

X-ray Crystallography and Modelling Analyses of MHC Antigen Binding Affinity

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Project Description: MHC (Major Histocompatibility Complex) genes encode cell-surface molecules with an important function in the recognition part of the immune defense system. These genes are the most variable coding genes in our genome. Their importance for fitness traits such as disease resistance and mate choice have opened up a new research field among evolutionary ecologists, leading to several studies of MHC variation and evolution in natural vertebrate populations. MHC genes are well studied in several model organisms such as humans, mice and chickens. However, the extent and importance of MHC variation in natural vertebrate populations are still poorly understood. At the protein level, studies are still restricted to classical model species. Hence the structure of MHC molecules is only known from humans and mice. The antigen-binding residues (ABR) have only been characterized in human MHC molecules. Therefore, all studies of MHC variation in other vertebrate species assume ABRs identical with human ABRs. However, it is very likely that the ABRs have changed slightly during evolution from fish to humans.

In this project, I aim at solving the three-dimensional structure of MHC class II molecules from fish (Atlantic salmon and three-spine stickleback) and to further study antigen-binding ability and evolution of antigen-binding residues (ABR) in MHC class II molecules. For this purpose I will use crystallisation techniques, X-ray crystallography and homology modelling.