Effects of progressive resistance training on the expression of long non-coding RNAs in skeletal muscle of young adults

## Abstract

## Background

Long non-coding RNAs (lncRNAs) are non-protein-coding RNAs of more than 200 nucleotides in length. Over 240,000 lncRNAs in humans have been curated (*1*) even though not much is known about majority of them hence its poor functional annotation. However, they are generally believed to regulate regulate different aspects of cellular physiology and function (*2*), (*3*) as well as the expression of protein-coding genes (*4*) (*5*) . Some lncRNAs have been reported to play roles in cell cycle regulation (*6*), differentiation (*7*), metabolism (*8*), and muscle regeneration (*9*). Despite lncRNAs low levels of expression and sequence conservation (*10*) , their expressions are highly tissue and condition-specific (*4*), (*11*).

There is currently significant uncertainty about the mechanisms of actions of lncRNAs. Figuring out those that are differentially expressed in a given condition could thus be the first step in a series of steps aimed towards elucidating their mechanisms of action. Most publicly available research on this group of RNAs are focused on their roles in diseases, especially cancers, . Relatively much less like (*11*) are available on their roles in health promotion. It perhaps pertinent to investigate the possible functional roles of lncRNAs in health promoting activities like resistance exercise training. This research is exploring the role of these groups of genes in health promotion,vis-a-vis resistance exercise training.

The skeletal muscle is important for physical health and vitality. It responds to both use and disuse by hypertrophying, and loss of muscle strength and mass respectively (*12*) . Progressive resistance exercise training (PRET); a type of exercise where the skeletal muscle is exercised against progressively increased types of resistance (*13*) such as free weights , is the most potent non-pharmacological method of stimulating muscle hypertrophy and countering the loss in muscle strength and mass (*12*). There is a dose dependent relationship between PRET volume and its outcomes (*14*). Besides volume, factors internal to an individual are the main regulators of the benefits of PRET (*12*) . These factors include ribosome biogenesis, transcriptome profile and responses, metabolites profile etc (*12*), (*15*).

Numerous studies have reported the gene expression patterns following PRET, but how these patterns are regulated is poorly understood. Since lncRNAs are said to play regulatory roles, it might be pertinent to understand the lncRNAs that might be playing regulatory roles in response to PRET. This knowledge could serve towards a deeper understanding of the mechanisms regulating the benefits of PRET, and perhaps optimising the benefits as well as personalizing an individual’s PRET regimen.

This study aims to identify lncRNAs that are differentially expressed following PRET based on exercise conditions, ie between the trained and untrained and between volumes among the trained. It will enhance the current knowledge about the responses to PRET and how these can be optimised and personalised for individual participants

## Methods

### Data and Data analyses

Study design , sample preparation and RNA sequencing were done as described by Hamarsland et al (in\_view). FastQc (v0.11.5) was used to check the quality of the FastQ files . Reads mapping to human genome(GRCh 38) with gencode v40 primary assembly annotation were counted using RSEM (v.1.3.3-foss-2019b). Data extraction and statistical analyses were done using RStudio (2023.06.2 Build 561) . A diagram showing the overview of data analyses steps is shown in Figure 1

### Models and visualization

To compare the influence of the effective library size of all the genes, versus only those annotated as lncRNAs, two types of negative binomial regression models were built using Seq\_Wrapper, an R package developed in-house, one normalized using lncRNAs alone, and another using the full genes counts. All genes annotated as lncRNA by the Ensemble database in BioMart were extracted

Two models were built, one to determine the effect of training by grouping the participants’ legs into trained and untrained. The other model was designed to investigate the effect of the different exercise conditions , that is set 6, set 3 and set 0. lncRNAs with p values less than or below 0.05, and log fold 2 change above 0.5 were extracted

Flow diagram sowing steps in analysis

## Results

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