



CNS DISEASES IN SWINE TECHNICAL PAPER

Cambridge Technologies

KEY POINTS:

- 1** NEUROLOGICAL DISEASES LIKE SAPELOVIRUS AND ATYPICAL PORCINE PESTIVIRUS CAN BE DIFFICULT TO IDENTIFY AND ISOLATE.
- 2** NEXT GENERATION SEQUENCING TECHNIQUES SUCH AS METAGENOMICS HAVE BEEN VITAL IN DISCOVERING PREVIOUSLY UNKNOWN VIRUSES.
- 3** AN AUTOGENOUS VACCINE MAY BE THE ONLY OPTION AVAILABLE FOR VACCINATION AGAINST CNS DISEASE SINCE THERE ARE CURRENTLY NO COMMERCIAL VACCINES.
- 4** USING A CUSTOM VACCINE MANUFACTURER WITH EXPERTISE IN NEXT GENERATION DIAGNOSTICS IS AN IMPORTANT CONSIDERATION IN DEVELOPING A SOLUTION TO CNS DISEASE.

INTRODUCTION

Viral-based neurological diseases continue to present new challenges for pork producers and veterinarians. Pathogens such as Teschovirus, Sapelovirus, Atypical Porcine Pestivirus, Astrovirus, and PRRSV can be difficult to identify and isolate, and often there is not a commercial vaccine available.

Cambridge Technologies uses Precision Vaccinology™ to assist producers and veterinarians with these challenges. By combining Next Generation Sequencing in our diagnostic laboratory with state of the art manufacturing, Cambridge can identify and characterize these emerging pathogens and if needed, develop a custom vaccine for the herd veterinarian to implement a vaccination program to meet these threats.

TESCHOVIRUS

A non-enveloped RNA virus, Porcine Teschovirus (PTV) has 13 known serotypes. Strains of PTV are associated with diseases such as Talfan disease, teschovirus encephalomyelitis, SMEDI syndrome, diarrhea, and respiratory and cardiovascular issues⁸.

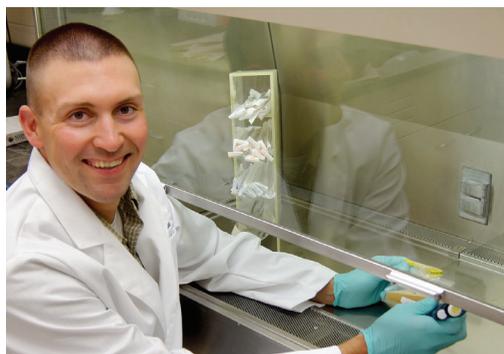
Diagnosis of PTV is relatively straightforward. Virus isolation and neutralization have long been the standard for identification⁴. However, forward-thinking laboratories such as Cambridge Technologies have recently begun to identify PTV and classify specific strains using metagenomic sequencing of brain and spinal cord samples.

At one time, there were commercially-available vaccines to counter PTV-in-

duced disease. However, as those diseases have decreased in incidence, the vaccines have been removed from the market⁴. Today, a custom vaccine would be the only option to combat this re-emerging threat.

SAPELOVIRUS

Sapelo virus (PSV) was previously known as Porcine Enterovirus A⁹. Similar to PTV, PSV is a non-enveloped single-strand RNA virus that can cause polioencephalomyelitis with ataxia and eventual limb paralysis⁵. SMEDI syndrome can also come from a PSV infection⁹. Incidence of the virus increased dramatically in 2017, leading the Swine Health Information Center to raise the virus on their Swine Disease Matrix from an average risk score of 1.0 in May



2017 to 4.0 in December⁷.

Dr. Ben Hause, now Vice President of Research, Development, and Diagnostics at Cambridge Technologies, was on the team that first detected sapelovirus associated with polioencephalomyelitis, using next-generation sequencing². Virus neutralization and IFA can be used for identification, while RT-PCR can distinguish between PSV and other viruses⁹.

