Swine Day 2017
Rowland Lab Research Update

Raymond (Bob) Rowland

K-State Swine Day Progress Report

November 17, 2016

Manhattan

North American PRRS Symposium on PRRS, Emerging and Foreign Animal Diseases and National Swine Improvement Federation NAPRRS-NSIF Joint Conference

December 1-3, 2017
Intercontinental Chicago Magnificent Mile

November 24, 2017- Conference registration deadline

Genetic approaches for improving swine health in response to PRRSV infection

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Collaborators

Randy Prather, University of Missouri- Genetically modified pigs that are disease resistant

Jack Dekkers, Iowa State University- Genomic markers for breeding disease resistance

Joan Lunney, ARS-USDA- Genetics of the response of pigs to infection

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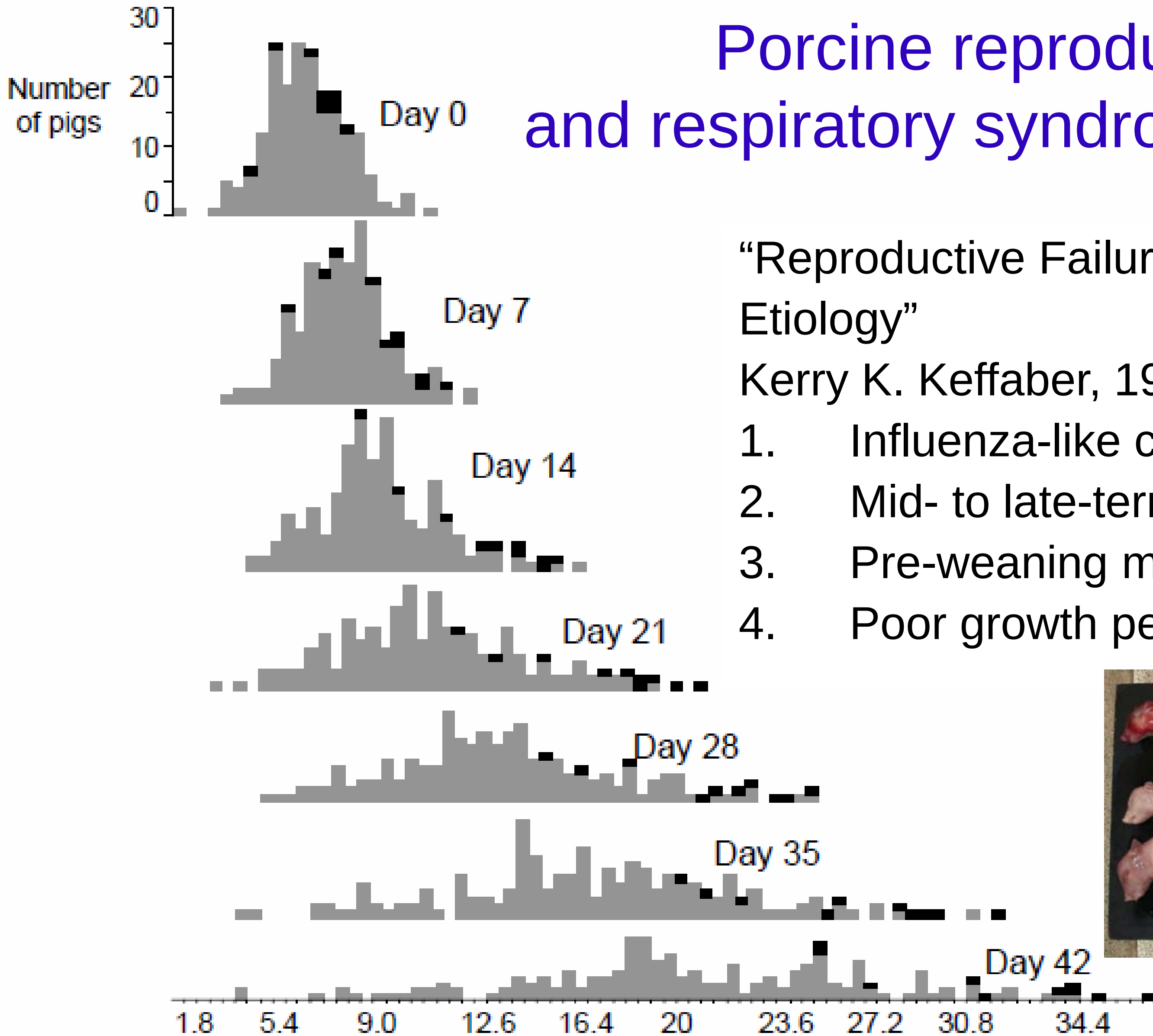
Porcine reproductive and respiratory syndrome (PRRS)



