

# Role of natural killer cells during herpes virus infection in a non mammalian host

## Background:

Herpesviruses are an ancient family of viruses that have been found in all vertebrate species [1]. Each herpesvirus has a very narrow host range and is thought to have co-evolved with their host during evolution.

Marek's Disease Virus (MDV) is an avian oncogenic herpesvirus causing Marek's Disease (MD) that shares biological characteristics with human herpesviruses like EBV [2]. MD is a major disease affecting poultry worldwide. Since the 1960's, chickens are vaccinated but due to vaccination new virus variants with higher virulence continue to emerge [3, 4]. Infection with MDV results in activation of both early and late immune responses [5]. One of the cell types that are involved in the MDV specific immune response are natural killer (NK) cells. Infection with MDV results in enhanced NK-cell activation. Studying NK-cell responses in chickens is challenging due to the limited knowledge of non-mammalian NK cells. In a recent study, we identified new markers that are expressed on chicken NK cells and developed assays to measure NK-cell degranulation and killing [6].

Interestingly, some chicken strains are resistant to MDV infection. This is associated with differences in expression of major histocompatibility complex (MHC) genes. Since low levels of MHC I expression makes a cell susceptible to NK cell mediated killing, NK cells may be one of the factors contributing to MDV resistance. Studies in mammals have shown that herpesviruses are able to evade the immune response, for example by encoding proteins that inhibit NK cells. We hypothesize that the emergence of more virulent strains may be a consequence of immune evasion strategies of MDV, and that NK cells are involved in this process

## Research question:

Is the enhanced virulence of MDV upon vaccination related to NK-cell function?

## Experimental approach and anticipated results

NK cells will be isolated from different organs of 4 week old chickens. These cells will be stimulated *in vitro* with different strains of MDV and NK-cell activation will be analysed to investigate the relation between virulence and NK-cell activation. Next, we will perform *in vivo* experiments in which chickens will be infected with different strains of MDV. We will isolate NK cells from different organs, measure their function and look for differences in the NK-cell response against various MDV strains.

## Techniques:

Cell culture, flowcytometry, cell sorting, quantitative PCR, ELISA, immunohistochemistry

**Duration:** 6-9 months

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