ABSTRACT OF PhD DISSERTATION

Immunogenetical analyses of MHC (class I) related resistance to viral diseases in chickens

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ABSTRACT

The PhD dissertation was published at the Institute of Medical Biology, University of Southern Denmark. The dissertation contains the results of studies carried out at the Department of Animal Health and Welfare, Danish Institute of Agricultural Sciences, during the years 1999-2003, and consists of three articles.

The purpose of the study was to elucidate the mechanisms involved in tissue type-related disease resistance against viral diseases in chickens by means of immunogenetical analyses of inbred lines of tissue type specific chickens defined by their major histocompatibility complex (MHC) haplotype.

In chickens, MHC-related resistance towards several viral diseases has been described. Marek's disease (MD) was one of the first diseases studied, and it remains one of the strongest examples of variation in MHC-related disease resistance regardless of species. The project was based on the identification of differences between MD-resistant and susceptible MHC haplotypes, and the focus was on MHC-I genes and genes involved in antigen presentation via MHC-I.

It was demonstrated that there is a correlation between MD susceptibility and the amount of MHC-I antigens on the surface of lymphocyte subpopulations in the spleen; the most important peripheral lymphoid organ in the chicken. Thus, MD-resistant animals showed low MHC-I expression, which is also observed on lymphocytes in peripheral blood. The chicken has only two classical MHC-I isogenes. It was demonstrated that one of the genes were expressed to a very limited extent in MD-susceptible animals, whereas this gene was relatively more active in MD-resistant animals. The gene showed some similarity to the human HLA-C gene, the product of which is involved in the regulation of natural killer (NK) cell activity.

Expression analyses of both MHC-I genes showed an increased systemic number of mRNA variants with a shortened 3' untranslated region (UTR) in MD-resistant animals. The chicken HLA-C-like gene preferentially expressed this mRNA form. Infection studies with MD virus showed that MD-resistant animals via alternative polyadenylation can up-regulate the expression of the shortened mRNA variant. Variations in the 3′ UTR may result in differences in mRNA stability and translation efficiency. Furthermore, in MD-susceptible animals mRNA variants without exon 7 were detected, which may result in reduced peptide optimisation in antigen presentation.

The study concludes that a significant variation in the expression pattern of MHC-I genes exists between MD-resistant and susceptible animals with potential influence on the cytotoxic T-cell response as well as on NK cell activity.