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Review paper

Immune responses and vaccine-induced immunity against Porcine circovirus type 2

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ABSTRACT

Porcine circovirus type 2 (PCV2) is essential but not sufficient for postweaning multisystemic wasting syndrome (PMWS) occurrence in pigs. The outcome of PCV2 infection depends on the specific immune responses that are developing during the infection. Diseased pigs are immunosupressed and unable to mount effective immune responses to clear the virus from circulation. In the final stage, PMWS-affected pigs suffer from extensive lymphoid lesions and altered cytokine expression patterns in peripheral blood mononuclear cells (PBMCs) and lymphoid organs. PCV2 infection can also be asymptomatic, demonstrating that not every infection will guarantee the occurrence of severe immunopathological disturbances. Asymptomatic animals have higher virus specific and neutralising antibody titres than PMWS-affected animals. Recent results have pointed out that the mechanisms by which PCV2 can affect the immune responses involve the induction of IL-10, virus accumulation into and modulation of plasmacytoid dendritic cells and the role of viral DNA in regulation of immune cell functions. Fourteen years after the first description of PMWS in Canada, efficient commercial vaccines against PCV2 are available. The vaccine success is based on activated humoral and cellular immune responses against PCV2. This review focuses on the recent research on immunological aspects during PCV2 infections and summarizes what is currently known about the vaccine-induced immunity.

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1. Introduction

Porcine circoviruses are circular single-stranded DNA viruses belonging to the genus *Circovirus* in the family of *Circoviridae*. *Porcine circovirus type 2* (PCV2) is the primary causative agent of porcine circovirus diseases (PCVD) (Segalés et al., 2005), such as postweaning multisystemic wasting syndrome (PMWS), the most economically important one worldwide. PCV2 is widespread, even ubiquitous in certain regions (Allan and Ellis, 2000; Segalés et al., 2004b), being present in both diseased and non-diseased farms. This widespread distribution of PCV2, particularly its association with asymptomatic animals, indicates that additional triggering factors must be associated for the occurrence of PCVD. Although certain co-factors have been identified, they are not all characterized. In fact, an experimental infection model consistently reproducible in different laboratories is still lacking (Tomás et al., 2008), complicating the investigation of the disease.

Detailed disease descriptions of PCVDs have been published elsewhere (Segalés et al., 2005; Opriessnig et al., 2007; Madec et al., 2008; Ramamoorthy and Meng, 2009). Among PCVDs, PMWS is the most extensively characterized. It affects pigs mainly between 6 and 18 weeks of age; symptomatic animals suffer from wasting, growth retardation, dyspnoea and enlargement of superficial inguinal lymph nodes (Segalés et al., 2005). The clinical symptoms indicate involvement of immunopathological features (Clark, 1997; Rosell et al., 1999; Shibahara et al., 2000; Nielsen et al., 2003). Indeed, PMWS-affected pigs have depletion of T- and B-lymphocytes (Darwich et al., 2002; Nielsen et al., 2003), increased numbers of cells of the monocyte/macrophage lineage (Chianini et al., 2003), and an altered pattern of cytokine responses (Darwich et al., 2003a). With an impaired immune system, diseased animals are more susceptible to opportunistic pathogens (Carrasco et al., 2000; Nunez et al., 2003; Segalés et al., 2003; Ellis et al., 2004).

Pigs can also be asymptomatically infected, demonstrating that not every infection will guarantee the onset of severe immunopathological disturbance. Indeed, animals surviving PCV2 infection develop immunity against the virus (Allan and Ellis, 2000; Krakowka et al., 2002; Ladekjaer-Mikkelsen et al., 2002). Subclinically infected pigs seroconvert with higher virus specific and neutralising antibody titres than PMWS-affected animals (Ladekjaer-Mikkelsen et al., 2002; Rovira et al., 2002; Okuda et al., 2003; Hasslung et al., 2005; Meerts et al., 2006; Fort et al., 2007).

Recently, commercial vaccines against PCV2 have proven to be efficacious at protecting against PMWS development by reducing significantly the mortality rates of nursery and fattening pigs in vaccinated farms, and increasing the daily weight gain (Fachinger et al., 2008; Kixmöller et al., 2008; Opriessnig et al., 2009; Segalés et al., 2009). Also, microscopic lymphoid lesions typifying PMWS, as well as viremia, are reduced (Fachinger et al., 2008; Fort et al., 2008; Kixmöller et al., 2008; Opriessnig et al., 2009).

In contrast to articles reviewing the symptoms and aetiology of PMWS, there have been only a few review articles focusing on the characteristics of PCV2 interaction with the immune system (Darwich et al., 2004; Segalés et al., 2004a). With the marked expansion of this particular research field the last 5 years, the present article reviews current knowledge on PCV2 immunology, in terms of both innate and acquired immune responses as well as vaccination.

2. Early immunological events following infection by PCV2

Recent work has suggested that the discrepancy in the outcome of PCV2 infection relates to how the virus influences the innate immune system. In infected animals, PCV2 is most frequently associated with monocytes, macrophages and dendritic cells (DC), which have critical roles in immune defence development and regulation (Darwich et al., 2004).

2.1. Effects of PCV2 infection on dendritic cells in vitro

In vitro analyses have confirmed the predilection of PCV2 for DC and macrophages (Gilpin et al., 2003; Vincent et al., 2003). Interestingly, these cells accumulated both viral antigen and DNA for prolonged periods, without efficient replication of the virus and are thus regarded playing a major role in viral persistence and transmission (Gilpin et al., 2003; Vincent et al., 2003; Pérez-Martín et al., 2007).

In DCs the presence of live PCV2 does not appear detrimental to DC survival (Vincent et al., 2003), nor is the virus transmitted from DCs to lymphocytes (Vincent et al., 2003).