**MicroRNA, the small rock in my shoe**

MicroRNAs (miRNAs) are small single-stranded RNAs playing an important role in the regulation of gene expression and participating in various biological processes.

**Why is selecting candidates hard?**

Identifying miRNAs that are specific to a particular disease or tissue is still a challenge since many miRNAs have overlapping functions and can regulate multiple genes and not all potential miRNAs are functionally relevant in a given cell.

Time consumption

Overlapping functions and can regulate multiple genes

Bias towards more studied

Hard to find complex cause-effect relationships

**Sarcopenia; a matter of time**

Sarcopenia is the progressive muscle wasting due to aging. Target identification and validation is a pressing challenge, with many targets failing or showing poor association with the disease.

Computational prediction of therapeutic targets could decrease the attrition rates in the drug discovery pipeline by reducing the initial search phase.

**What can we do?**

There are more than 160 different tools, apps, and databases dedicated to the study of microRNAs. miRBase, miRWalk, and miRNet areas some of the most popular.

miRBase is the state-of-the-art database of microRNA sequence annotations.

miRNet integrating users' data with existing knowledge via network-based visual analytics

miRWalk is an online resource for the prediction of microRNA (miRNA) target interactions and integrates results from TargetScan, miRDB, miRanda, and other popular databases.

During the development of this project, we are also creating miRKat, a software to select miRNAs involved in the specific condition of Sarcopenia.

**How to select effective miRNAs**

We collect an initial set of genes from RNAseq and microarray data from five published studies, with 246 samples of skeletal muscle from healthy participants with ages ranging from 19 to 85 years old.

Is known that gene expression changes with age, and one should consider changes in gene expression with age when studying aging and age-related diseases.

We analyzed young, middle age, and older adults and determined differential express genes among the age groups, calling these genes the original genes (OG).

Then we use tools like GeneMania and IntAct to find the interactions among those genes, alongside adding other genes that have important interactions with the OGs, then we added the miRNAs that target those genes by using different miRNAs databases like mirWalk, miRDB and mirTarbase.

Finally, we calculate the closeness and pageRank centralities of each node, setting a threshold to select the nodes considered relevant. This was integrated into miRKat, our own miRNA selection tool.

**Obtained differentially expressed genes**

We got 245 differentially expressed genes distributed in the 5 experiments, the 6 combinations of ages, and up and down-regulated genes. For this poster, we are going to focus on up-regulated genes in old (>65) compared to middle age (>35).

**Networks generated; middle age to old**

**Selected microRNAs**

We got more than 60 different miRNAs across all techniques.

Using Closeness centrality and IntAct we see 29 miRNAs, 3 of which appear in more than one stage of life.

The models within miRKat lack access to information on miRNAs expression in tissues or enriched pathways, however, more than 20% of them are found in muscle. Comparable with miRNet which is based on empirical sampling for enrichment analysis.

**Conclusion and future work**

miRNAs are important regulators of gene expression and potential targets for therapeutics, but their selection for specific conditions such as sarcopenia remains a challenge due to their complex functions and interactions.

To select miRNAs, is necessary to evaluate the quality of the output, a challenge that is still present in our design, since most of the evaluation methods imply a bias towards known miRNAs and genes.

Once the final selection of miRNAs and genes is established, we aim to incorporate the timestamps on the model and show the progression of the interaction as a function of time.

The process is planned to be part of miRKat so it can be publicly available. Meanwhile, news on the process can be found at https://github.com/GuerreroVazquez