



COLLEGE OF VETERINARY MEDICINE
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

Colloquium on Prospects for Development of an Effective PRRS Virus Vaccine

Development of economical and effective control strategies for Porcine Reproductive and Respiratory Syndrome (PRRS) remains an important goal for the swine industry.

On June 1 and 2, 2007, a meeting was held at the University of Illinois College of Veterinary Medicine to discuss the state of current knowledge about PRRS vaccination. The meeting was attended by invited experts in PRRS, virology, immunology, and vaccinology and included clinical veterinarians, academics, and vaccine industry scientists (see list of attendees below).

Three general questions were posed to the group:

1. What is the efficacy of current PRRS vaccines?
2. What are the knowledge gaps that need to be filled to develop improved/novel vaccines? and
3. What is the probability that successful PRRS vaccines can be developed?

Following are the consensus opinions regarding each question. This document provides a useful tool to guide future PRRS virus vaccine research in the most promising directions.

What is the efficacy of current PRRS vaccines?

A clear consensus was that modified-live (MLV) PRRS vaccines confer solid protection against homologous reinfection. Their efficacy against heterologous reinfection was thought to be more variable, although the question of how to define “heterologous” in the context of PRRS virus variability remains unanswered (see below). Killed-virus PRRSV vaccines were considered ineffective or of limited efficacy at best, even against homologous challenge, though some thought that this may be improved. The practice of serum inoculation, in which naïve gilts entering the breeding herd are purposely infected with virus strains currently circulating on the farm, has also shown some efficacy. Current vaccine practices appear to be efficacious against homologous challenge, providing support for vaccination as a viable control strategy for PRRS.

While vaccination may be protective, field experience indicates that current vaccines are inadequate for PRRSV control in production settings. Properties of an improved PRRS vaccine may include rapid induction of immunity, protection against most currently prevalent PRRSV strains, no adverse outcomes to swine health and ability to differentiate vaccinated from infected animals. Simplicity of administration to ensure compliance within production units is essential. These properties define the goals for PRRS vaccine research and development.

What are the knowledge gaps which are impeding PRRS vaccine development?

Given that effective vaccination is possible, what researchable questions need to be answered before improved vaccines are developed?

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1. PRRS vaccines may be efficacious against homologous challenge yet knowledge about what mediates this protection is incomplete. What are the determinants of *protective* immunity? There is evidence that antibody alone is capable of mediating protection but we don't know whether solid protection is primarily or partially antibody-mediated, or much about the role of cell-mediated immunity in protection against PRRSV. Which viral proteins bear the B- and T-cell epitopes capable of inducing a protective response? What is the structure of these epitopes? Are there viral factors which impair or modulate host immune responses, including innate responses, to reduce vaccine efficacy? Definition of all of the PRRSV components which have a role on induction of protective immunity and their compatibility with bona fide vector or other delivery systems is an important research goal.
2. There is certainly a lack of protective efficacy of current vaccines against heterologous PRRSV strains. However, it is unclear what defines a heterologous strain in terms of protective immunity. Recent work indicates that there are serogroups of PRRSV based on cross-neutralization studies but the relationship of these serogroups to protection remains to be determined. How does immune evasion by PRRSV occur? In general, we need to know what determines functional variability between PRRSV strains relative to protective immunity and how PRRSV quasispecies distributions affect immunity. Additionally we must know if there are more conserved epitopes which may be exploited to increase the breadth of protection.
3. To prevent adverse health outcomes and prevent reversion to virulence, it is important that we understand how PRRSV causes disease so that safe and stable vaccine candidates may be rationally developed. What are the PRRSV determinants of virulence, replication and host range? Can these be rationally modulated to reduce virulence and/or increase immune responses? What are the effects of viral proteins on macrophage function? How do environment, health status, nutrition and other host factors influence virulence and immunity?

What is the probability that successful PRRS vaccines can be developed?

Most participants agreed that successful vaccination against PRRSV can be achieved and improved, with current MLV vaccines as the standard by which improvement is defined. There was considerable discussion about the various types of vaccines, their likelihood of success and issues related to field efficacy. While there was some consensus that replicating vaccines showed the most promise, at this point all options remain open as to vaccination modes, antigens, adjuvants, etc., with achievement of the efficacy, safety, and logistical goals the primary criteria for success. Estimates of the time required to reach these goals and get a vaccine to market vary widely, largely because it is difficult to predict research outcomes. However, once a candidate vaccine is identified, the development, regulatory and production process is predicted to take 2-3 years for standard MLV and subunit vaccines or 4-6 years for genetically-modified live vaccines. A *realistic* estimate is to have improved vaccines in the hands of producers within 5-10 years.

Conclusions

- PRRS vaccines are effective against homologous challenge.
- Current vaccines are not adequate for producer needs.
- Important research questions that need to be addressed to improve PRRSV vaccines have been identified.
- Improved PRRSV vaccines should be available in 5-10 years.

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Attendees

- Dr. Dave Benfield, *Associate Director, Ohio Agricultural Research and Development Center, The Ohio State University*
- Dr. Jay Calvert, *Associate Research Fellow, Pfizer Animal Health*
- Dr. Shafiqul Chowdhury, *Professor, Diagnostic Medicine/Pathobiology, Kansas State University*
- Dr. Gustavo Delhon, *Research Assistant Professor, Department of Pathobiology, University of Illinois*
- Dr. Tony Goldberg, *Associate Professor, Department of Pathobiology, University of Illinois*
- Dr. Dick Hesse, *Associate Professor, Diagnostic Medicine Pathobiology, Kansas State University*
- Dr. Wally Hoffmann, *Interim Director, Veterinary Diagnostic Laboratory, University of Illinois*
- Dr. Marcus Kehrli, *Research Leader, Virus and Prion Diseases of Livestock Research Unit, National Animal Disease Center, USDA/ARS*
- Dr. Mark Kuhlenschmidt, *Professor & Assistant Head, Department of Pathobiology, University of Illinois*
- Dr. Will Laegreid, *Professor, Department of Pathobiology, University of Illinois*
- Dr. Osvaldo Lopez, *Associate Professor, Biology, Northern Michigan University*
- Dr. James Lowe, *Director, Health & Production Services at The Maschboffs, Inc.; Veterinarian/Owner at Carthage Veterinary Service, Ltd.; and Manager/Owner at Professional Swine Management, LLC.*
- Dr. Monte McCaw, *Associate Professor, Department of Population Health and Pathobiology, North Carolina State University*
- Dr. Eric Nelson, *Professor, Department of Veterinary Science, South Dakota State University*
- Dr. Fernando Osorio, *Professor, Nebraska Center for Virology & Department of Veterinary and Biomedical Sciences, University of Nebraska at Lincoln*
- Dr. Guillermo Risatti, *Assistant Professor, Pathobiology, University of Connecticut*
- Dr. Dan Rock, *Professor & Head, Department of Pathobiology, University of Illinois*
- Dr. Raymond Rowland, *Professor, Diagnostic Medicine/Pathobiology, Kansas State University*
- Dr. Randy Simonson, *Chief Operating Officer, Newport Laboratories*
- Dr. Jonathan Smith, *Chief Scientific Officer, AlphaVax, Inc.*
- Dr. Dongwan Yoo, *Professor & Head, Department of Pathobiology, University of Illinois*
- Dr. Pam Zaabel, *Director of Swine Health Information and Research, National Pork Board*
- Dr. Federico Zuckermann, *Professor, Department of Pathobiology, University of Illinois*