Investigation of a novel protein ADTRP and its role in coronary artery disease

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Background: The novel protein, androgen-dependent TFPI regulating protein (ADTRP) was found to regulate TFPI in an androgen-dependent manner and intronic SNP, rs6903956 of the ADTRP gene was associated with CAD. More recently, ADTRP was recognized as a hydrolytic enzyme that breaks down a class of lipids known as FAHFA which were shown to have anti-diabetic and anti-inflammatory effects.

Purpose: We aim to investigate the possible regulatory effect of ADTRP on genes that may be involved in biological pathways related to CAD.

Methods: Human endothelial cell line, EA.hy926 was stimulated with androgen and recombinant ADTRP respectively, and mRNA expression of ADTRP and TFPI was measured using real-time RT-PCR. Plasma ADTRP levels in CAD and non-CAD patients were measured using ELISA. Global gene expression profiling of EA.hy926 cells stimulated with recombinant ADTRP was performed using microarray.

Results: We observed an up-regulation of both ADTRP and TFPI mRNA expression upon stimulation with androgen. However, stimulation of EA.hy926 with recombinant ADTRP did not cause a significant up-regulation of TFPI. CAD patients were found to have significantly lower plasma ADTRP as compared to non-CAD patients (p=0.004). Gene expression profiling demonstrated that ADTRP stimulation regulates a diverse set of genes involved in inflammatory signaling, cell cycle, apoptosis, histone modifications and olfactory receptor activity.

Conclusions: Our results indicate that ADTRP may not have a direct effect in regulation of TFPI and the gene expression data highlights the possible functions of ADTRP in multiple biological pathways that may be involved in the pathogenesis of CAD.