RESEARCH ABSTRACT

SWINE HEALTH

Title: Improvement of Interferon Biotherapeutics for Foot-and-mouth Disease in Swine – NPB #14-014

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Scientific Abstract:

Foot-and-mouth disease virus (FMDV) is one of the most contagious animal viruses with potential devastating economic effect. There are commercial FMD vaccines available; however, it usually takes a week for the vaccines to induce protective immunity. Biotherapeutics using a replication-defective adenovirus inserted with an interferon gene can completely protect pigs from FMDV infection. However, the disadvantages of this biotherapeutics are the requirement of high dose and short-lasting effect. To improve it, we used two strategies: (1) to identify the most potent interferon gene for use in the biotherapeutics, (2) to enhance interferon production and (3) to develop novel biotherapeutics using interferon regulatory factor (IRF) genes. Thirty-seven porcine interferon genes were transiently expressed in cell culture and their anti-FMDV activities were compared using a CPE reduction assay. The highest and the lowest antiviral activities of genes differed more than one thousand times. Adenovirus inserted with the top interferon gene induced an anti-FMDV activity four-fold higher in cell culture than the previous one. To increase interferon production, an adenovirus tripartite sequence and a porcine SOCS1 gene with an EF1a promoter were inserted into the adenovirus. This new recombinant virus induced up to 170-fold higher anti-FMDV activity in cell culture than the previous adenovirus. Among three constitutively active IRF genes tested, IRF2 induced the highest anti-FMDV activity. The recombinant adenovirus inserted with IRF2 also induced a higher anti-FMDV activity than the one previously tested. These two new and the previous tested recombinant adenoviruses were compared in pigs. The results of anti-FMDV activity in the sera of treated pigs indicated that the adenovirus inserted with the best IFN and SOCS1 gene is the best biotherapeutics with the improvement of greater than 20 fold in potency. This new recombinant adenovirus not only enhanced the magnitude of antiviral activity but also prolonged the duration of the activity.