RESEARCH ABSTRACT

SWINE HEALTH

Title: Genogroup A, B and C porcine rotaviruses: Prevalence and implications for effective vaccines – **NPB #12-094**

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Scientific Abstract:

Fecal samples collected in different seasons of 2004 and 2011 from diarrheic and healthy nursing piglets from 5 selected swine farms in the US were screened for PRV groups A (PRVA) and C (PRVC) using RT-PCR. RVs were identified in 27.4% (65/237) of the samples, with 7.6% and 21.5% positive for Gp A and C RVs, respectively. The highest overall prevalence was in summer (35.2%) followed by winter (27.4%) [2004, spring (23.9%) and summer (19.4%); 2011 winter (61.9%) and summer (43.9%)]. The dominant G-P combination was G9P[13] found in 60.9% of positive samples. The other combinations were G9P[7] (8.7%), G4P[13] (8.7%), G11P[13] (4.3%), and G11P[7] (4.3%). Sequence analysis of partial VP7 genes of selected strains revealed that the G4 strains were closely related to one another (95%) and, to a lesser extent, to human (82 to 84%) and porcine (84 to 86%) G4 strains. Of the 128 samples collected in 2012, 23.5% from nursing piglets and 8.5% from weaned piglets were PRVC positive, with a higher PRVC frequency in diarrheic (28.4%) than in non-diarrheic (6.6%) piglets. Partial sequencing and phylogenetic analysis of the VP6 gene of selected PRVC from different farms (historic and recent) revealed high nucleotide sequence identity with reference human (82.5-86%) and porcine (86.2-97.2%) RVC. For two strains (RVC/Pig-wt/USA/RV0104/2011/G3PX and RVC/Pig-wt/USA/RV0143/2012/G6Px) from two different farms full length sequences of the inner capsid VP6, enterotoxin NSP4 and the outer capsid VP7 and VP4 (partial for RV0104) genes were determined. The VP6 gene of the two strains showed high (99%) nucleotide identity to one another, 84-91% identity to other porcine RVC strains and 81-82% identity to human and bovine RVC strains. The NSP4 gene analysis revealed that RVC/Pig-wt/USA/RV0104/2011/G3PX and RVC/Pig-wt/USA/RV0143/2012/G6Px strains were not closely related to each other (87% identity), but shared higher identity with prototype RVC/Pig-wt/USA/Cowden/1980/G1Px strain (93% and 89%, respectively). The VP7 gene analysis indicated that the two strains were distantly related to one another (72% identity). RVC/Pig-wt/USA/RV0143/2012/G6Px was most closely related to porcine RVC G6 strains (82-86% identity), whereas RVC/Pig-wt/USA/RV0104/2011/G3PX was most closely related to porcine HF (G3) strain (94% identity). Analysis of the full length nucleotide sequence of the VP4 gene revealed that RVC/Pig-wt/USA/RV0143/2012/G6Px was distantly related to porcine (75%), bovine (74%) and human (70%) strains.

Comparative sequence analysis of the full genome constellations of the selected dominant G9P[13] and G9P[7] field PRVA strains revealed that the P[13] strain genome constellation was G9-P[13]-I5-R1-C1-M1-A8-N1-T1-E1-H1, while that of the P[7] strain was G9-P[7]-I5-R1-C1-M1-A8-N1-T7-E1-H1. Remarkably, four (VP2, VP3, NSP2 and NSP4) and five (VP7, VP2, VP3, NSP2 and NSP4) genome segments of the G9P[13] and the G9P[7], respectively, shared the highest nucleotide identity (89.5-95.6%) with the respective genes of PRV OSU. Only NSP1 genes of both G9 strains and NSP3 of the G9P[13] strain shared the highest nucleotide identity (~91-92%) with PRV Gottfried NSP1 and NSP3, respectively. The G9P[7] NSP3 gene was most closely related to RVA/Cow-tc/GBR/UK/1973/G6P5 with 93.4% of similarity. This suggests that both prototype vaccine strains might have contributed some genetic material to the currently circulating field PRV diversity via multiple reassortment events. It is also of interest that VP7 genes of both G9 strains were most closely related to human G9 strains with nucleotide identity of over 92%.

The sera of gnotobiotic (Gn) pigs inoculated with one of the dominant PRVA G9P[13] contained high levels of homologous but very low levels of heterologous virus neutralizing (VN) antibodies (Ab) against several human (porcine-like) and PRVAs. Similarly, reference PRVA OSU and Gottfried (prototype vaccine) strains induced low heterologous VN Ab titers against PRVA G9P[13] and human RV Wa. **This suggests that only limited cross-protection may be conferred by the current PRV vaccines against the circulating wild-type PRVAs**. Consistent with the higher overall nucleotide identity between OSU and the G9 strains, higher levels of cross-neutralizing Abs were observed between the G9P[13] strain and OSU as compared to Gottfried strains. Additionally, when we assessed the one-way cross-reactivity between the historic cell-culture adapted PRVC Cowden (G1) and the newly identified field PRVC (G6), only limited cross-neutralizing Ab titers were detected. The heterologous VN Ab titer for Cowden strain was ~150 lower than for the homologous strain.
Thus, our results demonstrate the high genetic and antigenic diversity and the shift in dominant genotype prevalence among PRVAs and PRVCs, may provide a possible explanation why the current vaccines may lack efficacy. Additionally, our findings suggest that the currently dominant G9 PRVAs may be natural reassortants between RVs from multiple hosts including swine, bovine and human. **Therefore, epidemiological studies on the prevalence and genetic diversity of PRVs are of utmost importance to design updated RV vaccines based on the dominant RV genotypes circulating in swine and to control RV infection in swine and humans.**