Changes in Weight Distribution after Infection

"Reproductive Failure of Unknown Etiology"

Kerry K. Keffaber, 1989, AASP

1. Influenza-like clinical signs
2. Mid- to late-term abortions
3. Pre-weaning mortality
4. Poor growth performance

$14 billion in losses ($600million/year)

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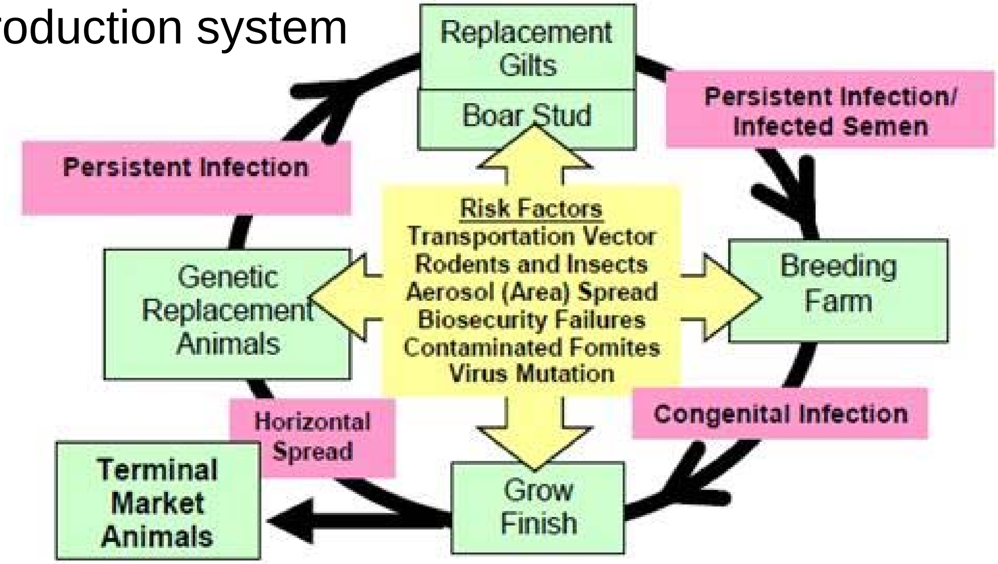
PRRS is a production system disease

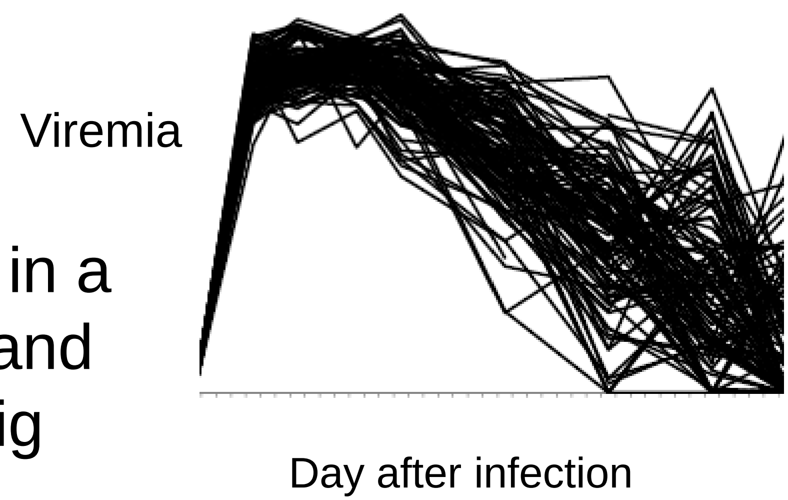
Endemic phase with outbreaks of severe disease

Persistence in a production system



2003-Eric Neumann

Stealthy
Easily transmitted
Persistent
Participates in polymicrobial diseases



Persistence in a population and within a pig

The greatest cost of PRRSV is wasted feed

Sick and dead pigs
Slow growing pigs
Secondary infections

Nutritional, Environmental and Social Impacts

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Integrated approach for PRRS control

