Leicester Kidney Exercise Team

Differential microRNA expression in skeletal muscle of human CKD patients and healthy controls

Watson EL[1], Sylvius N[2], Viana JL[3], Greening N[1], Barratt J[1], and Smith AC[1]
[1]Leicester Kidney Exercise Team, University of Leicester and University Hospitals of Leicester, United Kingdom
[2] Centre for Core Biotechnology Services, Department of Genetics, University of Leicester, United Kingdom
[3]Research Center in Sports Sciences, Health and Human Development (CIDESD), University Institute of Maia (ISMAI), Portugal

Introduction

- Patients with advanced Chronic Kidney Disease (CKD) experience significant muscle wasting that negatively impacts upon quality of life, morbidity and mortality; however the causes of this muscle wasting are poorly understood.
- Many factors could play a role, but one possible mechanism is through dysregulation of microRNA (miRNAs) expression.
- MiRNAs are short non-coding RNA molecules that regulate gene and protein expression and have been implicated in human disease. Moreover, they have also been shown to directly regulate protein synthesis, degradation and myogenic pathways, making them possible candidates for a role in muscle wasting in CKD.
- miRNA's have an important role in the pathophysiological pathways that cause primary muscle disorders.

Aim

To investigate differential expression of miRNA's in skeletal muscle of human CKD patients and healthy controls to identify possible regulators of muscle wasting in this disease population

Hypothesis

There will be a significantly differential expression of important microRNA's known to have roles in the maintenance of muscle in CKD Vs healthy controls.

Methods

- Vastus Lateralis muscle biopsies collected from 5 CKD patients (3b-5) and 5 aged and sex matched healthy controls
- Samples collected under rested and fasted conditions

Group	Number	Age	Males	Females
CKD Patients	5	59 [46-74]	4	1
Healthy Controls	5	59 [46-74]	4	1

Table 1. Participant Characteristics

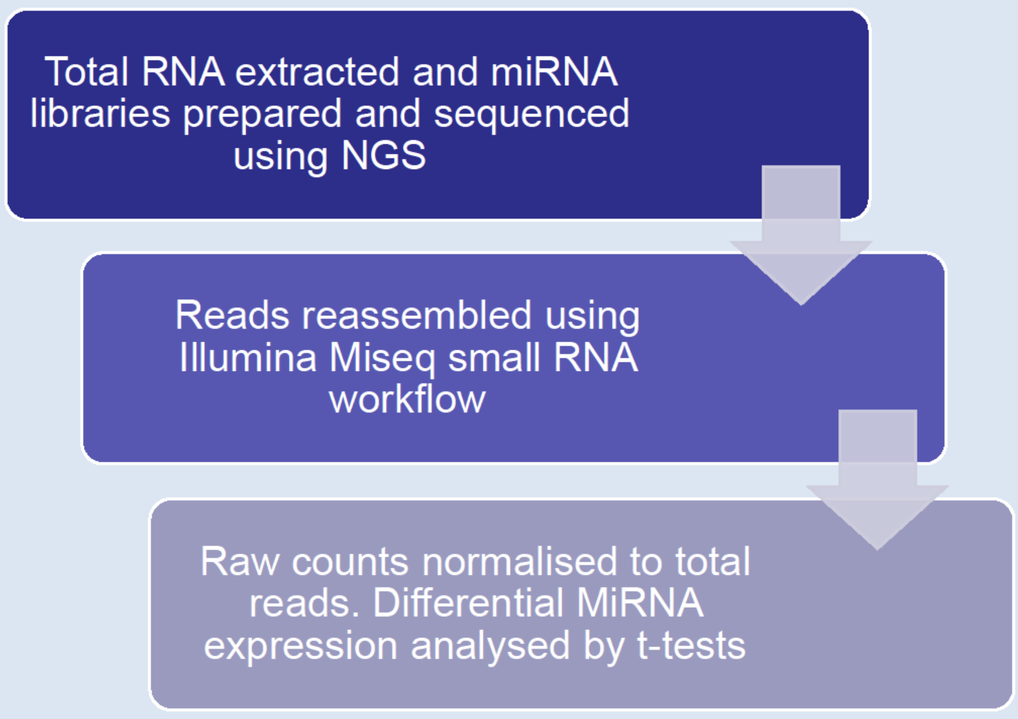

Figure 1. Flow diagram depicting methods

- MiRNA's were discounted from further analysis if they had less than 100 reads

Results

Number of miRNA's read	496
Number of miRNA's discounted	398
Number of miRNA's to analyse	98

