miRStress: Unveiling the conserved role of stress-regulated miRNA-family on mitochondrial response in aquatic organisms

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Abstract

In 2024, the Nobel Prize in Physiology or Medicine was awarded "for the discovery of microRNA and its role in post-transcriptional gene regulation", highlighting the expansion and relevance of this field since their discovery. MicroRNAs (miRNAs) are small, non-coding RNA molecules that play a crucial role in regulating gene expression. These molecules, typically 22 nucleotides long, can bind to messenger RNAs (mRNAs) and inhibit their translation or promote their degradation. As a result, miRNAs are involved in the pleiotropic control of various biological processes, including cell development, differentiation, apoptosis, and response to stress, essential for normal cell homeostasis, and enabled the evolution of increasingly complex organisms. In my laboratory, we focus the attention on a group of selected miRNAs reported to be de-regulated in response to hypoxia (OxymiRs) in marine organisms, as well as in mammals, trying to understand their roles in metabolic regulation in stress conditions. Our preliminary data allowed us to identify the positive effect of MIR-17~92 family down-regulation on mitochondria in metabolic stressed human cells. The **miRStress project** aims to characterize the response and the activity of these miRNAs to different stress conditions in two teleost species, to investigate the molecular mechanism's conservation among teleost fishes from marine and brackish environments (marine Fugu *Takifugu rubripes* and brackish medakafish *Oryzias latipes*). To this purpose, we will analyze their conservation and expression pattern in different Teleost species (via MirGeneDB3.0 and FISHmiRNA) and their levels in response to different stress conditions (e.g. oxidative stress; hypoxia; starvation) in the Fugu cell line from eye tissue (AIM1). Their functional role will be analysed by gain- and loss-of-function experiments in Fugu cells (AIM2) and medakafish primary eye cells (AIM3), focusing in particular on mitochondrial response activities. The underlying molecular mechanisms of their effect will be investigated via transcriptome analysis to identify their direct and indirect targets. Overall, the project will lay the bases for further analyses about the signals and the molecular mechanisms that during the evolution worked to ensure the complex regulation of miRNAs in response to adaptation to different environments and stress responses.