THE EXPRESSION OF HEART-RELATED GENES IS ALTERED IN DIABETIC AND NON DIABETIC RAT HEARTS PERFUSED WITH HIGH LEVELS OF GLUCOSE

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Diabetes mellitus is characterized by an increased risk of death after cardiovascular diseases related to hyperglycemia. To investigate the pathogenetic mechanisms underlying these cardiovascular complications, we studied gene expression changes in isolated diabetic(STZ 70 mg/Kg i.p.) and non diabetic rat hearts perfused with high glucose solution. Rat hearts were cannulated *via* the aorta and perfused for 2 h with control Krebs solution (glucose 11.1 mmol/l) and high glucose Krebs solution (glucose 33.3 mmol/l). Total RNA was extracted using the RNeasy kit (Qiagen). We studied gene expression profile by Microarray technique with Applied Biosystems 1700 Chemiluminescent analyzer and Real Time PCR (RT PCR) TaqMan assays (Applied Biosystems). Statistical analysis in microarray experiments has been performed on the complete series of experiments using Spotfire software. We studied biological processes, molecular functions and pathways with PANTHER classification system. In microarray (MC) studies we identified a series of genes significantly up and down regulated ($p<0.05$). In particular, we observed a change of expression of 167 genes in non diabetic rat hearts and of 368 genes in diabetic rat hearts (control *vs* high glucose concentration) and a change of expression of 2,742 genes in diabetic *vs* non diabetic rat hearts both exposed to high glucose concentration. Among them we selected genes with a fold change >2 and studied their biological processes and molecular functions. In particular, in our experimental model, we observed a significative change of expression of genes involved in: ion trasport, mRNA transcription, signal transduction, cytokine and chemokine mediated signaling pathway, protein, fatty acid and steroid metabolism, apoptosis and immunity defense. RT PCR data (in non diabetic rat hearts) confirmed gene expression changes of: Ucp1 (uncoupling protein 1) (MC: +5.6 ; RT PCR: +261.4); IL6 (interleukin 6) (MC: +4.05 ; RT PCR: +3.81); Ccl7 (chemokine (C-C motif) ligand 7) (MC: +3.5 ; RT PCR: +2.51); Ccl2 (chemokine (C-C motif) ligand 2) (MC: +3.6 ; RT PCR: +5.49); Has1 (hyaluronan synthase1) (MC: +2.1 ; RT PCR: +1.94); Has2 (hyaluronan synthase2) (MC: +3.5; RT PCR: +2.38) and down-regulation of TRPC3 (transient receptor potential cation channel member 3) (MC: -0.33 ; RT PCR: -0.60). Others RT PCR experiments are in course to validate microarrays results. Our results demonstrate that high glucose modifies the expression of some genes involved in the regulation of important cell functions. These genes could shed light on new therapeutic targets for cardiovascular desease induced by high glucose levels and diabetes.