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PCV2 vaccination induces IFN-γ/TNF-α co-producing T cells with a potential role in protection

Hanna C Koinig[1,2], Stephanie C Talker[2], Maria Stadler[2], Andrea Ladinig[1], Robert Graage[1,3], Mathias Ritzmann[1,4], Isabel Hennig-Pauka[1], Wilhelm Gerner[2†] and Armin Saalmüller[2*†]

Abstract

Porcine circovirus type 2 (PCV2) is one of the economically most important pathogens for swine production worldwide. Vaccination is a powerful tool to control porcine circovirus diseases (PCVD). However, it is not fully understood how PCV2 vaccination interacts with the porcine immune system. Especially knowledge on the cellular immune response against PCV2 is sparse. In this study we analysed antigen-specific T cell responses against PCV2 in a controlled vaccination and infection experiment. We focused on the ability of $CD4^+$ T cells to produce cytokines using multicolour flow cytometry (FCM). Vaccination with a PCV2 subunit vaccine (Ingelvac CircoFLEX®) induced PCV2-specific antibodies only in five out of 12 animals. Conversely, vaccine-antigen specific $CD4^+$ T cells which simultaneously produced IFN-γ and TNF-α and had a phenotype of central and effector memory T cells were detected in all vaccinated piglets. After challenge, seroconversion occurred earlier in vaccinated and infected pigs compared to the non-vaccinated, infected group. Vaccinated pigs were fully protected against viremia after subsequent challenge. Therefore, our data suggests that the induction of IFN-γ/TNF-α co-producing T cells by PCV2 vaccination may serve as a potential correlate of protection for this type of vaccine.

Introduction

Since the first description of porcine circovirus by Tischer et al. in 1982 [1], porcine circovirus type 2 (PCV2) has become one of the most important pathogens affecting the swine industry worldwide [2]. PCV2 is the causative agent of a number of disease syndromes summarized as porcine circovirus diseases (PCVD) among which postweaning multisystemic wasting syndrome (PMWS) is the economically most important [3,4]. Single PCV2 infection rarely results in clinical disease [5]. In the majority of cases pigs are subclinically infected [4]. However, coinfections with porcine reproductive and respiratory syndrome virus (PRRSV), porcine parvovirus (PPV) or *Mycoplasma hyopneumoniae* (*M. hyo*) are common and lead to more severe clinical symptoms [6,7].

In 2006 the first commercial PCV2 vaccines were introduced to the market [8]. Open reading frame 2 (ORF2) encoded capsid proteins were found to be immunogenic which made them suitable for vaccine development [9,10]. Indeed, two of four commercial PCV2 vaccines are based on recombinant ORF2 capsid proteins. Currently, PCV2 vaccination is widely used to combat PCVD. Different vaccines are commercially available and have successfully contributed to a decrease in mortality and an increase in growth parameters [11], probably via a reduction of PMWS severity [12]. Therefore, they are considered as an efficient tool to control PMWS [13].

The majority of domestic pigs are seropositive for PCV2-specific antibodies [12,14]. Of note, viremia is frequently detected in seropositive pigs. This led to the assumption that antibodies against PCV2 are not fully protective [15,16]. Furthermore, previous studies indicated that the analysis of antibody titres is often not sufficient to evaluate a protective immune response against PCV2 [17]. Other findings underline the importance of neutralizing antibodies. PMWS-affected pigs have lower titres of neutralizing antibodies than subclinically infected animals [18] and high titres of neutralizing antibodies are inversely

* Correspondence: armin.saalmueller@vetmeduni.ac.at
†Equal contributors
[2]Institute of Immunology, Department of Pathobiology, University of Veterinary Medicine, Vienna, Austria
Full list of author information is available at the end of the article