Does Resistance Exercise Training Significantly Alter Skeletal Muscle Gene Expression in Humans?

Group 4

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1. Academic Paper Summaries

Paper A: Phillips BE et al. (2013). Molecular Networks of Human Muscle Adaptation to Exercise and Age. *PLoS Genetics* 9(3): e1003389.

This study examined how physical activity and aging affect skeletal muscle at the molecular level using genome-wide transcript analysis. Researchers studied 44 individuals undergoing 20 weeks of resistance training, observing lean mass gains ranging from 3% to 28%. Counterintuitively, those with the greatest muscle growth showed an inhibited mTOR activation signature, including down-regulation of ribosomal RNAs. The analysis identified all-trans-retinoic acid (ATRA) signaling as a key exercise-responsive pathway. Using continuous age analysis across 97 subjects (ages 18–78), researchers identified approximately 500 age-related genes enriched in post-transcriptional processes. The study concludes that aging and exercise activate separate molecular networks in human muscle. Notably, this paper is the original source of the GSE47881 dataset we use in our analysis.

Paper B: Kumar V et al. (2009). Age-related differences in the dose–response relationship of muscle protein synthesis to resistance exercise in young and old men. *The Journal of Physiology* 587(1): 211–217.

This study investigated how myofibrillar protein synthesis (MPS) and muscle anabolic signaling respond to resistance exercise at varying intensities (20–90% of 1RM) in young (24 $\pm$ 6 years) versus older (70 $\pm$ 5 years) men with identical body mass indices. Results showed a sigmoidal dose-response relationship between exercise intensity and MPS at 1–2 hours post-exercise, but this relationship was significantly blunted in older men ($P < 0.05$). The authors concluded that older men exhibit "anabolic resistance" in signaling and MPS to resistance exercise, suggesting age-related impairment in muscle's molecular response to training.

2. Data Description

2.1. Why This Dataset Answers Our Research Question

The GSE47881 dataset (DERBY BBSRC RET Study) directly addresses our research question by providing paired pre- and post-training skeletal muscle gene expression measurements from a controlled 20-week resistance exercise intervention. This is the same dataset analyzed in Phillips et al. (2013), allowing us to replicate and extend their findings using our own statistical approach. This design allows us to quantify exercise-induced gene expression changes within individuals, test whether these molecular responses differ systematically by age, and identify specific genes significantly altered by resistance training. As this dataset has been

previously analyzed in a peer-reviewed publication, we can validate our statistical approach by comparing our findings to those reported by Phillips et al.

2.2. Dataset Size

The dataset contains 45 observations (participants) and 54,677 variables. After removing one participant who did not complete the program, we have 44 complete cases. Variables include subject_id, age, and 54,675 gene expression difference values (Post − Pre).

2.3. Variable Descriptions

Raw Dataset Variables (89 samples: 44 pre-training, 44 post-training, 1 baseline):

- **Accession** (Categorical): GEO sample identifier (e.g., GSM1161771).

- **Patientid** (Categorical): Unique participant identifier (e.g., AC033).

- **Age** (Numerical): Participant age in years (range: 20–75).

- **Time** (Categorical): Training status, either "pre-training" or "post-training."

- **Tissue** (Categorical): Sample source (skeletal muscle biopsy for all samples).

- **Gene expression values** (Numerical): 54,675 probe intensities per sample measured via Affymetrix microarray.

Processed Dataset Variables (44 participants):

- **subject_id** (Categorical): Unique participant identifier.

- **age** (Numerical): Participant age in years at study enrollment (range: 18–75).

- **Gene probe differences** (Numerical): Expression change (Post − Pre) for each of 54,675 gene probes. Positive values indicate upregulation after training; negative values indicate downregulation.