

P056 IL-1-antagonism prevents IL-1-mediated inhibition of striated muscle gene-expression involved in antigen-presentation and differentiation in Type 2 diabetes

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Background: Systemic blockade of IL-1 β with IL-1 receptor antagonist (IL-1Ra) lowers HbA1c, improves β -cell function and reduces circulating IL-6 levels in patients with Type 2 diabetes. To investigate IL-1Ra effects in insulin-sensitive tissue, muscle biopsies from patients from the above mentioned study were analysed by microarray. Methods: Gene expression profiles in vastus lateralis biopsies from six patients before and after 13 weeks of IL-1Ra treatment were determined using AffymetrixU133Plus2.0 GeneChips and analyzed with dChip and Ingenuity software. Results: After IL-1Ra treatment, 47 genes were differentially expressed (P-value<0.05). Fold changes were from 1.20-2.67 for both up- and downregulated genes (23 and 24 genes, respectively). Class I antigen presentation and Notch signalling pathways were significantly upregulated (Ingenuity, P-values: 4.14E-05 and 2.2E-03, respectively). HLA-A and adhesion protein 1 were among the upregulated genes, while heat-shock protein 70 and cyclin-dependent kinase-inhibitor1C were among the downregulated genes. Conclusion: IL-1 reduces the expression of genes regulating muscle tissue antigen presentation and regeneration/differentiation in Type 2 diabetes and these changes are prevented by IL-1Ra.