

# Natural killer cells as key players in the vaccine-induced immune response against bovine GI nematodes

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## Introduction

Immunological control of worm infections through vaccination is often put forward as a valuable alternative for anthelmintics to control helminth infections in livestock. In recent years, our research group has been able to develop protective experimental vaccines against the two most important and prevalent gastrointestinal nematodes in cattle: the abomasal nematode *Ostertagia ostertagi* and the intestinal nematode *Cooperia oncophora*, based on activation-associated proteins (ASP) purified from the excretory-secretory material of adult worms.

## Aim of the study

The general aim of our research project is to define the vaccine-induced immune response by both *O. ostertagi* and *C. oncophora* antigens since the development of the vaccines is largely hampered by the lack of knowledge on the protective immune response needed against these parasites.

## *Ostertagia ostertagi*

## *Cooperia oncophora*

## Experimental set up

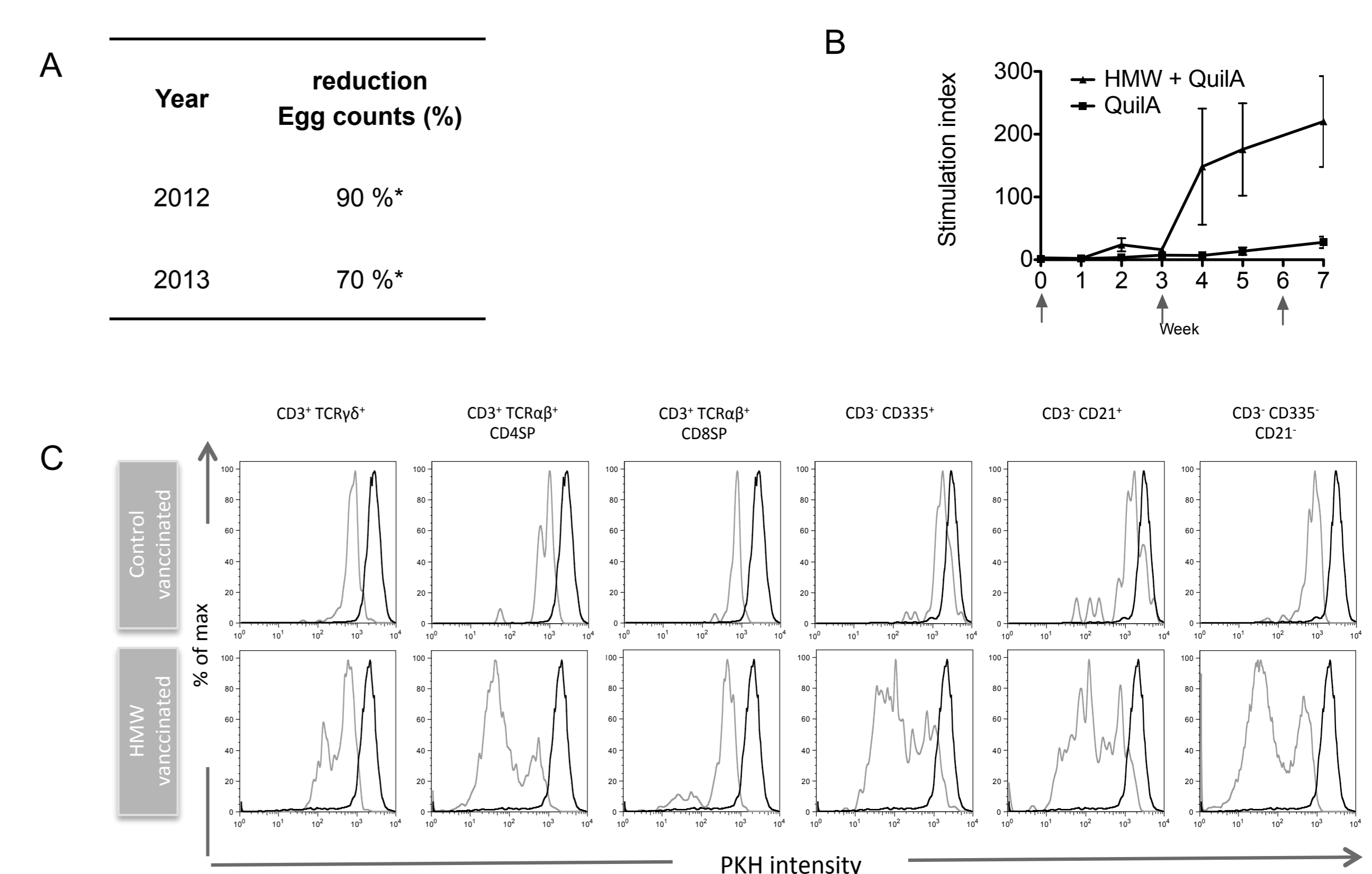
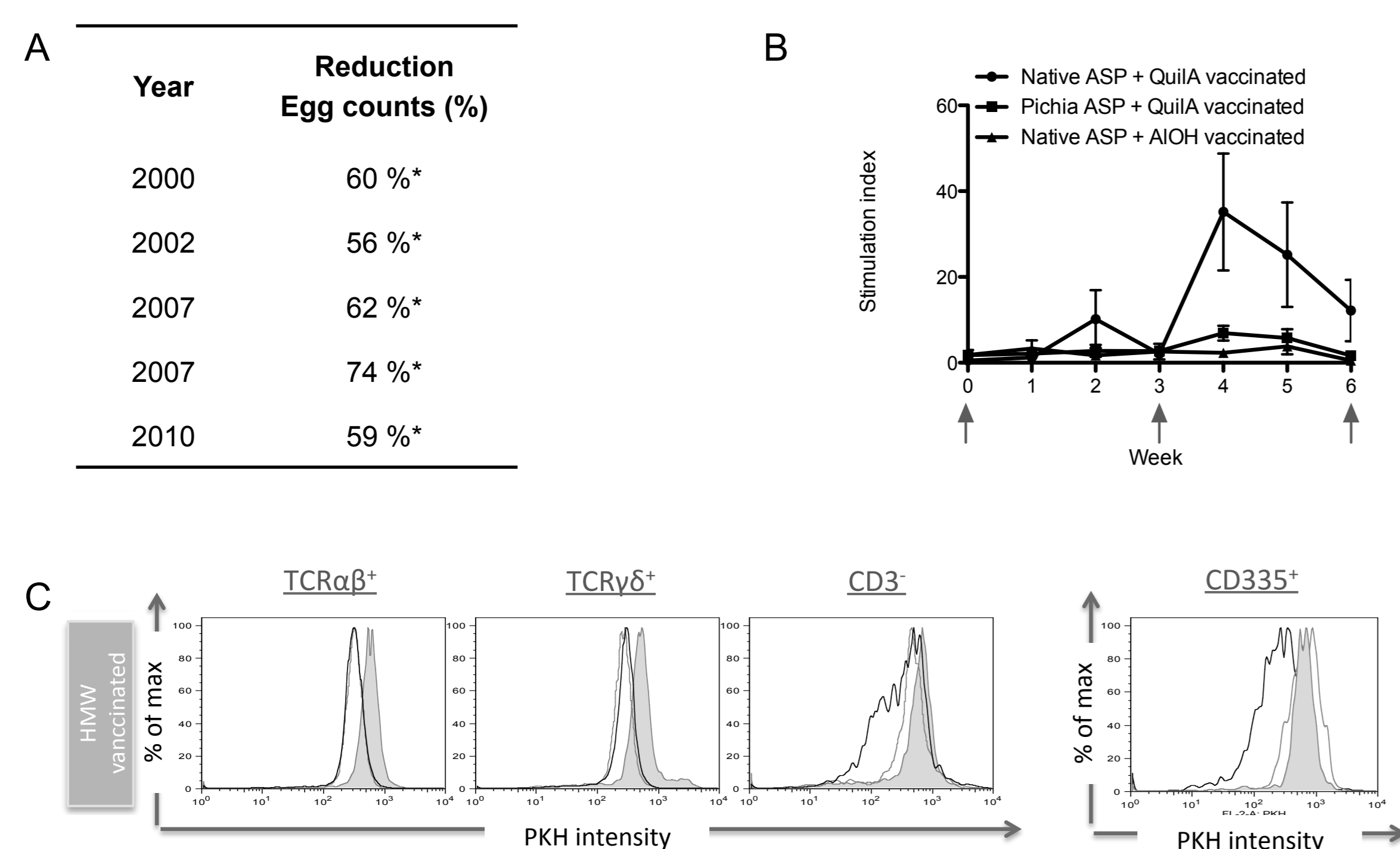
- Five groups of 4 animals:
  - QuilA control
  - nASP/QuilA
  - pASP/QuilA
  - nASP /Alum

