid mediators, including Resolvins (RvE1) and Maresins (MaR1) are key regulators of the resolution phase of inflammation. Despite their known anti-inflammatory effects, their impact on nitric oxide (NO) and prostacyclin (PGI2) levels in human umbilical vein endothelial cells (HUVECs) remains underexplored. This study investigates the effects of RvE1 and MaR1 on vascular inflammation, focusing on NO and PGI2 in HUVECs.
Methods: An in vitro inflammatory model was established by incubating HUVECs with lipopolysaccharides (LPS, 100 µg/mL) and interleukin-1 beta (IL-1β, 100 ng/mL) for 24 hours. RvE1 and MaR1 (100 nM) were then applied under the same conditions. Levels of tumor necrosis factor-alpha (TNF-α), total nitrite-nitrate, and the stable PGI2 metabolite 6- keto-PGF1α were measured in the incubation medium using ELISA.
Results and Discussion: LPS and IL-1β significantly increased TNF-α levels, confirming the inflammatory response. RvE1 and MaR1 significantly reduced nitrite-nitrate levels, suggesting their role in mitigating vascular inflammation. However, no significant changes were observed in 6-keto-PGF1α levels (n=3-4, p>0.05). These findings highlight the selective effects of RvE1 and MaR1 on different pathways involved in endothelial inflammation.
Conclusion: This preliminary study demonstrates that RvE1 and MaR1 appear to reduce nitrite-nitrate levels, their lack of impact on 6-keto-PGF1α suggests distinct pathway-specific actions that warrant further investigation. Future studies with larger sample sizes, varied inflammatory conditions, are essential to confirm these findings and better understand their therapeutic potential.
Relevance to AtheroNET: This research aligns with AtheroNET's goal of exploring novel anti-inflammatory strategies, emphasizing the importance of pro-resolving lipid mediators in vascular health.

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Proteomic analysis for prediction of type 2 diabetes identifies cardiovascular disease-related proteins

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Introduction and Aim: Cardiovascular disease (CVD) and type 2 diabetes (T2D) are interconnected chronic conditions which cause significant global health challenges and mortality. T2D is a risk factor for CVD characterized by insulin resistance and beta-cell dysfunction. This study aims to investigate the association between the blood plasma proteome and T2D in the Trøndelag Health (HUNT) Study.
Methods: The HUNT Study is a population-based cohort with four waves of enrollment beginning in 1984. 5,402 samples from HUNT3 were analysed with SomaScan including 3,221 on SomaScanv4.0 (~5,000 proteins) and 2,181 on SomaScanv4.1 (~7,000 proteins). T2D was defined based on self-reported disease from questionnaires. Binary logistic regression analysis was performed to test the associations of protein concentrations with T2D. Models included adjustment by sex, age, waist-hip-ratio (WHR), smoking status, and comorbidities.
Results and Discussion: We identified 584 proteins that are significantly associated with T2D. From these proteins, CILP2 and MXRA8 are associated with decreased risk, while PLXB2 and NFASC are associated with increased risk for having T2D. The most significant pathway from GO enrichment analysis includes proteins related to lipid catabolic process (FDR adjusted p-value: 0.000054). Indeed, several proteins significantly associated with T2D are known for their role in lipid metabolism, for instance Adiponectin (OR 0.55; 95% CI 0.46 - 0.65), Apo A – IV (1.57;1.37 - 1.81), Apo B (0.63; 0.55 - 0.73), Apo C – I (0.73; 0.64 - 0.84), and Apo D (0.49; 0.38 - 0.63).
Conclusion: The proteins and pathways identified represent insights into the underlying molecular mechanism of T2D and may serve as potential biomarkers for risk prediction and prevention for CVD.
Relevance for AtheroNET: The findings suggest that early identification of these proteins could mitigate cardiovascular risks in individuals with or at risk for T2D.