How do we design an innovative treatment for **Myotonic Dystrophy type 1 (MD1)**?

THE ROLE OF GENETICS

Muscleblind proteins play an important role in the cellular metabolism of neurons and muscle cells in humans.

WHAT HAPPENS TO THESE PROTEINS IN MD1?

THEY ARE SEQUESTERED

Inside the cells of patients with **MD1**, there is a mutation in the **DMPK gene**.

The mutated gene promotes the synthesis of **toxic RNAs**.

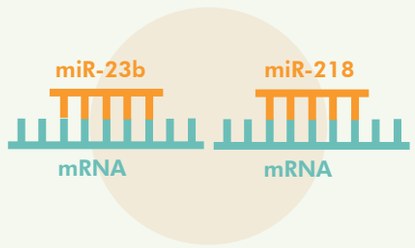
The structure of the toxic RNAs, which are loop-shaped, **sequesters** the **Muscleblind proteins**.

Their inactivity triggers the symptoms of the MD1.

THEY AREN'T SYNTHESISED

The Translational Genomics Group at the University of Valencia has identified a new mechanism connected to MD1.

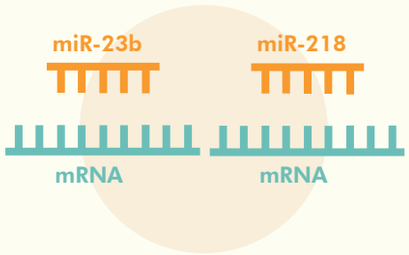
Two **microRNAs (miR-23b, miR-218)** inhibit the synthesis of Muscleblind proteins when they bind with **their messenger RNA (mRNA)**.



This mechanism, activated in the cells of **patients with MD1**, contributes to the fact that only a small number of **Muscleblind proteins** are active.

BUT... WHAT WOULD HAPPEN IF THE ACTION OF THE microRNAs COULD BE UNBLOCKED?

This is what the **TATAMI project** sets out to do, through the use of synthetic molecules, called **antagomiRs**.

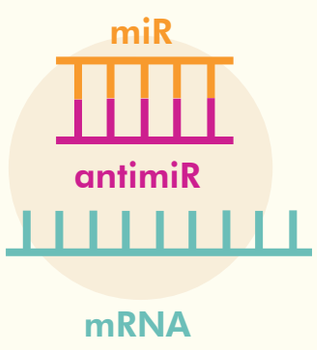


antagomiRs, CUSTOM-MADE DRUGS

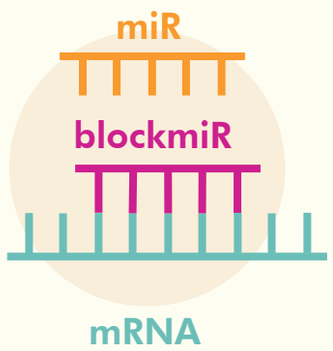
The **TATAMI project** is designing **antagomiRs**, drugs that prevent microRNAs and the messenger RNA of Muscleblind proteins from binding.

They are evaluating almost
100 different molecules.

Some, called **antimiRs**, directly bind to the **microRNAs**, blocking their action.

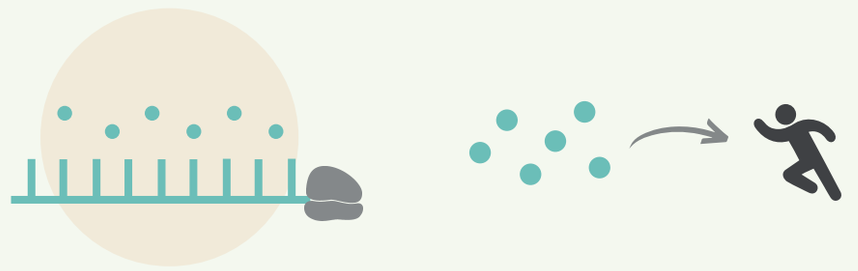


Others, called **blockmiRs**, bind to the **messenger RNA** of Muscleblind proteins, thus preventing **microRNAs** from binding to it.



In both cases, the objective is to **promote an increase in Muscleblind protein synthesis**.

As a result, symptoms of the MD1 can be **reversed**.



THE IDEAL CANDIDATE WILL BE THE MOST SPECIFIC, MOST EFFECTIVE AND LEAST TOXIC DRUG FOR THE PATIENT.