- Three intramuscular injections followed by a five trickle infection with *O. ostertagi*

- Two groups of 7 animals:
  - QuilA control
  - HMW/QuilA

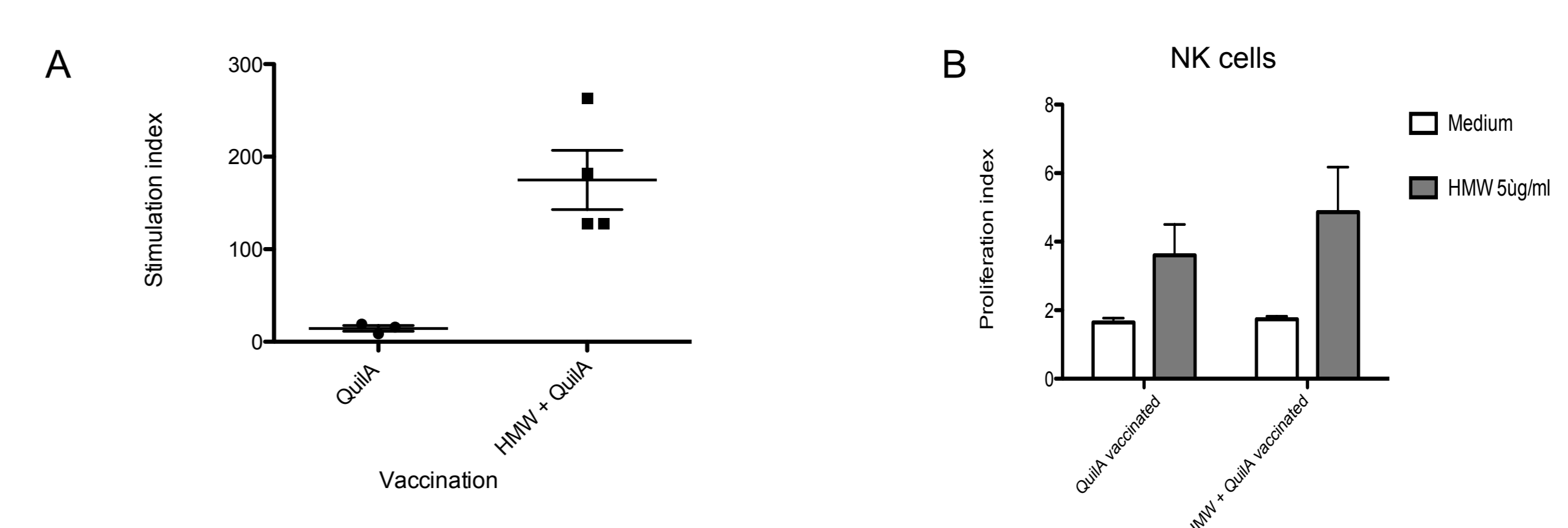
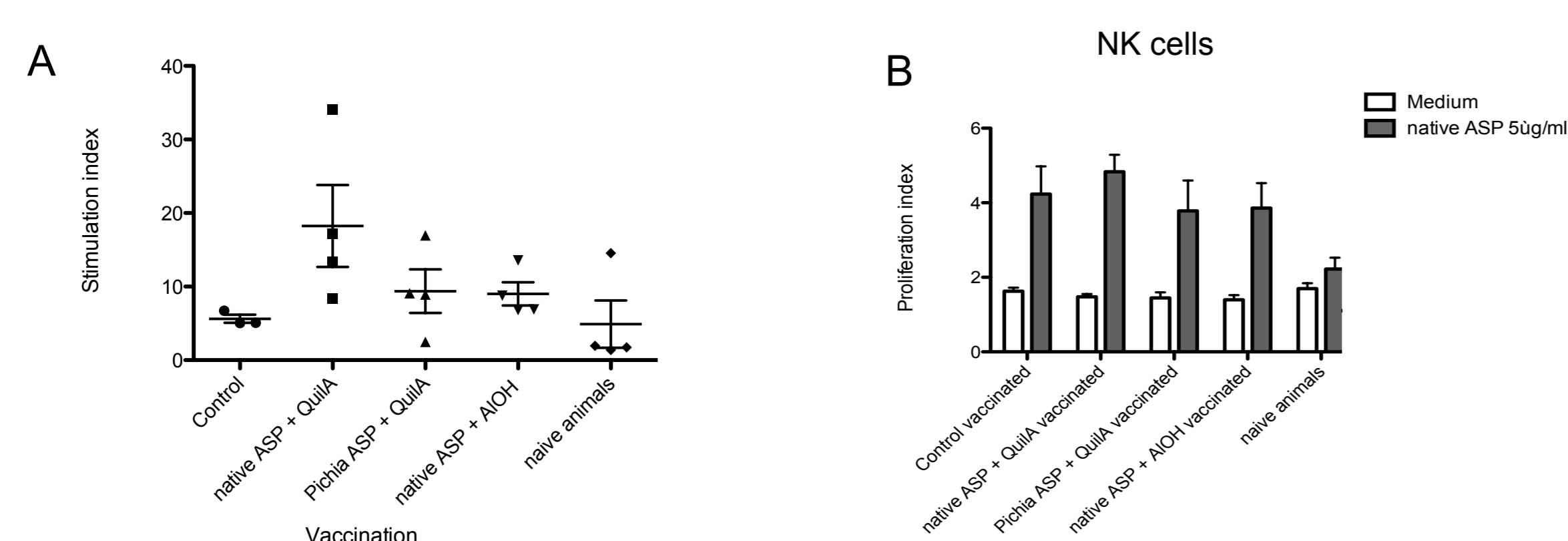
- Three intramuscular injections followed by a five trickle infection with *C. oncophora*

