

# Training the innate immune system in order to enhance the vaccine mediated protection

## Background:

Immunological memory is a mechanism used by the immune system to realize a more effective response to pathogens that the host has encountered earlier. Traditionally, this memory formation is a property of the adaptive immune system and is mediated via B and T cells. Recent studies demonstrate that also the innate immune system exhibits immunological memory. This process, initially reported in plants and invertebrates (1), is called trained immunity (2). Several cells of the innate immune system including monocytes, macrophages and NK cells have been reported to be involved. Stimulation of these cells with LPS or  $\beta$ -glucans leads to enhanced antimicrobial and inflammatory properties of these innate immune cells, resulting in an enhanced response to subsequent infections and improved survival of the host.

Although trained immunity has been reported in plants, humans and mice, little is known on this process in veterinary species such as chickens. This is surprising, since repeated vaccination with live virus in young chickens results in long-term protection. In this first period of life, the adaptive immune system responsible for the specific memory formation is not fully developed which suggests that innate immune cells are somehow involved in this long term protection.

We developed tools to investigate the innate immune response in chickens, including assays to analyze the function of NK cells (3) and antigen presenting cells (the chicken equivalent of monocytes, macrophages and dendritic cells (4)).

These tools will be used to develop an *in vitro* model to study trained immunity in chickens and characterize the contribution of the different innate immune cells to this process.

## Research question:

How can we train the chicken innate immune system to enhance the vaccine mediated protection?

## Experimental approach and anticipated results

We will adapt the human *in vitro* assay to measure trained immunity to the chicken system. To this end, cells from the innate immune system will be isolated, cultured and trained for a short period by the addition of LPS or  $\beta$ -glucans. Next, the stimulus will be washed away and the cells will be cultured for 5-6 days followed by restimulation. Activation of the immune cells will be measured by flowcytometry and qPCR for immune-relevant genes. Next, trained immune cells will be incubated with viruses and the anti-viral effect will be determined.

## Techniques:

Isolation of primary cells, cell culture, functional cellular assays, flowcytometry, ELISA, qPCR, immunohistochemistry

## Duration:

6-9 months

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## References

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