Title: Selection of miRNA candidates

for the treatment of Sarcopenia using network-

based analysis and differential expression scoring

Authors: Karen Guerrero Vazquez, Pilib Ó Broin, Katarzyna Whysall

Affiliations: University of Galway

Abstract:

Sarcopenia is a natural consequence of aging and leads to progressive muscle wasting. Currently, there is no cure for this condition, and target identification and validation remain pressing challenges. Many potential therapeutic targets have failed in clinical trials or shown poor association with the disease. This project aims to address this challenge by creating a model of microRNA:target interactions for more efficient in silico selection of potential therapeutic targets for sarcopenia.

We conducted a novel analysis of microRNA involvement in aging using RNAseq data, microarray analysis, and network analysis. Our approach includes five different experiments with a total of 246 samples of skeletal muscle from healthy patients with age ranges from 19 to 85 years old. We analyzed the differentially expressed genes in young, middle age and old individuals and determined gene interactions and the microRNAs that target them using data from target prediction repositories such as targetScan, mirDB, and mirTarbase and other metadata like expression levels in different tissues and the presence of diseases. All the metadata is stored in a MySQL database.

We measured the relevance of the nodes with different scores and centralities to identify the most important microRNAs and their relationships with genes during aging. Our approach extends the original set of differentially expressed genes plus the involved microRNAs. This novel model of microRNA-target interactions offers a valuable computer-based approach to target identification and validation, which has significant potential for advancing our understanding and treatment of sarcopenia.

Our model of microRNA-target interactions is specifically tailored to the context of muscle aging and offers a more comprehensive and accurate representation of the complex regulatory mechanisms involved in muscle aging than existing tools, as it integrates multiple layers of biological information. By identifying a few tens of microRNAs and genes with potential therapeutic power, our model offers a valuable and efficient approach to target identification and validation for the treatment of sarcopenia.