McArdle's disease is a genetic disease, inherited in autosomal, recessive way. Is referred as muscle glycogen phosphorylase (PYGM) deficiency syndrome. This disease **is caused by mutations in both alleles of the *PYGM* gene**. It is mainly manifested by **intolerance to physical exercises, muscle cramps and pain**. The occurrence of onset in patient life and their severity depends on the individual variability. In extreme cases, muscle damage or even necrosis is observed. This disease is most often diagnosed after the age of 30. **Despite the efforts towards searching for treatment, it has not yet been possible to invent an effective method that could help patients suffering from this disease.**

The zebrafish (*danio rerio*) has become a **promising model organism** used in many research fields such as neurology, developmental biology, toxicology and genetic research. This small, aquarium fish has **many advantages as a model organism, such as: small size, which require not much space, and a relatively low cost of breeding, a large number of offspring and short lifecycle**. The body of the fish is transparent in early stages of development, which allows observation of internal organs. However, the most important feature is the **high degree of similarity between the fish and the human genome**. Most genes, as much as 80%, have a human counterpart. Also, many biochemical pathways run in a similar way to humans. The ease of genetic modification in zebrafish is an additional advantage.

The goal of our research is to create an animal model of human McArdle's disease. The zebrafish has two forms of the enzyme: pygma and pygmb, which have over 80% amino acid sequence identity to human PYGM. **Our initial research with zebrafish larvae showed that transient silencing of the *pygm* gene causes symptoms very similar to those observed in people suffering from McArdle's disease**. Patients' lack of adequate muscle glycogen phosphorylase function results in muscle glycogen deposition, changes in muscle structure and inability to physical effort. In fish, we also observed similar phenomena, such as glycogen accumulation, muscle deformations, and reduced mobility. Larvae with transient reduction of pygm gene expression also have changes in protein and mRNA levels.

In our future research, we want to use the CRISPR-Cas9 gene editing technique **to obtain an adult zebrafish with the silenced *pygm* gene**. Such an animal model of human McArdle disease will be a **precious tool to investigate the pathological mechanism responsible for disease symptoms**. We will use this model to search for efficient treatment. We will reach for drugs, which are already approved to use to treat patients with other glycogen storage diseases, but not McArdle. We will also check diet supplements or other substances potentially helpful in the McArdle disease treatment. Such approach **could be an relatively fast and efficient way to help McArdle patients**. **We will also widely share the zebrafish model and all data for non-commercial use all around the world**, hoping that other scientific centres could add their piece of puzzles toward understanding the McArdle disease.