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Isolation variation and its role in pathogenicity and disease control: Why does FDAH's Suvaxyn® PCV2 one dose vaccine work so well?

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Introduction

Porcine Circovirus Type 2 (PCV2)-Associated Disease (PCVAD) such as Postweaning Multisystemic Wasting Syndrome (PMWS) has recently emerged as a significant global swine disease. PMWS mainly affects pigs between 5 and 18 weeks of age, and its clinical signs include progressive weight loss, dyspnea, tachypnea, anemia, diarrhea, and jaundice. The PMWS-associated mortality rate is high up to 40% in some complicated field cases (5).

Porcine circovirus (PCV) can be classified into nonpathogenic PCV Type 1 (PCV1) and pathogenic PCV2. The PCV1, first discovered as a natural contaminant of Porcine Kidney (PK)-15 cells in 1974 (6), exists in approximately 50% of the herds, but does not cause any disease in pigs. The PCV2, first recognized in Canada in the later 1990s (2), is known as a primary but not sole causative agent of PMWS. The PCV2 shares similar genomic structure and approximately 75% DNA sequence identity with the PCV1. PCV, a single stranded DNA viral genome, consists of two major open reading frames (orf): orf1 encoding replicase for viral replication, and orf 2 encoding immunogenic viral capsid protein. The PCV2 orf2 capsid protein is found to be a protective immunogen in the vaccine development.

PCV2 variants

The PCV2 can be further classified into PCV2A (Genotype II, RFLP 422 or American-like strain) and PCV2B (Genotype I, RFLP 321 or European-like strain) by whole genome DNA sequencing analysis or PCR-coupled RFLP pattern of orf2. Recently PCV2B has been isolated from the PMWS pigs in Canada and USA. The PCV2A and 2B share more than 95% DNA sequence identity. The unique genomic feature of PCV2B (1,767 bp) is a thymidine (T) deletion at the nucleotide position 1,042 of PCV2A (1,768 bp), indicating only one nucleotide difference in genome size between these two genotypes. Although both PCV2A and PCV2B were found in the PMWS-sick pigs, PCV2A was mostly associated with the 'healthy' infected pigs. In some cases (i.e. PRRSV as co-infection factor), PCV2B was reported to be more virulent to pigs than PCV2A, resulting in higher mortality rate.

PCV is ubiquitous in global swine populations, but it is not always a pathogen in pigs. Two or more PCV variants can be found in the same sick or 'healthy' pigs without clinical signs. The PCV variants may have existed in herds in commensalisms for many years. This raises the question as to why PMWS has (re)emerged as a severe swine disease in just the past 10-15 years, and what happened to the pigs before 1990s. In addition to PCV2, what cofactors (other viral and bacterial pathogens, pig genetics, timing, or agent X) trigger the disease now? To understand the role of PCV2 variants in pathogenicity and disease control, interaction between the pig and different PCV2 genotypes at the molecular immunological and pathological levels merits further investigation.

Suvaxyn® PCV2 One Dose

In April 2006 Fort Dodge Animal Health (FDAH) was granted a first USDA full license for Suvaxyn® PCV2 One Dose for protection against PCV2 in pigs. Since launched Suvaxyn® PCV2 One Dose has showed excellent field performance in efficacy and safety. Suvaxyn® PCV2 One Dose contains inactivated Porcine Circovirus Type 1-Type 2 Chimera (3) formulated with FDAH's proprietary adjuvant. Suvaxyn® PCV2 One Dose is administered intramuscularly to healthy piglets at 4 weeks of age or older in a one-dose regimen.

In the early phase of vaccine development, different levels of viral antigen loads were optimized, and the effect of various adjuvants on vaccine efficacy and safety was evaluated. The optimized antigen load and the most effective adjuvant were chosen for use in the Suvaxyn® PCV2 One Dose vaccine. In addition, the unique genomic structure of the PCV Type 1-Type 2 Chimera (3) and its very "common" orf2 capsid protein were other key factors in successful development of the Suvaxyn® PCV2 One Dose vaccine.

Efficacy studies indicated significant protection in the prevention of PCV2 viremia and reduction of microscopic lymphoid depletion in Suvaxyn® PCV2 One Dose-vaccinated pigs as compared to the controls following a single vaccination. Furthermore, challenge studies demonstrated cross-protection against a genetically divergent French PCV2 strain (PCV2B) which shares 99.7% sequence identity with the new genotype Canadian isolates (7). In addition, maternal antibody override studies demonstrated that Suvaxyn® PCV2 One Dose is efficacious in pigs with low to high levels of maternal antibodies to PCV2 (4).

Field performance of the Suvaxyn® PCV2 One Dose vaccine was demonstrated in several commercial herds involving in a total of 6,830 vaccinated pigs and 3,750 unvaccinated controls. The results indicate that vaccination of Suvaxyn® PCV2 One Dose significantly decreased the total mortality rate related to PCVAD (1).

The safety of the Suvaxyn® PCV2 One Dose vaccine was demonstrated by a field safety trial involving a total of 1,110 doses of two prelicensing vaccine serials being administered according to label recommendations by private veterinarians. No adverse events associated with the vaccine were noted in the safety trial.

In summary, Suvaxyn® PCV2 One Dose is efficacious in the prevention of PCV2 infection as well as safe for pigs under field conditions. This may be due to the optimized antigen load, carefully selected adjuvant, unique chimeric construct and its highly-homologous orf2 capsid protein.

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