RESEARCH ABSTRACT

SWINE HEALTH

Title: Macrophage Activation and development of Porcine Circovirus Wasting Disease **NPB #00-014**.

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Abstract: Porcine circovirus (PCV)-2, a newly described single stranded circular DNA virus pathogen of swine is the cause of postweaning multisystemic wasting syndrome (PMWS). In gnotobiotic piglets, PCV-2 infection alone produces asymptomatic infection without evidence of overt PMWS. Gnotobiotic piglets infected with PCV-2 were injected with keyhole limpet hemocyanin in incomplete Freund's adjuvant (KLH/ICFA) and the effects on virus production and development of PMWS were determined. In the first experiment, piglets were injected subcutaneously on the left hip and shoulder and viral burden was assessed in regional lymph nodes draining the injection sites and in contralateral lymph nodes 13/14 days after infection. Immune activation increased the number of virus antigen-positive cells in draining lymph nodes and increased the amount of infectious virus recovered by 1-4 log10. In a second experiment, the effects of injections of KLH/ICFA with or without concurrent stimulation of peritoneal macrophages by intraperitoneal injections of thioglycollate broth on induction of PMWS was assessed. All immunized piglets developed moderate to severe PMWS whereas none of the piglets infected with PCV-2 alone developed PMWS. Greater than 107 infectious virus per gram of tissue was recovered from PMWS-affected piglets. In PMWS-affected piglets, extensive replication of PCV-2 in lymphoid tissues and liver was documented by both immunocytochemistry and quantitative viral titrations.

Lymph node and liver section replicates from experimental PMWS piglets and controls were dually stained for the distribution of PCV-2 structural protein, incorporated bromo-desoxyuridine (BrDU), TUNEL reactivity and cytoplasmic lysozyme. Viral antigen was primarily localized within the cytoplasm and occasional nuclei of lysozyme-positive histiocytes and macrophages. Cellular DNA synthesis was not mandatory for virus production as the majority of virus-positive histiocytes were negative for BrDU incorporation into cell nuclei. In the main, hepatocytes did not contain viral protein and, when detected, antigen was restricted to hepatocyte nuclei only. Apoptosis, as determined by TUNEL, was not a feature of hepatocyte loss in PMWS lesions. These data confirm the tropism of PCV-2 for macrophages and histiocytes and suggest that hepatocyte destruction, characteristic of experimental PMWS, is accomplished by progressive and widespread hepatocyte necrosis, not by apoptotic mechanisms. Thus, immune activation is a key component of the pathogenesis of PCV-2-associated PMWS in swine and this event is accompanied by upregulation of virus production in macrophages and spread of the virus to many organs and tissues.