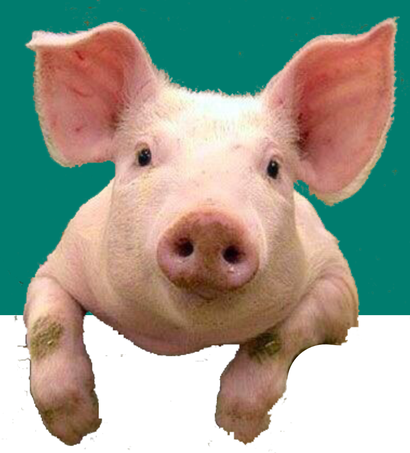
Pigs immunized with heterologous EPITOPE-prime, INACT-boost swine flu vaccine have fewer lung lesions and lower body temperature after challenge



A prime-boost concept using a T-cell epitope-driven DNA vaccine followed by a whole virus vaccine effectively protected pigs in the pandemic H1N1 pig challenge model

Joshua S. Hewitt[a], Anbu K. Karuppannan[a], Swan Tan[b], Phillip Gauger[a], Patrick G. Halbur[a], Priscilla F. Gerber[c], Anne S. De Groot[b,d], **Leonard Moise[b,d]**, Tanja Opriessnig[a,e*]

[a]Department of Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, IA, USA; [b]Institute for Immunology and Informatics, Department of Cell and Molecular Biology, University of Rhode Island, Providence, RI, USA; [c]Animal Science, School of Environmental and Rural Science, University of New England, Armidale, Australia; [d]EpiVax Inc., Providence, RI, USA; [e]The Roslin Institute and The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, UK

Introduction

In this pilot study, the efficacy of an intradermal pDNA vaccine composed of conserved SLA class I and class II T cell epitopes (EPITOPE) against a homosubtypic challenge was compared to an intramuscular commercial inactivated whole virus vaccine (INACT) and a heterologous prime boost approach using both vaccines.

Objectives

- ✓ Evaluate the PigMatrix cell-mediated immune response in swine
- ✓ Compare the efficacy of PigMatrix compared to a commercial inactivated IAV vaccine, and co-vaccination with PigMatrix and the commercial inactivated product.