Disease Control

- Vaccines
- Detection
- Ecology
- Epidemiology
- Biosecurity
- Sociology

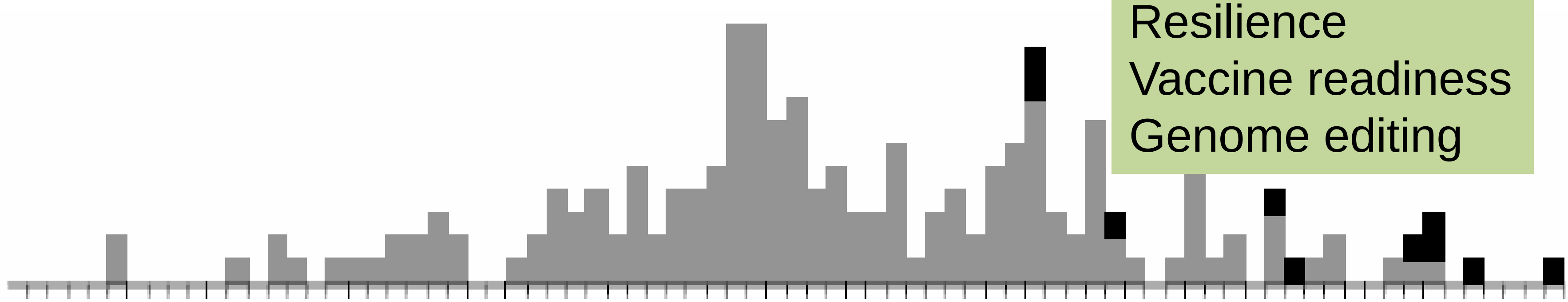
Nutrition

- Feed efficiency
- Feed formulation
- Microbiome

Pig Genetics

- Resistance
- Tolerance
- Resilience
- Vaccine readiness
- Genome editing

Getting back the 5-10% that PRRS takes



PRRS vaccines

- Modified live virus (MLV) vaccine introduced in the U.S.1994- approved for use in PRRSV-infected herds
- MLV limitations-virus shedding, persistent infection, incomplete immune protection, inability to differentiate infected from vaccinated animals (DIVA), potential for reversion to virulence
- Killed vaccines are not effective
- Subversion of host immunity and antigenic variation have made further advances in vaccines difficult to achieve

Conclusions: Vaccines are a poor option for disease control and eradication- Vaccinated animals cannot be transported to PRRSV-free regions.

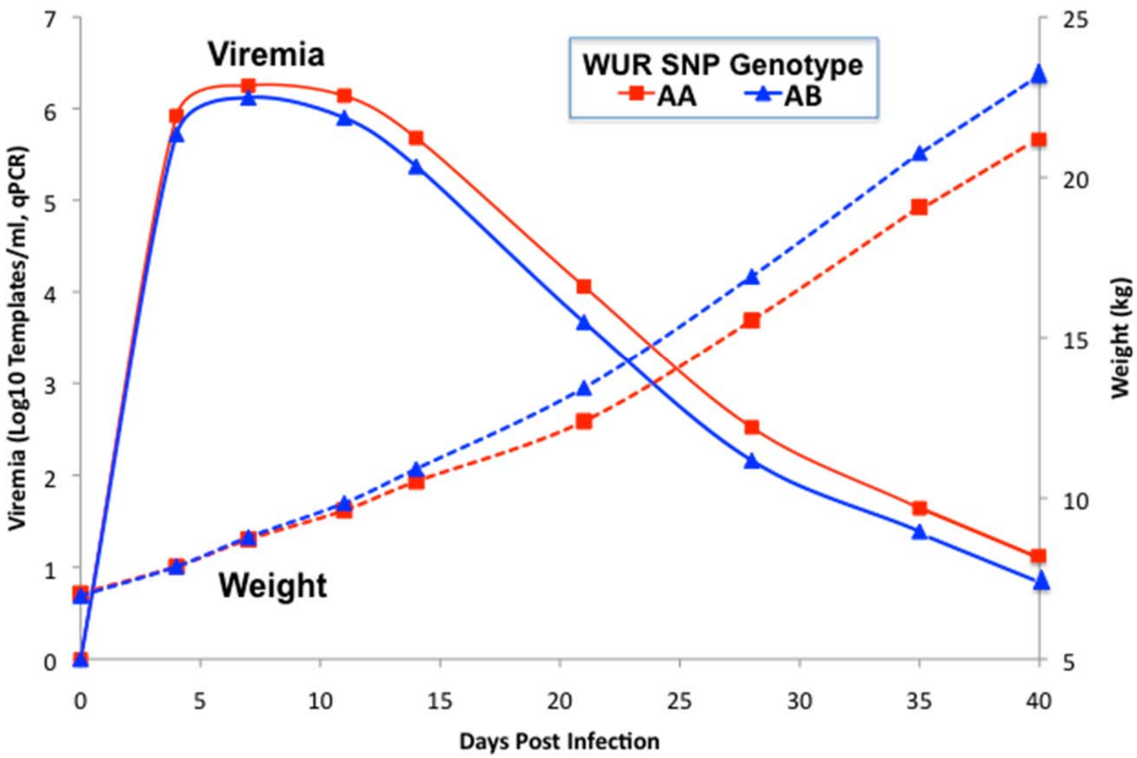
The application of genetics for improving animal health

