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Report to Pennsylvania Soybean Promotion Board

Title: Influenza D Virus in Pennsylvania Cattle
Final report: April 2, 2020
Principal Investigator: Dr Suresh Kuchipudi

Objectives:

The aim of this project was to isolate and characterize IDVs from PA cattle to evaluate the prevalence and genetic diversity of these viruses.

Progress report:

This project has led to identification of 35 influenza D virus (IDV) specimens from Pennsylvania and multiple other states. In our sampling, we found that most IDV was detected in nasal swabs. IDV was also detected in some lung tissue specimens but not in deep nasal swabs or trachea tissue. This finding will guide future IDV sampling/surveillance efforts in cattle and may be extended to other species.

When initiating an infection, IDVs bind to cells through interaction cell surface receptors with a viral surface protein called hemagglutinin-esterase fusion (HEF) protein. Differences in the amino acid sequences of HEF from various IDVs are used to categorize IDV isolates into "lineages." When we analyzed the amino acid sequences of the HEF proteins from PA IDV, we discovered that the receptor binding site of HEF differs significantly between IDV of different lineages. We analyzed the predicted structure of the HEF protein that these differences would provide and found that these changes in HEF between IDV lineages alter the conformation of specific portion of the HEF protein that attaches to the cell surface. We suspect that these variations in the binding site may affect the ability of IDV to bind specific cells in the bovine respiratory tract, and our initial studies of this in cell culture and tissue binding assays indicate it may in fact play a role. Changes in IDV's ability to bind to upper and lower respiratory tract cells could have major implications to virus transmission and development of respiratory disease, respectively. We hope to explore this in future studies.

Phylogenetic analysis of whole-genome sequences of our IDV isolates indicated that recent isolates from the Northeast (PA and surrounding states) are closely related to a swine isolate from 2017 in Kentucky. The Kentucky strain also has a modified HEF that is similar to our IDVs. Interestingly, a recent report in the scientific literature found their isolates also relate most directly to the Kentucky isolate. This could mean that the genetic/protein structure being used by these recent isolates is an advantage for the virus, which is causing the virus to consistently mutate to achieve this new state. The final analysis of the sequences and isolates derived from this project is examining these possibilities. Manuscripts reporting the genome sequences and molecular and structural analysis of the IDV HEF proteins are being completed at this time in order to report the results from this project.

The results of this project have provided novel insights into the viruses threatening PA cattle. Further monitoring of IDV in PA cattle is warranted to track the mutations that may increase transmission or virulence.

Sincerely,

Suresh Kuchipudi