Cultured endothelial cells response to extracellular diabetic–like environment: gene expression analysis

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Aims/hypothesis: High blood and tissue concentrations of glucose and advanced glycation end products (AGEs) are thought to play an important role in the development of vascular diabetic complications. Therefore the impact of extracellular AGEs and of different glucose concentrations was evaluated by studying the gene expressions and the underlying cellular pathways involved in the development of inflammatory processes observed in cultured endothelial cells.

Methods: Fresh human umbilical vein cord endothelial cells (HUVEC) were treated in the presence of elevated extracellular glucose concentrations (5.5-28 mmol/l) with and without AGEs-HSA. Affymetrix GeneChip® Human Gene 1.0 ST arrays were used for gene expression analysis (total 20 chips). Genes of interest differentially expressed ($p<0.05$) were further validated using Real-time PCR and Western Blot.

Results: Microarray analysis revealed significant changes in some gene expressions in the presence of the different stimuli, suggesting different pathways involved. Validation of the increased expressions of selected genes was examined as follows: thioredoxin – interacting protein (*TXNIP*), *NFKB*, interleukin 6 (*IL6*), interleukin 8 (*IL8*), and receptor of AGEs (*RAGE*). Interestingly it was found that the association of AGEs together with the highest pathophysiological concentrations of glucose diminished the expression of these specific genes.

Conclusion/interpretations: In the present model dealing with a diabetic like environment the relative short term experiments we used have shown an unexpected blunting action of AGEs in presence of the highest glucose concentrations. Further investigations will have to be performed to determine the cellular interactive pathways which have been involved in theses processes.