Title: Evaluation of the epitope driven pDNA vaccine PigMatrix EDV in the pig model as a candidate vaccine for universal flu protection – NPB #17-185

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Most commercial influenza A virus (IAV) vaccines provide homologous protection, but fail to prevent heterologous infections. In this study, the efficacy of an intradermal administered pDNA vaccine (EPITOPE) was evaluated and compared to an intramuscular commercial inactivated whole virus vaccine (INACT), and a combined vaccine regimen against virulent IAV challenge. Thirty-nine IAV-free, 3-week-old pigs were randomly assigned to one of five groups including a NEG-CONTROL group (unvaccinated, sham-challenged), an INACT-INACT-IAV group (vaccinated with FluSure XP® at 4 and 7 weeks, pH1N1 challenged), an EPITOPE-INACT-IAV group (vaccinated with PigMatrix EDV at 4 and FluSure XP® at 7 weeks, pH1N1 challenged), an EPITOPE-EPITOPE-IAV group (vaccinated with PigMatrix EDV at 4 and 7 weeks, pH1N1 challenged), and a POS-CONTROL group (unvaccinated, pH1N1 challenged). The challenge and sham-challenge were done at 9 weeks of age, and all pigs were necropsied at day post challenge (dpc) 5. At the time of challenge, all INACT-INACT-IAV pigs, and by dpc 5 all INACT-INACT-IAV and EPITOPE-INACT-IAV pigs, were seropositive for IAV. IFNγ secreting cells, recognizing T cell epitope specific vaccine peptides as well as pH1N1 challenge virus, were increased for the EPITOPE-INACT-IAV over the EPITOPE-EPITOPE-IAV and INACT-INACT-IAV groups at challenge. On dpc 1, EPITOPE-INACT-IAV pigs and INACT-INACT-IAV pigs had significantly lower body temperatures compared to the POS-CONTROL and EPITOPE-EPITOPE-IAV. 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 detectable IAV antigen in lung tissues at dpc 5 was observed in the EPITOPE-INACT-IAV group similar to naïve unchallenged pigs and different from all other challenged groups. These results suggest that the prime boost approach using an epitope driven DNA vaccine with inactivated vaccines merits further exploration as a practical control measure against IAV.