Serum sIL-6Rα Predicts Impairments in Cutaneous Nitric Oxide-Dependent Vasodilation in Humans.

[1]Kutz, J., [2]Cannon, J., [1]Kenney, W.L., FACSM, [1]Alexander-Holowatz, L,. FACSM. [1]The Pennsylvania State University, University Park, PA, [2]School of Allied Health Sciences, Medical College of Georgia, Augusta, GA.

jlk5268@psu.edu, jcannon@georgiahealth.edu, w7k@psu.edu, lma191@psu.edu

Purpose: Interleukin-6 (IL-6) contributes to atherosclerotic plaque development and plaque destabilization by promoting inflammation. Soluble IL-6 receptors (sIL-6R) are capable of stimulating a variety of cellular responses through trans-signaling including activation of inflammatory processes inducing endothelial dysfunction in the vasculature. The aim of the present study was to determine if sIL-6Rα was related to impairments in nitric oxide (NO)-dependent cutaneous vasodilation in humans across a broad range of serum low-density lipoprotein (LDL) concentrations. **Methods:** In 19 men and women, with a broad range of serum LDL concentrations (LDL: 75-233 mg/dl), skin blood flow (SkBF) was measured by laser-Doppler flowmetry during a standardized local heating protocol (42°C) to induce eNOS-dependent vasodilation. After full expression of SkBF during sustained local heating, NO-dependent vasodilation was quantified by perfusion of the NOS inhibitor L-NAME. All data were normalized as a percentage of maximum cutaneous vascular conductance (%CVC_{max} = laser-Doppler flux/ mean arterial pressure: 28mM sodium nitroprusside). Serum samples were analyzed for the inflammatory cytokines IL-6, sIL-6Rα and TNFα using a customized cytometric bead assay. **Results:** NO-dependent vasodilation ranged from 22 to 82 %CVC_{max} and sIL-6Rα values were measured from 13.8 to 31.6 ng/ml. NO-dependent vasodilation was negatively related to sIL-6Rα (R^2 = 0.368,p= 0.006) and to serum LDL concentrations (R^2 = 0.328,p= 0.01). IL-6 and TNFα were not related to NO-dependent vasodilation. Stepwise regression revealed that sIL-6Rα was the best predictor of NO-dependent vasodilation. **Conclusion:** Both sIL-6Rα and low-density lipoproteins are independently associated with impairments in cutaneous microvascular function. **Research funded by NIH Grant HL-089302-05.**