Project financed by the National Science Centre ***" The search for the novel mechanisms linking intracellular calcium flux regulation with insulin sensitivity response to regular physical exercise***

Supervisor: prof.dr hab. Marek Strączkowski

Insulin resistance is a risk factor for type 2 diabetes, dyslipidemia, hypertension, cardiovascular disease, neurodegenerative disorders, different forms of cancer. It is usually associated with obesity. Skeletal muscle is the main tissue responsible for insulin-stimulated glucose uptake, which is decreased in insulin resistance. Physical activity exerts beneficial effects on the prevention of insulin resistance-related diseases.

The main feature of skeletal muscle is the ability to make contractions, called contractility. Ca^{2+} plays an essential role in the initiation of muscle contraction. It may stimulate muscle glucose uptake independently of contraction and may regulate gene expression and mitochondrial biogenesis. In skeletal muscle, the cytosolic Ca^{2+} level is mainly determined by Ca^{2+} movements between the cytosol and the sarcoplasmic reticulum. In our preliminary research, we found that genes associated with intracellular Ca^{2+} flux have decreased skeletal muscle expression in the group of young subjects with low insulin sensitivity.

We hypothesize that factors associated with intracellular Ca^{2+} may regulate muscle contractility, insulin sensitivity and individual response to regular physical exercise.

The aim of the project is to assess the role of the genes associated with intracellular Ca^{2+} flux in the regulation of muscle contractility, insulin sensitivity and the metabolic response to regular physical exercise.

We plan to examine 60 individuals, 20 normal-weight with normal glucose tolerance, 20 obese with normal glucose tolerance and 20 obese with impaired glucose tolerance. Insulin sensitivity will be measured with hyperinsulinemic-euglycemic clamp. Vastus lateralis muscle biopsy will be performed at baseline and after 12-week regular exercise training.

We also plan to perform C2C12 myoblast cell culture with the silencing of the examined genes. Next, electric pulse stimulation (EPS) will be performed in the part of the developed myotubes. Myotubes will be studied with and without gene silencing as well as without EPS and after EPS. Cell glucose uptake will be measured. The studied proteins, calcium channels and sarcomere development will be studied with confocal microscopy in myotubes and in human muscle samples. Furthermore, in all the conditions studied, gene (RNA-seq and qPCR) and protein expression (Westen blot and co-immunoprecipitation) will be measured.

The project will allow to study the role of the novel factors in the pathogenesis of skeletal muscle insulin resistance and in the modulation of metabolic response to physical exercise.

PhD student in the Department of Prophylaxis of Metabolic Diseases

Requirements:
- MSc in biotechnology/biology/medical analytics
- fluency in English
- knowledge in molecular biology techniques.

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