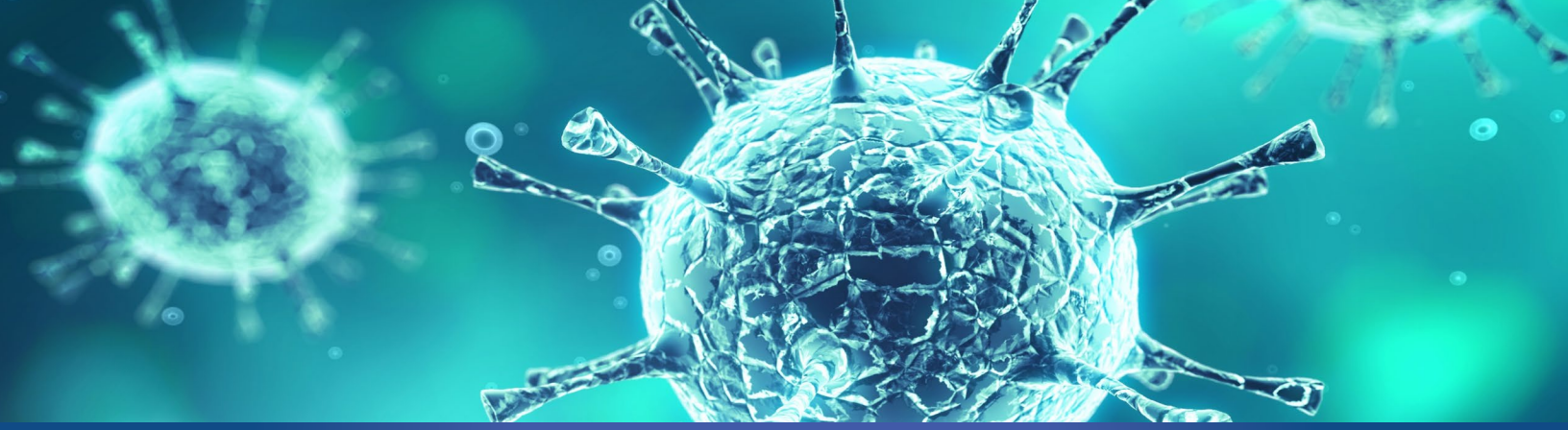
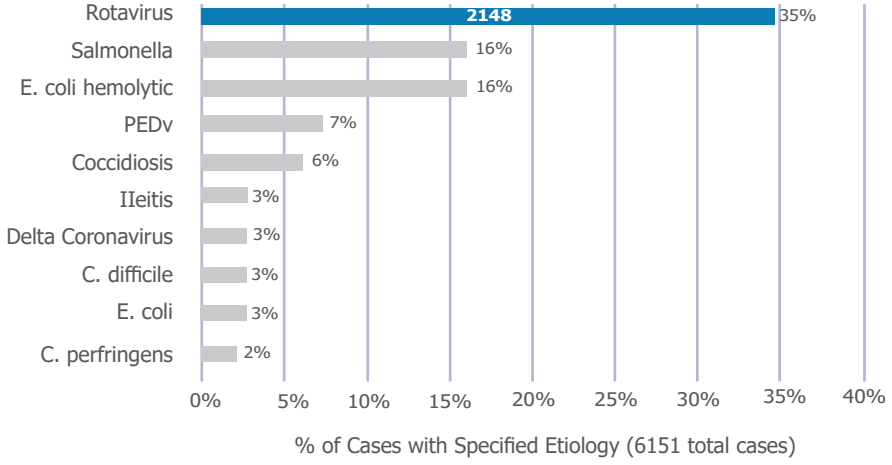


ROTAVIRUS PRODUCT SUMMARY

Porcine rotavirus is an important world-wide cause of diarrhea in piglets and is responsible for significant economic impact in today's swine herd. Of 6151 digestive disease diagnostic cases submitted to the Iowa State University Veterinary Diagnostic Laboratory between May 1, 2020 and April 30, 2021 with a specific cause identified, rotavirus was the most prevalent causative agent found. (Graphic 1.)

Graphic 1:

ISU-VDL Digestive Disease Dignostics
Top 10 Etiological Agents (Jan 2020 -Apr 2021)



Rotaviruses are antigenically diverse, with nine serogroups (A-D, F-J) (Graphic 2). Of these groups, Rotavirus serogroup A (RVA) has traditionally been the most common in swine. However, serogroups B and C (RVB and RVC) have been gaining in importance, with RVC in particular being implicated in cases of severe neonatal diarrhea.

Graphic 2:

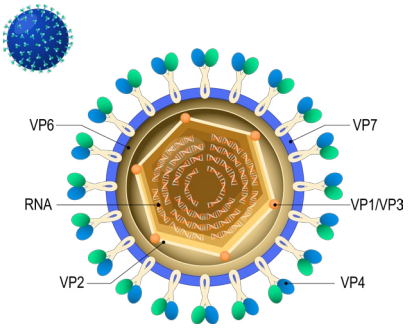
Rotavirus Strain Classification

9 Serogroups A-D, F-J	♦ Serological classification based primarily on epitopes in VP6 ♦ Rotavirus A, B and C are significant pathogens in swine & cattle. ♦ Reassortment does not occur between Serogroups.
Genotype 32 G types, 47 P types	♦ Nucleic acid sequence classification based on similarity of genes encoding for epitopes in VP7 (glycoprotein, G types) and VP4 (protease, P types)
Strain Diverse G,P combinations	♦ Reassortment occurs separately for VP7(G) and VP4(P) proteins. ♦ VP4 (spike protein) is more highly diverse than VP7. ♦ Analysis of VP4 and VP7 diversity is key to vaccine development.