## Systemic response



**Figure A:** The tables show the protection levels obtained with both native vaccines combined with QuilA in the different trials along the years. Protection levels are based in the reduction of the fecal egg counts. **Figure B:** As a measure of proliferation, <sup>3</sup>H-Thymidin (<sup>3</sup>HT) uptake by PBMCs was analyzed each week during the vaccination period. The stimulation index for each time point was calculated by dividing the mean counts per minute (CPM) of cultures stimulated with the antigen with the mean cpm of medium stimulated cultures. The combination of the native antigen with QuilA always gave the highest proliferation index. **Figure C:** Simultaneously to the <sup>3</sup>HT cultures, the proliferative cell fractions were identified by PKH labeling prior to culture.

## Mucosal response



**Figure A:** At the time of necropsy, mononuclear cells (MC) were isolated from the abomasal (*O. ostertagi*) or the small intestine (*C. oncophora*) draining lymph nodes and the proliferation index was calculated based on the <sup>3</sup>HT uptake as previously described for the systemic response. **Figure B:** MC were labeled with PKH to identify the proliferative cell populations.

## Conclusion

Natural killer cells may play a pivotal role on the protective vaccine-induced immune response against both *Ostertagia ostertagi* and *Cooperia oncophora*. In the case of *C. oncophora*, other immune cells such as CD4 T cells and B cells might also participate to induce a protective immune response at mucosal level, where only NK cell- proliferation is observed, whereas for *O. ostertagi* NK cells are the main responders both systemically and at the mucosal level.