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GENE EXPRESSION PROFILE OF CIRCULATING MONOCYTES IN FIRST-DEGREE RELATIVES OF TYPE 2 DIABETIC PATIENTS IN RESPONSE TO ORAL GLUCOSE TOLERANCE TEST

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Purpose: To study whether there exists genetic predisposition to alterations of immune status that is observed in type 2 diabetes (T2DM) patients. We investigated gene expression profile of circulating monocytes in response to oral glucose tolerance test (oGTT) in non-diabetic first degree relatives (FDR) of T2DM patients and in control subjects.

Methods: 12 non-diabetic male FDR and 12 control subjects without family history of diabetes matched for age and BMI underwent 2 hours' oGTT. Blood samples were taken before and at the end of oGTT, monocytes were isolated from peripheral blood mononuclear cells with anti-CD14 monoclonal antibody coated magnetic beads and gene expression profile analysis using RT-PCR was performed. *Results:* FDR subjects showed higher HOMA-IR index and higher Matsuda index of insulin resistance than controls. Significant downregulation of pyruvate dehydrogenase kinase isozyme 4 (PDK4) mRNA expression during oGTT was found in the two groups: this was taken as a positive control for oGTT effect. Among 8 immune-related genes analyzed, 4 genes were regulated during oGTT in at least one subject group (interleukine 8, tumor necrosis factor alpha (TNFalpha), chemokine (C-C motif) ligand 5 (CCL5) and chemokine (C-C motif) ligand 2 receptor). Among those, significantly different response to oGTT was found for TNFalpha and CCL5 gene: both were upregulated in FDR while downregulated in controls.

Conclusion: Results suggest an enhanced pro-inflammatory response to nutrient challenge in FDR. This pro-inflammatory response may be a feature of genetic predisposition to T2DM. *Supported by grants GACR 16-14048S and PROGRESS Q36*



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