

MHC MOLECULES

Cod's wallop? It's first class!

It is always fascinating to consider the distinct immune systems that have evolved in the natural world. A recent study in *Nature* has shown that, unlike other jawed vertebrates, the Atlantic cod does not encode MHC class II molecules. Instead, these fish rely on additional MHC class I molecules and a unique repertoire of Toll-like receptors (TLRs) to protect them from pathogens.

Compared with other teleost fish, Atlantic cod have greater numbers of neutrophils in the blood and higher levels of serum IgM, but they produce lower levels of specific antibodies in response to infection. By sequencing the whole genome of the Atlantic cod, Jakobsen and colleagues have shown that the weak antibody response generated by these fish can be attributed to the lack of a functional MHC class II antigen-presenting pathway. Atlantic cod do not possess any genes encoding MHC class II molecules or the invariant chain chaperone, and have a truncated pseudogene for the CD4 co-receptor. As such, these fish lack

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the classical adaptive immune pathway for responding to exogenous bacteria and parasites.

Despite this, Atlantic cod do not show increased disease susceptibility in the wild — the authors found that this could be partly explained by a marked increase in the number and diversity of its MHC class I loci. They suggest that the Atlantic cod may compensate for the loss of CD4⁺ T cells by using antigen cross-presentation to generate diverse CD8⁺ T cell subsets.

Atlantic cod also possess an unusual composition of TLR-encoding genes. These fish have strongly modified the repertoire of genes encoding TLRs that recognize bacterial surface antigens, as they lack *TLR1*, *TLR2* and *TLR5*, but possess *TLR1*-like genes, such as *TLR14* and *TLR18*.

In addition, Atlantic cod show a marked expansion in the number of genes encoding nucleic acid-detecting TLRs, such as *TLR7*, *TLR8*, *TLR9* and *TLR22*. The increased number of *TLR9* genes found in the Atlantic cod's

genome is accompanied by an expansion in the number of interleukin-8 (*IL8*) genes. As *IL-8* has been shown to be induced directly by *TLR9* signalling in human neutrophils, the authors propose that *TLR9*-mediated recognition of bacterial DNA may be particularly important for immune protection in these fish.

The authors' findings suggest that adaptive immune responses in the Atlantic cod are initiated and regulated in a distinct way from those in other teleost fish. This has important implications for vaccine design and disease management in Atlantic cod, in commercial fisheries as well as in the wild.

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ORIGINAL RESEARCH PAPER Star, B. et al. The genome sequence of Atlantic cod reveals a unique immune system. *Nature* 10 Aug 2011 (doi:10.1038/nature10342)
FURTHER READING Boehm, T. Design principles of adaptive immune systems. *Nature Rev. Immunol.* 11, 307–317 (2011)

