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LARGE-SCALE ANALYSIS OF SKELETAL MUSCLE GENE EXPRESSION AFTER EXERCISE IN OBESE, DIABETIC PSAMMOMYS OBESUS (ISRAELI SAND RATS)

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Exercise has been shown to ameliorate the severity and symptoms of obesity and type 2 diabetes. Using cDNA microarrays we investigated skeletal muscle gene expression after exercise training in obese, diabetic Psammomys obesus, a unique polygenic animal model of obesity and type 2 diabetes. A group of 15 male obese, diabetic P. obesus (blood glucose 12.4±1.1 mmol/L) underwent exercise training (running 1km/day in 1hr) for 3 weeks, resulting in significant reduction in glycemia (to 9.1±1.1 mmol/L; p=0.02). Mean plasma insulin concentration also decreased by 34% after exercise training (702±76 to 463±45 mU/L). The heterogeneity of outbred P. obesus was evident from their variable response to exercise training. The reduction in blood glucose after training ranged from 0.3 to 10.7 mmol/L (2-74%). All animals underwent indirect calorimetry for 24hr before and after exercise training. Exercise training resulted in increased whole-body carbohydrate oxidation (by 13%) and decreased fat oxidation (by 15%) and physical activity (by 14%). A separate group of 8 untrained male obese, diabetic P. obesus (blood glucose 12.3±1.5 mmol/L) were used as controls. At the completion of the study, RNA was extracted from the red gastrocnemius muscle and hybridised to custom-made P. obesus cDNA microarrays of approximately 12,000 features. Microarray data was extracted using GenePixPro4 (Axon Instruments, CA) and analysed using GeneSight3 (BioDiscovery, CA) and Acuity1 (Axon Instruments). Statistical analysis revealed that 107 genes showed evidence of differential expression between exercise-trained and control animals. A number of these genes have been sequence identified and analysed further using bioinformatics and expression profiling. Skeletal muscle genes regulated by exercise in obese, diabetic P. obesus include some expected genes such as cytochrome b and GAPDH as well a number of unknown genes that are currently undergoing further investigation.