Reg. No: 2015/18/E/NZ6/00516; Principal Investigator: dr Krzysztof Łukasz Rakus

The role of the immune system is to protect the organism against pathogen infections. When functioning properly, via different types of pathogen recognizing receptors (PRRs) the immune system identifies a variety of pathogens, including viruses, bacteria and parasites. Viruses are recognized based on the presence of viral nucleic acids (DNA and RNA) by corresponding groups of receptors including, members of Toll-like receptors (TLRs), the retinoic acid-inducible gene I (RIG-I)-like receptors (RLRs), nucleotide-binding domain and leucine-rich repeat containing molecules (NLRs), and intracellular DNA sensors. Recently, several non-RLR DExD/H-box RNA helicases (such as, for instance DDX1, DDX3 and DHX9), have been also shown in mammals to play important role in sensing of viral nucleic acids in the cytoplasm. However, the mechanisms of their action are still not fully understood, and their role in the anti-viral immune response in fish has never been studied.
The main aim of this project is to identify, for the first time in fish, the role of DExD/H-box RNA helicases (DDX1, DDX3 and DHX9) in the activation of the anti-viral immune response. Experimental strategies will take advantage of the complementary characteristics of two teleost fish species: common carp (Cyprinus carpio) and zebrafish (Danio rerio). Both common carp and zebrafish belongs to cyprinid family and are widely used in research devoted to study the fish immunity. Zebrafish is a powerful laboratory model organism for which many advanced research techniques were developed. Common carp is economically important fish species being one of the most cultivated fish for human consumption worldwide. In addition its colorful ornamental varieties (koi carp), grown for personal pleasure and competitive exhibitions, represent one of the most expensive markets for individual freshwater fish, with some prize-winners being sold for US$10,000-1,000,000. From the research point of view, the large body size of common carp allows to study the immune response on the level of different immuno-related organs and leukocyte populations which is very difficult in small fish species such as zebrafish.
In the present project, we will study the expression of DDX1, DDX3 and DHX9 in fish leukocytes and verify how cell infection with spring viraemia of carp virus (SVCV) or their stimulation with poly I:C (synthetic dsRNA, mimicking viral infection) will affect receptor expression. Using zebrafish model we will use advance molecular techniques to either increase gene expression of DDX1, DDX3 and DHX9 or silence those genes. This experimental strategy will allow us to define the role DDX1, DDX3 and DHX9 in the activation of interferon (IFN) of type I, molecules involve in the first line of cellular defense against viruses. Identification of the underlying mechanisms associated with anti-viral response could lead to the better protection of the fish against virus infections. Thus more detailed recognition of the mechanisms involved in anti-viral response will allow to develop and to improve strategies for fish health control. This is becoming more and more important in view of the progress in the fish farming industry.