Table 2. Results from Next Generation Sequencing

A 18-miRNA signature specific to CKD was identified in which:
- 2 MiRNA's were significantly upregulated
- 16 MiRNA's were significantly downregulated

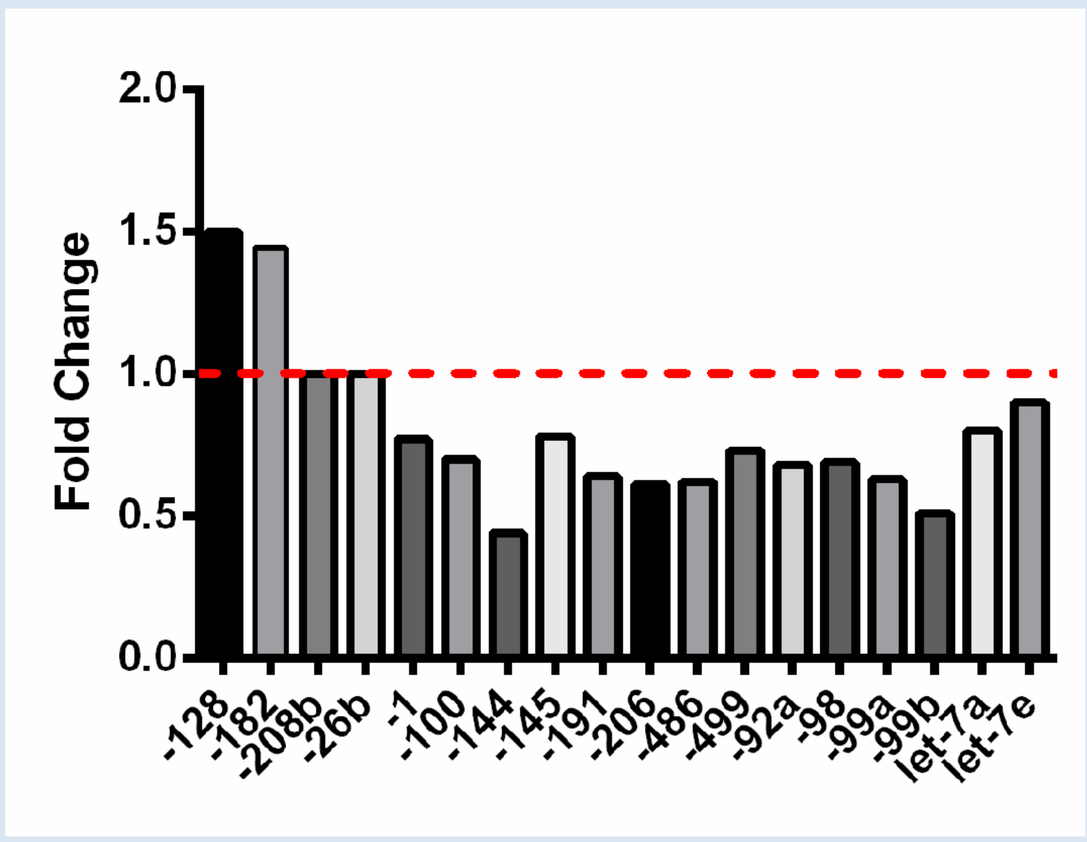

Figure 2. 18 MiRNA's that are differentially regulated in skeletal muscle in CKD. Results are presented as fold change,

Biological Relevance

miR-206
- One of the best characterized and most studied miRNA's to date
- Has been cited as a key regulator of muscle development
- Dysregulation of expression has been seen in other primary muscle disorders such as Duchene's Muscular Dystrophy
- Has an important role in satellite cell differentiation and muscle repair
- For these reasons has been identified as a potential therapeutic target in other myopathies

miR-1
- Administration of miR-1 to a rat injury model helped induce myoblast differentiation

miR-486
- Shown to increase satellite cell differentiation
- miR-486 mimics seen to prevent muscle atrophy in an animal model of CKD

Conclusions

- This study has identified 18 miRNA's that are differentially expressed in skeletal muscle of CKD patients
- Of particular interest to future work is the suppression of miR-1, miR-206 and miR-486, which may partly explain the cause of muscle wasting in CKD
- These are early results, which need to be confirmed by real-time PCR in a much larger population.

Emma Watson ec174@le.ac.uk

53 ERA
401--MP
Chronic Kidney Disease. Rehabilitation.
Emma Watson
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th, 2016
Held jointly with Österreichische Gesellschaft für Nephrologie
PosterSessionOnline.com