Developing effective vaccines to control rotavirus has traditionally been extremely difficult, due to a number of factors. Both RVB and RVC are nearly impossible to grow in tissue culture, meaning that traditional vaccines, either commercial or autogenous, have not been possible. The diverse genome of rotavirus, due to reassortment and recombination, means that traditional RVA vaccines containing only one or two virus isolates are not likely to provide coverage against the many diverse viruses found in the field.

Rotavirus has a complex structure (Graphic 3) that can change due to reassortment. These changes matter most when they occur at epitopes that are important antigenically such as VP4 and VP7 on the outside of the virus structure. These epitopes can be very diverse and understanding this diversity is necessary for vaccine development. As you move inwardly the more internal structures such as VP1, VP2, VP3, VP6 and RNA are more conserved and less involved in the immune response to the virus.

Graphic 3:



Using bioinformatics and cutting-edge technology, Medgene has developed a unique methodology to understand both sequence homology and protein structure of the Rotavirus to overcome these vaccine obstacles. Medgene works with reference laboratories to determine genetic sequences that will produce specific proteins leading to a targeted immune response. These genes of interest (GOI) are then inserted into our baculovirus vector. This construct of GOI and vector is the basis for producing the

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SWINE ROTAVIRUS

antigenic proteins for prescription platform vaccines tailored to swine herds and the Rotavirus strains affecting them. Continued work, conducted in collaboration with respected university researchers, has also shown the ability of our platform vaccines to develop immune responses to RVC strains, something that has not been previously possible due to the inability of these important pathogens to be cultured in laboratory settings.

Medgene's research into structural variability has determined that there are very specific regions, or structural barcodes, in the genes of interest that are critical in developing cross-reactive immune responses. As can be seen in the table (Graphic 4), the sequence similarity between construct 1 and Rotaviruses 3, 5 and 6 is less than 85%, however the immune response was positive (greater than 1:100 is considered positive in this assay). This indicates that although the sequence similarity was lower than expected to stimulate a cross reactive immune response, the structural similarity was high enough to generate a positive response. Understanding not only the sequence homology (% similarity described in the table) of the virus to the construct but also the protein structure (structural barcode) of the virus compared to the construct is important in vaccine development. Medgene scientists use this unique analysis of structural proteins to develop the best vaccine possible for a herd.

Graphic 4:

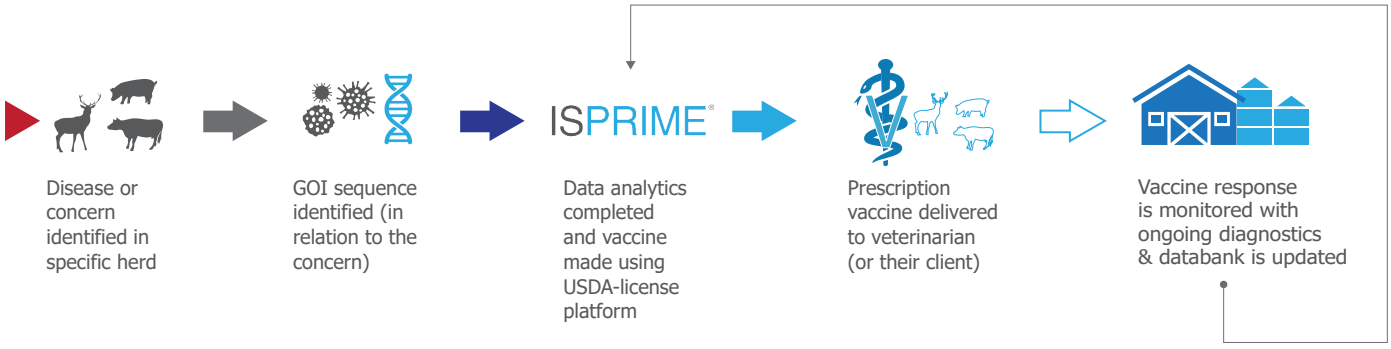
Sequence Homology Alone is not Predictive of Protection

Camparison of Baculovirus vaccine constructs to six Rotavirus A Isolates

	RVA 1	RVA 2	RVA 3	RVA 4	RVA 5	RVA 6
% Homology to Vaccine Construct 1	82.3%	82.0%	**77.9%**	82.8%	**82.3%**	**77.8%**
% Homology to Vaccine Construct 2	78.8%	78.5%	95.4%	81.9%	N/A	N/A
Vaccine Construct 1 + 2 Antibody Titer	Neg	Neg	**1:525**	Neg	**1:390**	**1:431**
Vaccine Construct 1 Antibody Titer	Neg	Neg	**1:593**	Neg	**1:403**	**1:403**
Vaccine Construct 2 Antibody Titer	Neg	Neg	1:80	Neg	Neg	Neg
Sham Antibody Titer	Neg	Neg	1:48	Neg	Neg	Neg

Medgene's ISPRIME® program provides a complete service to veterinarians, starting with identifying a specific disease to developing a targeted vaccine to herd monitoring.

ISPRIME® Process



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