RESEARCH REPORT
SWINE HEALTH

Title: Rational Design of a New Generation of PRRSV Differential (Marker) Vaccines (Renewal, 2007), **NPB 07-232**

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Scientific Abstract
A major research goal of our laboratory is the development of a new generation of PRRSV differential marker vaccines. Based on the use reverse genetics technology, we are pursuing the following 3 main objectives: 1) obtain molecularly attenuated vaccine strains, 2) produce a molecular enhancement of the immunogenicity of these novel vaccines and 3) develop a marker differential vaccine system for this new generation of vaccines currently under development. An additional long-term objective began to be addressed by this NPB project **(NPB 07-232)**. Such goal consists of the design of novel vaccines up to standards of satisfactory protective coverage against infection by **homologous or heterologous** PRRSV strains. It is still unclear what defines a heterologous PRRSV strain in terms of protective immunity. Previous work conducted at our laboratory **(NPB 04-174)**, had indicated that there may be serogroups of PRRSV strains defined on the basis of cross-neutralization studies. In this project **(NPB 07-232)**, by use of eight reference strains and their respective mono-specific antisera , we have been able to determine that at least 63 % of all the isolates studied may be typed with at least one of the reference antisera. More importantly, hierarchical clustering analysis of the pattern of cross-reactivity using six of the reference strains allows classifying the entire population of strains studied by us in eight clusters or groups. The patterns of reactivity among these groups vary widely, ranging from one of significant cross neutralization profile (n=1 group), to the minimal or no cross-neutralization profile (n=2). Importantly the prototype strain for the high cross neutralization profile group exhibits a unique pattern of high neutralizing reactivity after inoculation in vivo. Experimental inoculation and molecular studies of this strain indicate that this isolate is a naturally occurring field strain that is stably deglycosylated in one site of both GP3 and GP5 each. Further reverse genetics studies involving this naturally deglycosylated PRRSV strain are ongoing in our laboratory, which may shed light on the role of glycosylation in preventing neutralization as well as the role of GP3 (in addition of GP5) in such function.
This NPB project has permitted, by the first time, to describe the variability of PRRSV strains through an objective, biologically meaningful and immunologically measurable parameter. Until now, variability of PRRSV strains had been defined exclusively in terms of genetic sequencing of a small segment of the PRRSV genome (i.e. the GP5 gene). Perhaps the most significant output of this NPB-funded project is that it provided preliminary results that helped to substantiate a larger scale project (of @ 1million dollar) that PRRSV CAP2 recently awarded to a consortium of 4 universities, amongst which we are included. This larger scale project will center on correlating our immunological characterization of the PRRSV strains with the overall variation of their entire genome and their actual cross-protection in vivo. We anticipate that this research will help to define which sero-groups are important to be represented in the formulation of new vaccines to reach, by single or multivalent combinations, a broad cross-reactive protection.