MiR92b-3p as a potential therapeutic snippet of RNA for the cure of liver injury in fish

Cyanotoxin microcystin-LR (MC-LR) is a naturally occurring chemical. Chemicals like this can contaminate water and food of both animals and humans. If these kinds of chemicals are consumed they can cause fatal liver damage an even cancer. Despite recent scientific advances the way these toxins interact with the body's molecular structure are still unclear and science still has to discover how the toxins interact with different organs of the body, how cells react to them, how it travels through the system, etc. Research into how the toxin interacts with the body could help develop innovative therapies for liver disorders as well as methods and technology for predicting the effects of contamination.

Our recent studies of whitefish exposed to MC-LR showed that long term effects include severe liver damage but then a regeneration of the liver and a resistance to the toxin. However, this also involved changes to hepatic microRNAs (miRNAs) which control a suite of processes related with fundamental aspects of cells' life. Among them we found a microRNA molecule, MiR92b-3p, which in humans has a significant impact on the cell behavior. For example, its excess in the liver cells leads them to divide uncontrollably.

This project asks which genes are controlled by MiR92b to influence pathways through the body's system which are specifically important for certain types of liver damage in fish. The project will also ask whether too much or too little MiR92b-3p has a specific effect on MC-LR-induced liver damage in fish and whether it is possible to reduce such damage by controlling the levels of the miRNA. To do this we need to identify and characterize the functions of hepatic MiR92b-3p and how it works. We also aim to evaluate how effective MiR92b-3p might be as a therapy in fish.

Toward the ambitious objectives of our proposal, we will carry out research on both the cells of fish (*in vitro*) under laboratory conditions and on the fish themselves (*in vivo*) simultaneously. After a suite of biochemical, physiological, anatomical, and transcriptomic analyses we will show how MiR92b-3p works in a damaged liver and which processes it targets. Finally, the research will confirm if and how MiR92b-3p works therapeutically. We expect it to be shown effective enough to pave a way for its use as a tool for treatment for liver damage in fish. We believe, it is not a question of *if* RNA based therapeutics will become a reality, but *when*.