Commercial manufacturers have yet to develop a vaccine for PSV, and little is known about cross-protection between strains⁹. Cambridge Technologies uses Precision Vaccinology™ to identify and characterize the strain of PSV found



in the herd and then produce a custom vaccine to use against it. Custom vaccines made under the direction of the herd veterinarian, are the only option for pork producers looking to vaccinate against this challenge.

ATYPICAL PORCINE PESTIVIRUS

An enveloped RNA virus, Atypical Porcine Pestivirus (APPV) is a novel isolate containing some characteristics of more known pestiviruses such as the one causing classical swine fever. However, it is highly divergent and has not officially been accepted as a pestivirus specie¹⁰. The virus can contribute to tremors in young pigs under 14 weeks of age¹⁰.

APPV was first identified in 2015 by a team led by Dr. Hause using metagenomic sequencing³. To date, it has only been found in the United States. Due in part to the emerging nature of the virus, diagnostic tests are not commonly commercially available¹⁰. Next-generation sequencing and qRT-PCR are currently

used for diagnosis and identification. Dr. Hause's team also developed an ELISA for detection of APPV³.

No commercial vaccine is available for APPV. Cambridge Technologies is at the forefront of research on this new threat, and can work with veterinarians to develop an autogenous solution.

ASTROVIRUS

Porcine astrovirus (PAstV) is a non-enveloped RNA virus with five known strains. While astrovirus infections are commonly associated with gastrointestinal diseases, cases of poliomyelitis have recently been reported¹¹. Neurological diseases associated with PAstV have a 75-100 percent mortality rate¹.

Virus isolation of PAstV has proven to be quite difficult¹¹. However, it can be identified and characterized using next-generation sequencing, such as was done by Dr. Hause and cohorts¹.

Being a relatively new emerging disease, no commercial vaccine has been developed for porcine astrovirus. The strains that have been identified to date have all shown great genetic diversity⁶, thus cross-protection from a single-strain vaccine would be unlikely. An autogenous vaccine, possibly including multiple strains, could be developed by innovative manufacturers such as Cambridge Technologies.

PRRSV

Since first being discovered in the 1980s, Porcine Respiratory and Respiratory Syndrome Virus (PRRSV) has remained one of the most problematic diseases threatening pigs worldwide. In 2006, a highly pathogenic virus emerged in China¹². These strains cause disease similar to the traditional PRRSV, as well as neurological signs and erythematous blanching rash. These new variants, which have spread throughout southeast Asia, can cause clinical disease and death in all ages of swine including adult pigs and pregnant sows¹³.



PRRS is generally detected via PCR and viral isolation. New RT-PCR assays developed in China are capable of differentiation between traditional PRRSV and the newer, highly-pathogenic strains¹². Modern diagnostic facilities such as Cambridge Technologies are utilizing metagenomic sequencing for both detection of the virus and strain identification/selection.

There are several different commercial vaccines available for PRRSV, including both inactivated and modified live formulations. However, these products have traditionally been seen as incon-

sistent in offering protection¹⁴. Autogenous products offer options not available from commercial manufacturers. A key factor in building an inactivated PRRSV vaccine is the ability to maintain the integrity of the viral protein structure, which generates immune response. Cambridge Technologies uses Precision Vaccinology™ which includes a manufacturing process that is designed to protect this structure, keeping it as close as possible to the originally isolated virus.

DISCUSSION

The viruses being discussed in this paper are all very different, but two consistencies stand out: the need for

cutting-edge diagnostic technology and the lack of commercial vaccine options. Cambridge Technologies has set the standard in using next-generation sequencing capabilities to identify emerging diseases. Dr. Ben Hause, who was a member of the teams to first identify several of these viruses, leads our diagnostic and research teams and is available to veterinarians and producers as a resource as they struggle with these developing threats. Precision Vaccinology™ at Cambridge Technologies uses next generation diagnostics enabling us to identify and characterize individual strains, answer questions about cross-immunity and select strains for manufacturing state of the art custom vaccines.

SOURCES

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