- Marker selected breeding to improving response

- Modify genes involved in response to infection
  - Insertion of genes to promote resistance
  - <u>Deletion of genes involved in virus susceptibility</u>

“Genome Editing”

The favorable SSC4 marker, WUR, results in a 10% increase in weight and a decrease in viremia



Boddicker, et al. 2012. Evidence for a major QTL associated with host response to porcine reproductive and respiratory syndrome virus challenge. J Anim Sci. 90:1733-1746

Resistance
Tolerance
Resilience

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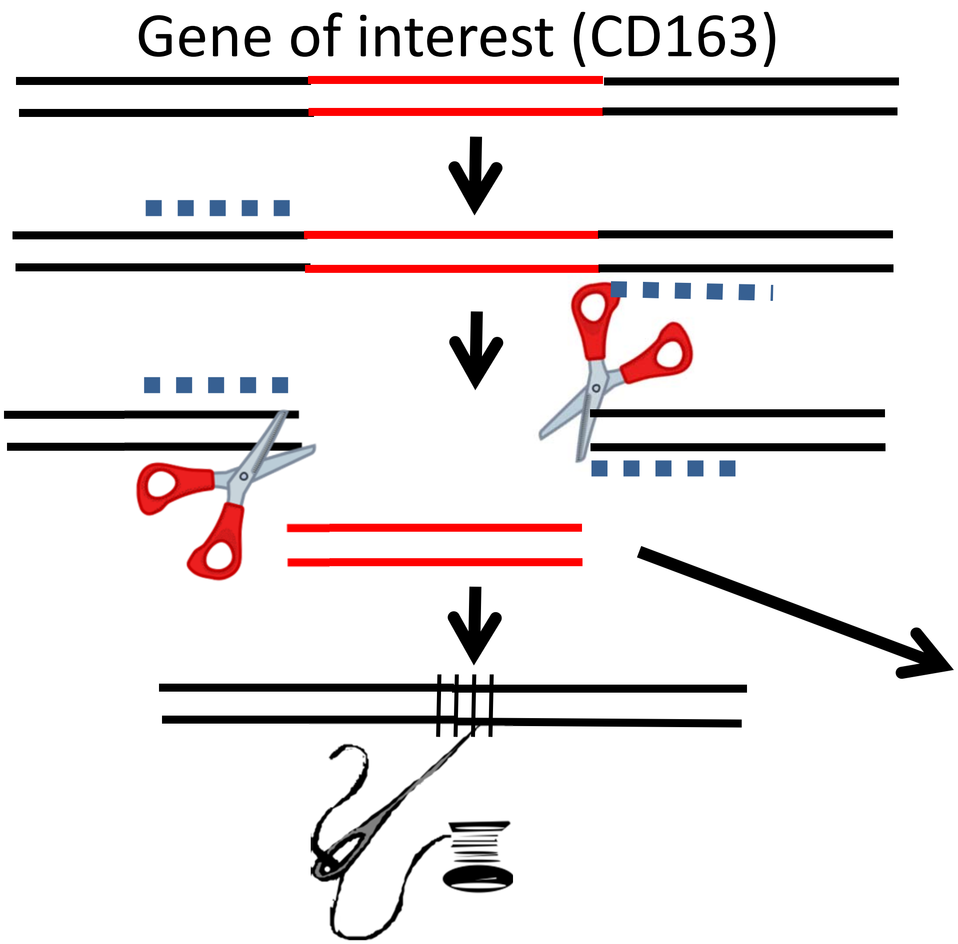
Genetic modification
CRISPR/Cas 9 system



Guide sequences direct were the genome is cut

Molecular scissors cut out DNA segment

Segment is removed and the DNA ends rejoined

Guide sequence ....

