

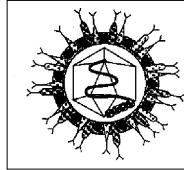
## Current Progress of US PRRS Host Genetics Consortium

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EADGENE Genomics for Animal Health:  
 Outlook for the Future

Muséum National d'Histoire Naturelle,  
 Paris, France  
 October 13, 2009

## Porcine Reproductive and Respiratory Syndrome Virus (PRRSV)



PRRSV = arterivirus, enveloped particle with positive polarity single-strand RNA

- When present in a herd, PRRS causes increased abortions, stillbirths, mummies and chronic respiratory problems in pigs at all stages of production.
- Type 1 (Lelystad) and type 2 (North American) PRRSV first appeared in the late 1980's
- Outbreak of porcine high fever disease (PHFD) in China, 2006, affected >2,000,000 pigs with ~400,000 fatal cases; correlated with unique PRRSV
- Economically, PRRS hits producers hard; cost estimates of \$700M US (2008 prices), with losses in an acute outbreak ranging from \$250 to >\$500 per sow. [Neumann et al. JAVMA 227: 385, 2005.]

## US PRRS Host Genetics Consortium (PHGC)

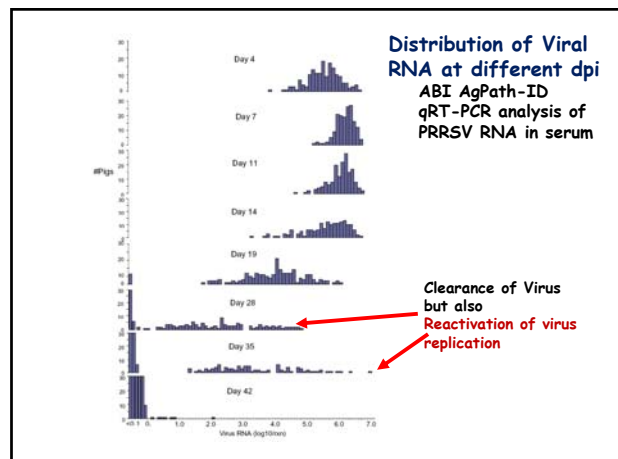
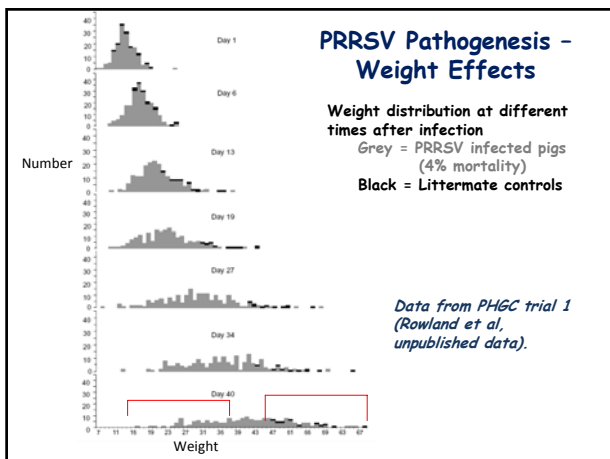
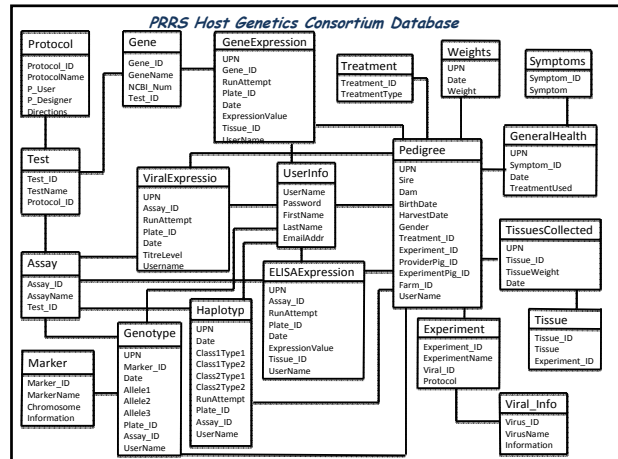
Plan: Use genotyping and phenotyping tools to determine if there are host genes that control resistance/susceptibility to PRRSV infection and associated growth effects

CoPIs NPB Phenotyping grant: R Rowland, Kansas State U; J Lunney, BARC; J Reecy, Iowa State (ISU); R Johnson, UNE

Nursery Pig Model - 5th round of 200 pigs started Oct. 1<sup>st</sup>  
 Sampling Plan: Infect at ~28 days age with well characterized PRRSV isolate (Osorio). Pigs followed for 42 days post infection (dpi) (bleed and weigh at -7, 0, 4, 7, 10, 14, 21, 28, 35, 42 dpi). Serum and Tempus tube (RNA) blood samples aliquoted, stored or sent to testing labs.

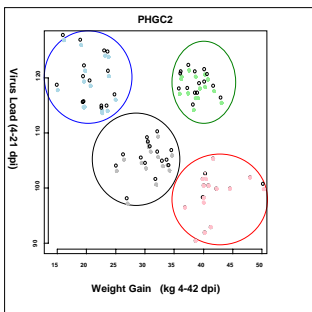
Basic phenotyping tests: viral levels by PCR (ABI), serum antibody (IDEXX and neutralizing), weight, and cytokines (IFN $\gamma$ , IL-8)

Data Storage: secure PHGC Database open to members  
 Overall Plan: perform testing on >1500 pigs so that genetic responses can be evaluated statistically and QTL identified.



