The ticking of the clock never stops, every moment we get older, and one of the most striking effects of age is probably the involuntary loss of muscle mass, strength, and function. This is called Sarcopenia.

Sarcopenia is a fundamental cause of and contributor to disability in older people. And mass decreases approximately 3–8\% per decade after the age of 30 and this rate of decline is even higher after the age of 60 (Brocklehurst, 1976).

Several factors, including chronic inflammation, increased reactive oxidative species, increased fibrosis of muscle, and increased loss of motor neurons, have been reported to contribute to development of sarcopenia (Yanai, 2020), therefore, it makes sense to aim for a therapeutic that also targets multiple genes and/or pathways. ****** NEEDS IMPROVEMENT

The approach that this project takes it on the hand of micro RNAs.

Mircro RNA or miRNA are conserved small non-coding RNAs that play an important role in the regulation of gene expression, they are short nucleotide single stranded RNAs (ssRNAs), between 14 and 33, with an average of 20 as MirBase suggest today.

It is likely that miRNAs naturally build regulatory networks that control different cellular functions, if this is the case, it would make sense to represent this interaction on a mathematical way in the shape of a network. And using computing methodologies, it would be possible to identify the participation of the mirnas in the system, allowing to filter and selecting the best candidates for further experimentation in lab for muscle wasting treatment. *** NEEDS IPROVEMENT

Therefore, our hypothesis is:

There’s a computer representation of the microRNAs and their interaction that allows the identification of micro RNA for the treatment of Sarcopenia.

In order to create a good model, we need to think in the inputs, the process and the expected output. First, let’s talk about the inputs.

Is commonly known in Computer Science that if trash goes in, trash goes out, for this reason, we are taking care on what we are going to utilize.

The obvious input is the existent microRNA. This microRNA are obtained from mirBase, the database of microRNA, created since the discovery of miRNAs under the name of *The mircoRNA Registry*.

The second thing that is vital for this project is the relationship of this miRNAs in the system. What do miRNAs do? They target mRNAs to suppress expression. Then the first relationship that we see is miRNA:mRNA. One miRNA can modulate thousands of mRNA, adding this many amount of miRNAs only gets things more complex. Especially if we consider that the relationships of the mirna:mRNA can be just a prediction.

On the same logic, we can add the relationship mRNA:Pathway, mRNA:Tissue, mRNA:Condition of the conditions, tissues and Pathways associated to Sarcopenia looking on the levels of differential expression associated to them.

We are swimming in a sea of data, the quality of the information is something that is currently under process, from the sources of the data to the value to the project. This will be tuned alongside the design of the network itself.

We can interpret different types of nodes:

- miRNAs
- mRNAs
- Tissues
- Biological processes
- Conditions

And they have several biological relationships with each other. For example, Sarcopenia is specific of the muscle that regenerates via the myogenesis, that activates MyoD, that upregulate mir1. Human mir1 have almost 4 thousand target mRNA, etc. The longest it takes ta node to make sense to sarcopenia, the impact of this node is going to be left behind or if it has a lot of interconnection, will be stronger, for example, the more of these 4K genes are associated with sarcopenia, the stronger mir1 becomes in the network.

Many works had been done in the past to find the influence of micro RNA in different diseases, appealing to different measures and rules.

To define the rules that are going to specify what does it mean to be related to some other node. And for the measures, thanks to omics, we can actually give a weight to this relationship in the shape of differential expression. And we can implement the concept of distance and interconnection in order to interpret the impact of an miRNA. It will be possible to give a value, a degree to our nodes, Centrality Degree can give us a good starter, the betweennes centrality will be essential in order to determine the distance of the miRNA with the target condition; Sarcopenia, and Eigenvector centrality to know the influence of the nodes in the network. ****ESTO ESTA MUY COMPLEJO

The Network could be extremely complex at this point, however, different nodes are going to be similar, and within the network we are going to find structures like clicks that would allow us to cluster them. With these clusters we can filter at big scale and increment the granularity as the number of nodes decreases.

In theory, at the end of this process, we should have a handful of miRNAs with their interaction in the system, allowing experts to manually review the miRNAs and design the experiments in the lab.

However, it's important to mention that this is a model, and every model should prove their functionality. For this case, we had planned a 2 steps testing; the testing by knowledge and testing by scale.

During the testing by knowledge we will have several known scenarios. Our nodes are going to be miRNAS, mRNAs and Processes that we know how related they are.

We will have networks composed by nodes that have absolutely nothing to do one with other and networks with known relationships. This way we will know what to expect from them, the model should give non information from the unrelated network and solid relevance in networks that are well known. This test does not required to be

Sarcopenia related, since it’s the evaluation of the model to predict the impact of the miRNAS in the network and not Sarcopenia itself.

The second one, is by scaling, this is intended to start with just a few known mirnas of Sarcopenia, for example, the myomiRs, that are muscle-enriched microRNA, and they biological processes. Then gradually adding more nodes to the point that be able to add all the data recopilated at the beginning of the project to guarantee scalability and attach the label “High-throughput”