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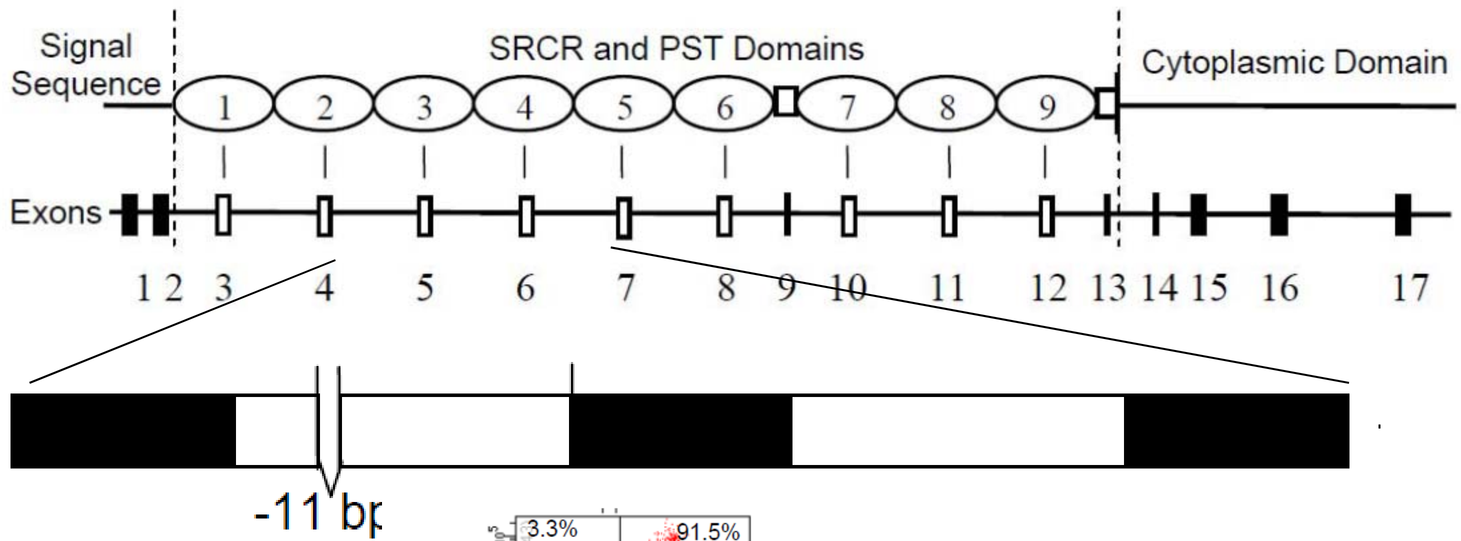
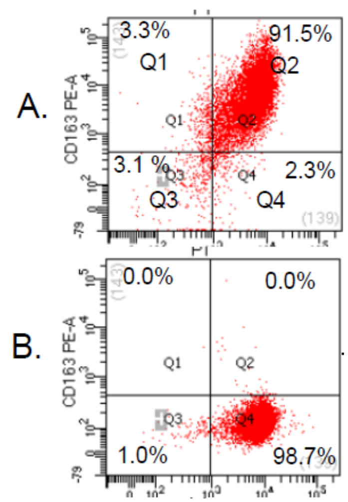
Knocking out CD163 by deleting 11of 2.7 billion bases of the pig genome (Randy Prather)





Normal pig
CD163 is present

CD163 knockout pig
CD163 is absent

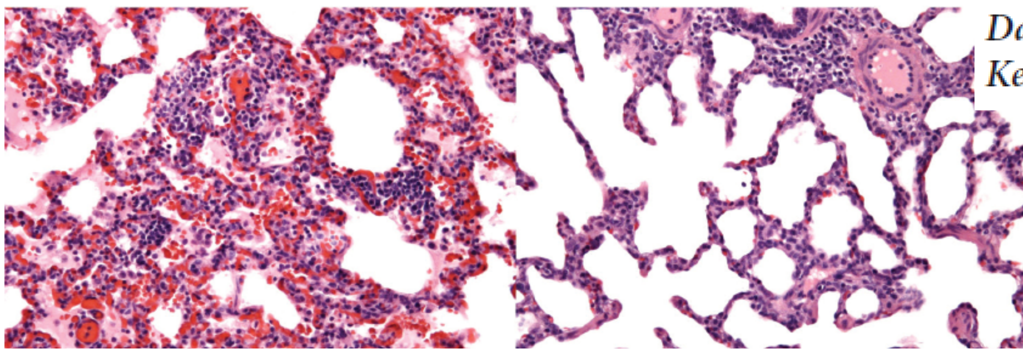
December 7, 2015

Gene-edited pigs are protected from porcine reproductive and respiratory syndrome virus