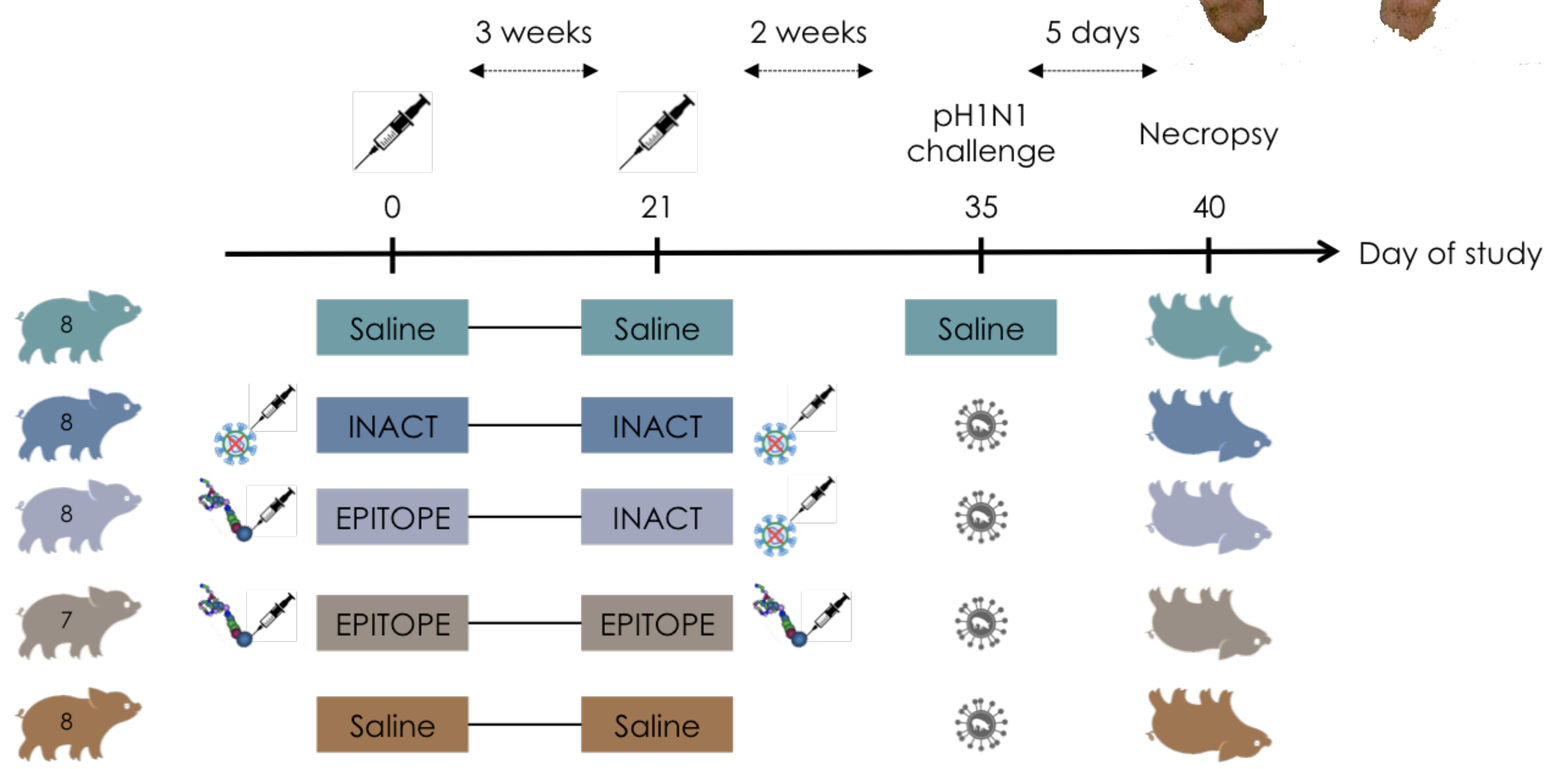
Results

Thirty-nine IAV-free, 3-week-old pigs were randomly assigned to one of five groups (Figure 1). All INACT-INACT-IAV pigs, and by dpc 5 all EPITOPE-INACT-IAV pigs were IAV seropositive at the time of challenge. IFNγ secreting cells, recognizing vaccine epitope-specific peptides and pH1N1 challenge virus were highest in the EPITOPE-INACT-IAV pigs at challenge (Figure 2). Macroscopic lung lesion scores were reduced in all EPITOPE-INACT-IAV pigs while INACT-INACT-IAV pigs exhibited a bimodal distribution of low and high scores akin to naïve challenged animals. No IAV antigen in lung tissues was detected at necropsy in the EPITOPE-INACT-IAV group, which was similar to naïve unchallenged pigs and different from all other challenged groups (Figure 4A & B).

Conclusions

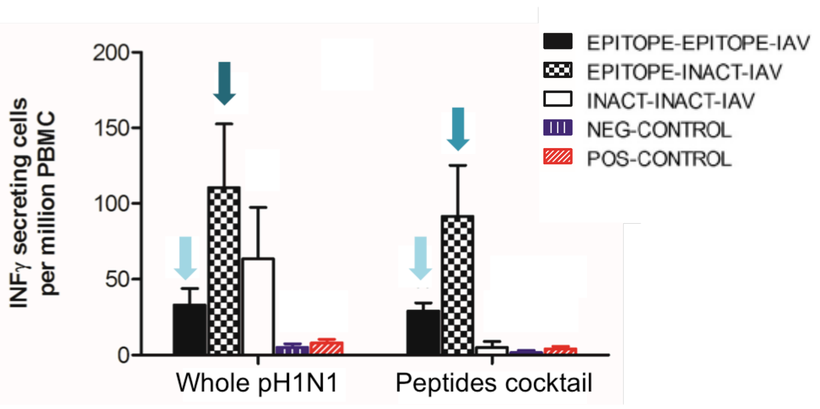
Results suggest that the heterologous prime boost approach using an epitope-driven DNA vaccine followed by an inactivated vaccine was effective against a homosubtypic challenge, and further exploration of this vaccine approach as a practical control measure against heterosubtypic IAV infections is warranted.

Figure 1 | Experimental design and treatment groups.



Thirty-nine IAV-free, 3-week-old pigs were randomly assigned to one of five groups including NEG-CONTROL, INACT-INACT-IAV, EPITOPE-INACT-IAV, EPITOPE-EPITOPE-IAV, and a POS-CONTROL group. The challenge was done at 9 weeks of age and pigs were necropsied at day post challenge (dpc) 5.

Figure 2 | Post-Vaccination CMI Response: IFNγ ELISpot.

