HUMAN PROSTACYCLIN RECEPTOR POLYMORPHISMS AND ATHEROGENESIS

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Selective inhibitors of cyclooxygenase 2 (COX-2) confer a small but absolute risk of myocardial infarction and stroke presumably through inhibition of COX-2-dependent prostacyclin (PGI_2). PGI_2 acts as a general restraint on endogenous stimuli to platelet activation, vascular proliferation and remodeling, hypertension, atherogenesis, and cardiac function risk. Development of genetic biomarkers will be useful to identify the patients uniquely susceptible at developing risk of cardiovascular complications by selective inhibition of COX-2. We aimed to investigate the association between 31 distinct single nucleotide polymorphisms (SNPs) in the human PGI_2 receptor (IP) and intima-media thickness(IMT) of the common carotid arteries, a surrogate measure for systemic vessel disease, in 40 individuals with a previous objectively confirmed deep vein thrombosis (DVT) and 21 controls, i.e. individuals without DVT but with comparable cardiovascular risk factors (cigarette smoking, diabetes, hypertensive status, lipid levels, body mass and systemic inflammatory status index, i.e. CRP, fibrinogen). We identified 5 SNPs which were not statistically significant different between the 2 groups (using Chi square test). Three were synonymous (no alteration in the coding amino acid sequence),V53V(DVT, 40% versus controls, 13%), V196 (DVT, 2.5% versus controls, 0%), S328S (DVT, 60% versus controls, 57%), and 2 were nonsynonymous (change in the coding amino acid sequence), P226T (DVT, 2.5% versus controls, 0%), and R212C (DVT, 7.5% versus controls, 5%). Interestingly, R212C polymorphism is associated with functional deficiencies. In DVT and controls, IMT values were not significantly different (1.12±0.45 and 1.13±0.28 mm, mean±SD). However, we found that the 4 individuals carriers of R212C polymorphism (3 in DVT and 1 in control group) were characterized by significant (P=0.006) higher IMT values versus all population (1.67±0.37 versus 1.08±0.37 mm). None of the 4 individuals were carriers of factor V Leiden. In conclusion, our results suggest a possible contribution of IP in the progression of atherosclerosis in human and pave the way to perform larger studies assessing a possible correlation between R212C polymorphism and vascular disease.