NATURE BIOTECHNOLOGY

Kristin M Whitworth[1], Raymond R R Rowland[2], Catherine L Ewen[2], Benjamin R Trible[2], Maureen A Kerrigan[2], Ada G Cino-Ozuna[2], Melissa S Samuel[1], Jonathan E Lightner[3], David G McLaren[3], Alan J Mileham[3], Kevin D Wells[1] & Randall S Prather[1]

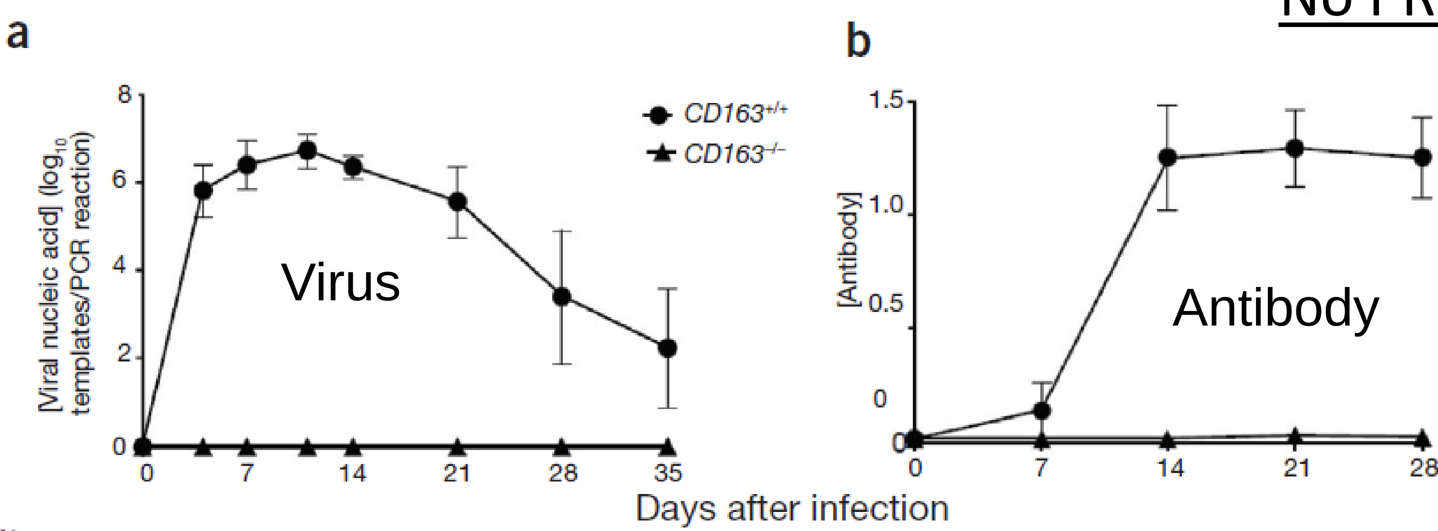
a CD163-Positive b No CD163



No CD163

No key-lock

No PRRSV



Reproductive PRRS
Infection of pregnant gilt/sow at 90 days of gestation

Prevention of reproductive PRRS
The end of a disease

Table 1. *CD163* parental and fetal genotypes used in this study

Gilt No.	*CD163* Genotype: Parents: Male	*CD163* Genotype: Parents: Dam	*CD163* Genotype: Fetus	Day of Infection*[1]	Day of Gestation*[2]	No.of Fetuses
138	+/+	+/+	+/+	91	106	16
139*[3]	+/+	+/+	+/+	91	106	14
140	+/+	+/+	+/+	91	106	12
84	+/+	-/-	+/-	89	109	14
87	+/+	-/-	+/-	89	109	17
122	+/+	-/-	+/-	89	109	11
86	-/-	-/-	-/-	90	109	7
121	-/-	-/-	-/-	90	109	9

*[1] Gestation day when dams were infected
*[2] Gestation day when fetuses were removed
*[3] PRRSV-infected dam aborted at 106 days of gestation

