



## Exercise Biochemistry Review

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### Adaptation of skeletal muscle to aerobic exercise: specific transcriptome response to acute exercise and training

Daniil Popov<sup>1,2</sup>, Pavel Makhnovskii<sup>1,2</sup>, Evgeny Lysenko<sup>1,2</sup>, Olga Vinogradova<sup>1,2</sup>

1. Institute of Biomedical problems of the RAS

2. Lomonosov Moscow State University

**Objective** Variety of processes including circadian rhythm and systemic factors affect expression of many genes in skeletal muscle during a day. Therefore, post-exercise gene expression depends on many factors: contractile activity *per se* as well as circadian rhythm, nerve activity, concentration of different substances in blood, feeding and fasting. In our study, we investigated specific for contractile activity changes in the transcriptome in untrained and trained (after an aerobic training programme) human skeletal muscle. The second goal was to examine effect of aerobic training on gene expression in muscle in basal state.

**Methods** Seven untrained males performed the one-legged knee extension exercise (for 60 min) with the same relative intensity before and after a 2 month aerobic training programme (1 h/day, 5/week). Biopsy samples were taken at rest (basal state, 48 h after the previous exercise), 1 and 4 h after one-legged exercise from *m. vastus lateralis* of either leg. This approach allowed us to evaluate specific changes in the transcriptome associated with contractile activity. RNA-sequencing (84 samples in total; ~42 million reads/sample) was performed by HiSeq 2500 (Illumina).

**Results** Two months aerobic training increased the aerobic capacity of the knee-extensor muscles (power at anaerobic threshold in incremental one-legged and cycling tests), the maximum rate of ADP-stimulated mitochondrial respiration in permeabilized muscle fibres and amounts of oxidative phosphorylation proteins. After one-legged exercise, expression of many genes was changed in exercised muscle (~1500) as well as in non-exercised muscle (~400). Pronounced changes in gene expression in non-exercised muscle may be associated with many factors, including circadian rhythm (result of GO analysis).

To examine transcriptome changes specific for contractile activity, the difference in gene expression between legs was examined. In untrained muscle, one-legged exercise changed expression of ~1200 genes specific for contractile activity at each time point. Despite the same relative intensity of one-legged exercise, transcriptomic response in trained muscle was markedly lower (~300 genes) compare to untrained.

We observed a strong overlap between transcriptomic responses (~250 genes) and particularly between enriched transcription factor binding sites in promoters of these genes in untrained and trained muscles. These sets of genes and transcription factors play the key role in adaptation of muscle to contractile activity independently on the level of muscular fitness.

Surprisingly, 2 months aerobic training changed the expression of more than 1500 genes in basal state. Noteworthy, these genes demonstrated a small overlap (~200 genes) with genes related to specific response to acute exercise. Moreover, these genes were associated with significantly different biological processes than genes related to specific response to acute exercise.

**Conclusions** Specific for contractile activity changes in the transcriptome in untrained and trained human skeletal muscle were revealed for the first time. After 2 month aerobic training, the specific transcriptome response to acute exercise become much less pronounced. A computational approach reveals common transcription factors important for adaptation of both untrained and trained muscle. We found out that adaptation of muscle to aerobic training associates not only with the transitory changes in gene expression after each exercise, but also with the marked changes in transcriptome in basal state.

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