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*Assignment of PHGC pigs to different virus/weight categories*



Results of multivariate analyses (principal components and partitioned cluster analyses) at MSU and BARC: effective in assigning PHGC pigs to 4 different virus/weight categories, i.e., the most desired low virus burden/maximal growth (LvHg red); versus high virus burden/maximal growth (HvHg green); low virus burden/reduced growth (LvLg black); and the least desired, high virus burden/reduced growth (HvLg blue).

Pigs from PHGC1 (179) and PHGC2 (167) were assessed for the two variables: 1) Weight gain (WG) from 1-42 days post infection (dpi) and 2) area under log-viral load curve from 0-19 (PHGC1) or 0-21 dpi (PHGC2). The top 15 animals in each cluster (based on their distance from the centroid and relative distance to animals in other clusters) were selected as shown by the colored dots. The figure clearly shows the separate groups for PHGC2.

*USDA PRRS CAP (Coordinated Ag Project) grant supported PRRS Host Genetics Consortium Genotyping*

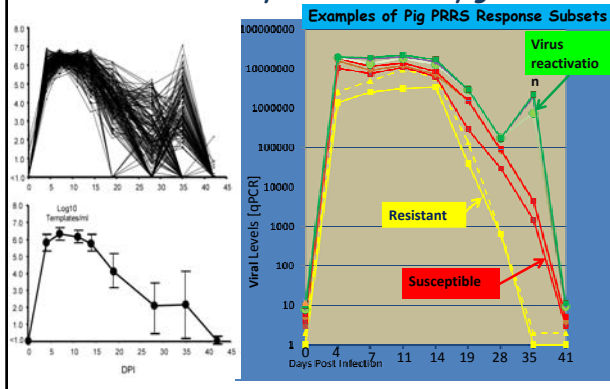
CoPIs: J Lunney, BARC; J Dekkers, JM Reecy, M Rothschild, C Tuggle, R Fernando, ISU; Z Jiang, WSU; H-C Liu, NCSU; R Pogranichniy, Purdue; R Rekeya, UGA; D Smith, U MI; JP Steibel, MSU

Plan: Use genotyping tools to determine if there are host genes that control resistance/susceptibility (PRRSV) infection

Progress: DNAs from pigs from PHGC1 to PHGC4, and their parents (850 pigs total), prepared, quality affirmed, sent to GeneSeek for single-nucleotide polymorphism (SNP) genotyping with Illumina's Porcine SNP60 BeadChip. Also testing for SLA genes, targeted SNPs. Support: US NRSP8 Swine genome. Since SNP chips will be used for genotyping decreased need for extensive family structure; better to use current pig genetics, e.g. progeny of 3-5 way crosses

WGAS (whole genome association studies) to characterize genetic variation in response to PRRSV infection (pigs with improved health, survivability and growth)

*Examples of different categories of anti-viral responses of PHGC pigs*



*USDA AFRI - PHGC Functional Genomics grant*

CoPIs: J Lunney, BARC; C Ernst, JP Steibel, MSU; V Honovar, C Tuggle, ISU; Z Jiang, WSU; R Pogranichniy, Purdue

Specific objectives

- 1) Identify genes and pathways that are associated with pigs that clear PRRS virus and that grow well despite PRRSV infection, using PHGC samples representing different virus/weight categories;
- 2) Select a gene-set and develop a classifier which predicts a pig's ability to clear PRRS infection and maintain weight gain;
- 3) Use quantitative PCR (QPCR) to verify differentially expressed (DE) genes that distinguish PRRS resistant, thrifty pigs from PRRS susceptible, unhealthy pigs, and to validate the classifier gene-set.

Arrays: updated NRSP8-Illumina 20,000 probes  
[www.pigoligoarray.org](http://www.pigoligoarray.org) Steibel et al. Animal Genetics, Epub

Progress to date: Statistical assignment of pigs to different virus/weight categories; quality affirmed RNA preps from Tempus tube samples

*Expected Outcomes of combined efforts of NPB, PRRS CAP2 and USDA AFRI supported research of PRRS Host Genetics Consortium*

- Define genomic regions, SNP alleles, or candidate genes [and source pig genetics] which are correlated with PRRS resistance/susceptibility quantitative trait loci (QTL)
- Use these QTL to develop selection procedures for pigs with lower PRRSV burden or persistence
- Utilize information gained to help uncover unique PRRSV resistance mechanisms and virus-host interactions, thus highlighting alternate vaccine and therapeutic approaches
- Determine why [some] pigs stay healthy despite PRRS.
- Identify pigs with improved resistance not just to PRRS but to respiratory infections

*Invitations:*

2008 International PRRS Symposium  
[www.prrssymposium.org](http://www.prrssymposium.org)

December 4-5, 2009  
 Chicago, IL, USA

2<sup>nd</sup> Animal Genetics of Animal Health  
 May 31-June 2, 2010  
 Paris, France

9<sup>th</sup> International Veterinary Immunology Symposium  
 August 16-20, 2010  
 Tokyo, Japan

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