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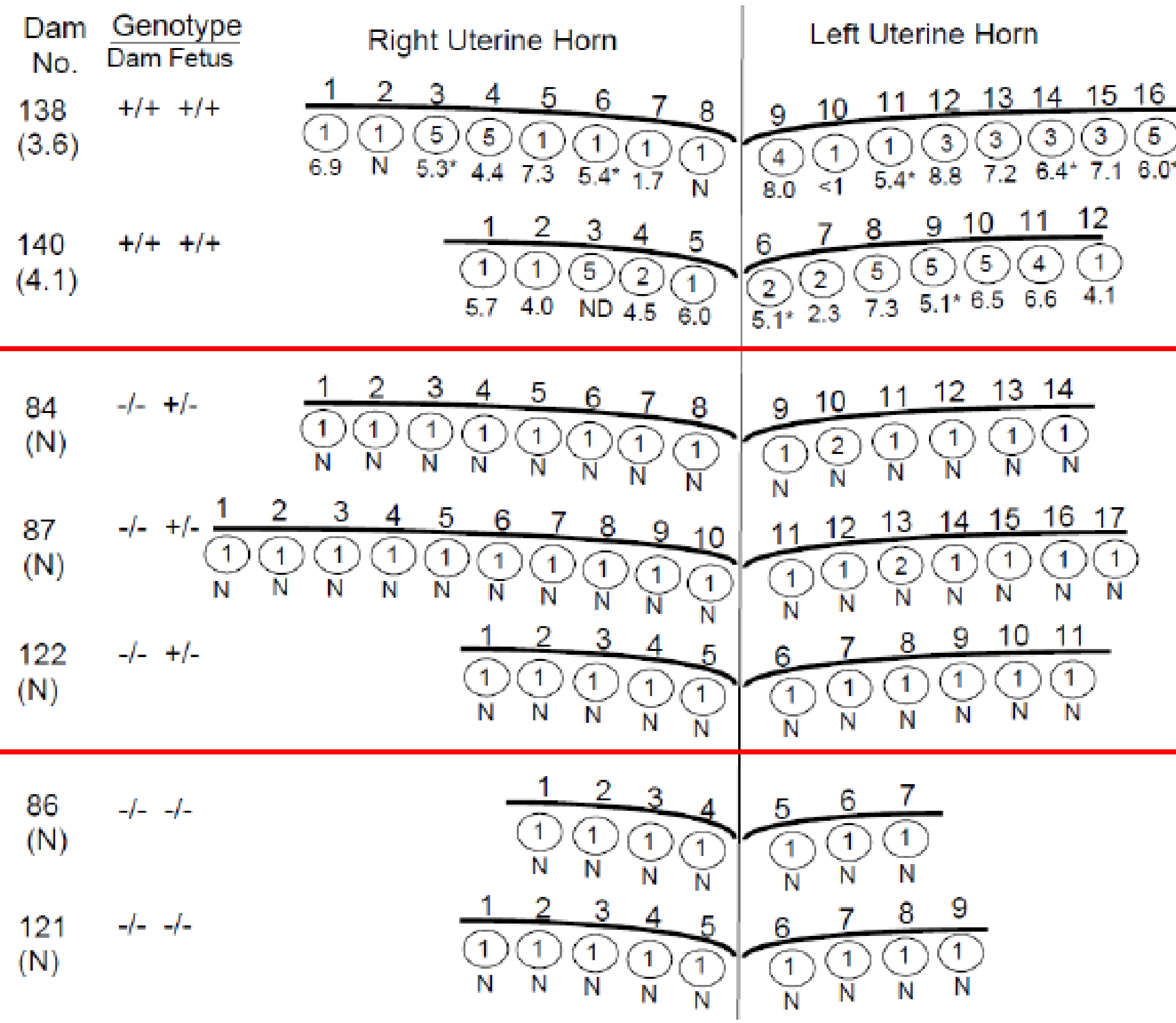
Prevention of reproductive PRRS
The end of a disease