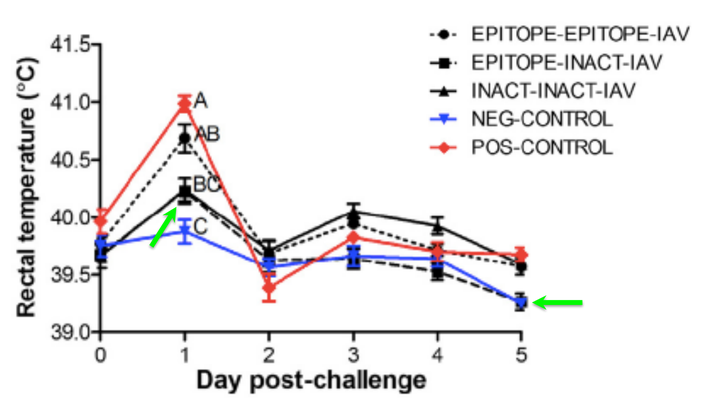


EPITOPE + EPITOPE pigs recall vaccine-matched peptides.

Response to epitope peptides boosted in EPITOPE + INACT pigs.

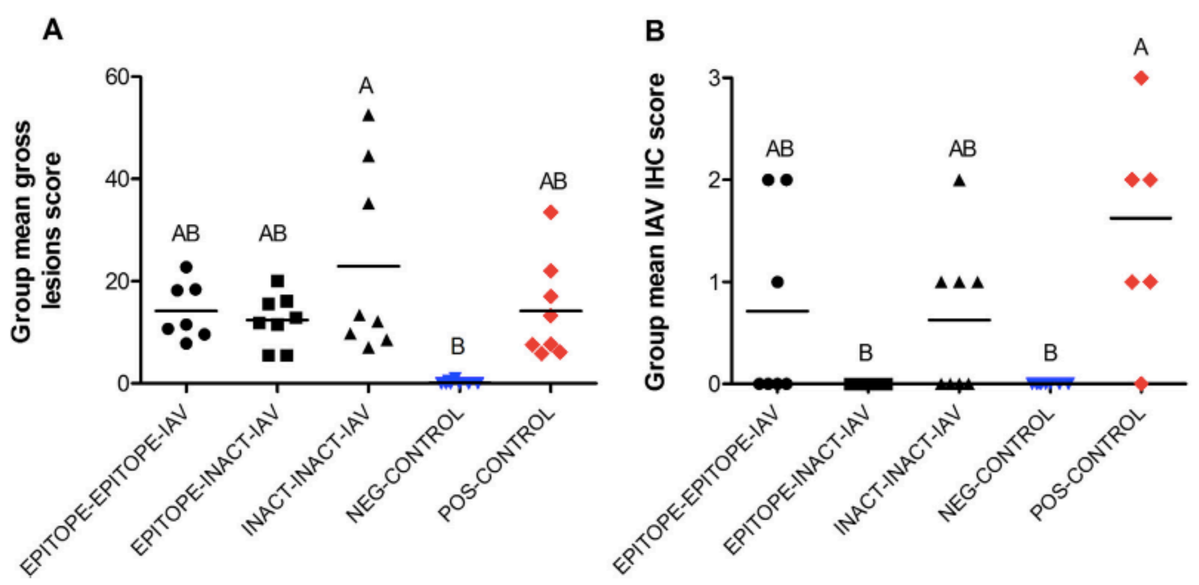
EPITOPE + INACT pigs mount strongest response to the pH1N1 challenge virus.

Figure 3 | Mean rectal temperatures ± SEM in the different treatment groups at certain dpc with pH1N1.



EPITOPE + INACT reduced body temperature at dpc 1 and reduced body temperature at dpc 3, 4 and 5.

Figure 4 | A. Group mean gross lung lesion scores ranging from 0 to 100% of the lung surface affected by consolidation with individual pig scores. B. Group mean IAV antigen in lungs as determined by immunohistochemistry with individual scores for each pig (score range from 0 = negative to 3 = abundant, multifocal IAV antigen present).



The EPITOPE-INACT-IAV group had lower lung lesion scores than the pigs in the POS-CONTROL group. There was also no detectable IAV antigen in lungs as the NEG-CONTROL group of pigs. This may be due to cytotoxic T cell response by CD8+ T cells stimulated by recall responses to the EPITOPE peptides, which are responsible for clearing the viral infection by killing infected cells.

References:

1) Hewitt JS, Karuppannan AK, Tan S, Gauger P, Halbur PG, Gerber PF, De Groot AS, Moise L, Opriessnig T. 2019. A prime-boost concept using a T-cell epitope-driven DNA vaccine followed by a whole virus vaccine effectively protected pigs in the pandemic H1N1 pig challenge model. Vaccine.
2) https://www.npr.org/sections/health-shots/2019/06/11/729314248/to-save-the-science-poster-researchers-want-to-kill-it-and-start-over

Contact information: Dr. Lenny Moise (lmoise@uri.edu)

Get poster handout

SCAN ME