Dam	Fetus
++	++
--	+/-
--	-/-



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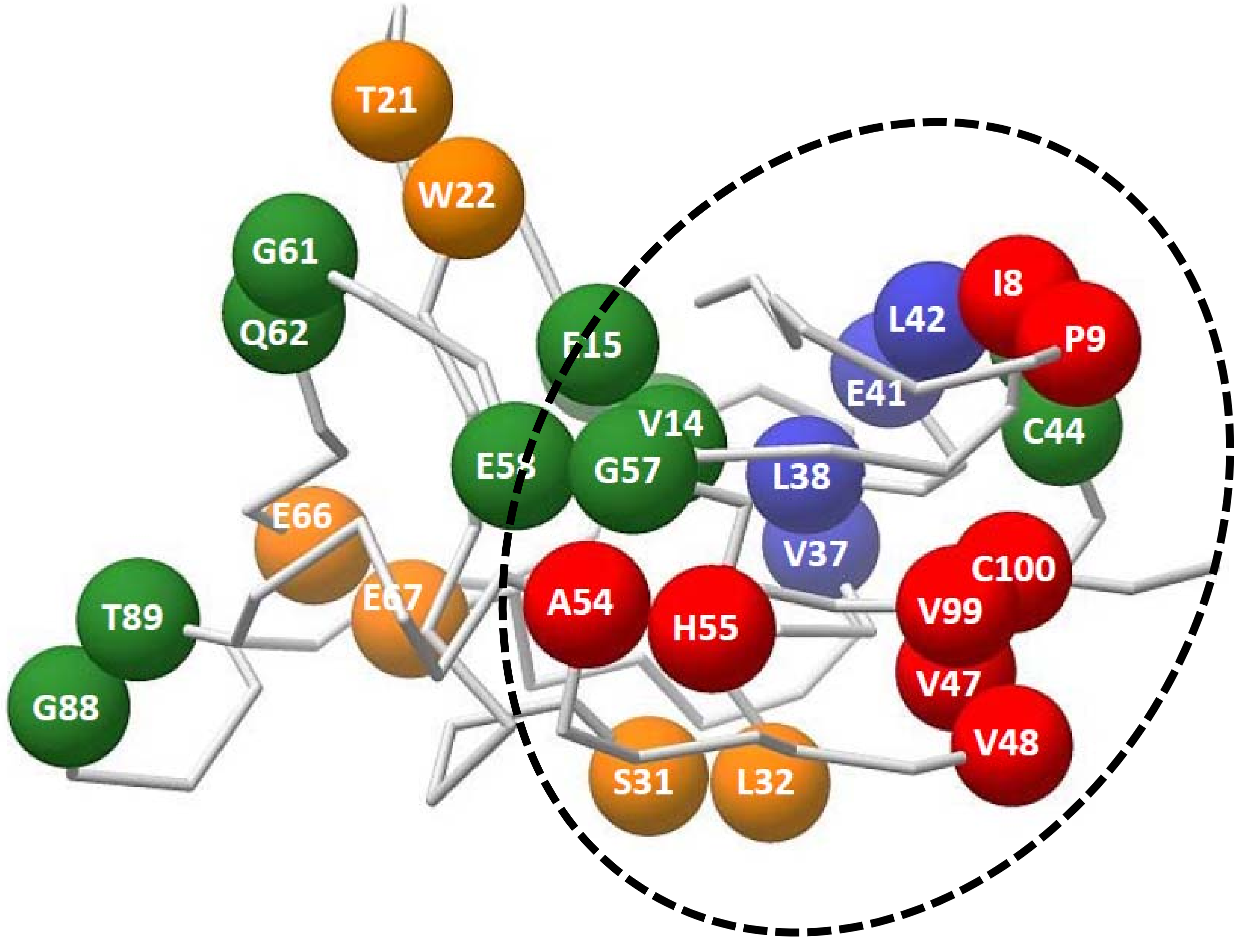
The end of a disease

- The absence of CD163 in the dam surrounds the developing fetus with a protective barrier, preventing infection with PRRSV
- The piglets are born with normal CD163 levels and are susceptible to PRRSV
- Still need that miracle vaccine

Mapping the regions where PRRSV interacts with CD163



Ana Stoian

NBAF

The NBAF, a new, state-of-the-art biosafety level (BSL) 3 & 4 facility located in Manhattan, KS, will enable the U.S. to conduct comprehensive research, develop vaccines and anti-virals, and provide enhanced diagnostic capabilities to protect our country from numerous foreign animal, emerging and zoonotic diseases to assist in protecting our food supply and the nation's agriculture economy and public health.

NBAF-associated projects in the Rowland lab (Biosecurity Research Institute)

African swine fever virus (ASFV) and classical swine fever virus (CSFV)

- Vaccines
- Diagnostics
- Genetics of disease resistance
- Risks for introduction

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PHGC

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Iowa State University
Jack Dekkers

Kansas NBAF Transition Fund

pork checkoff

- NIFA award #2013-68004-20362
- National Pork Board
- Genome Canada
- LLNL

USDA | NIFA