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discoveries

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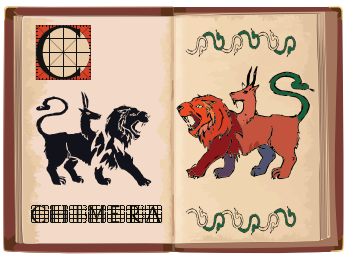

Chimera technology offers better path to protection for PCV2

Readers of Greek mythology know that a chimera is a fire-breathing, two-headed monster with a lion's head and claws, a goat's body and a serpent's tail. The same word is sometimes used to describe any creature composed of parts from various animals.

So, why is this mythical creature also used to describe some vaccines for animal and human medicine? And what does it have to do with Zoetis' newest vaccine, Fostera® Gold PCV MH?

The term chimera — or more specifically, "chimeric vaccines" — shouldn't be taken literally. It's strictly a colorful term that, like many medical words, has deep roots in the Greek language. Any association between the fabled chimera and modern-day vaccines ends there.

Dynamic duo

In the world of immunology, scientists join genetic material from different sources to maximize the immune response of an antigen. For example, they'll take a nonpathogenic virus and use it as the "backbone" for a vaccine. Then they'll take an immunogenic gene from another related virus and graft it to that backbone to, in essence, create a disease-fighting dynamic duo.

While the result of this process has drawn playful comparisons to the mythological chimera, in reality it combines strengths of two genetic forces that provide immunologists with the best traits of each component. In fact, chimeric vaccines have been described as "viruses with the replicative machinery of one virus and the protective antigens of another."[1]

"The backbone helps the vaccine get to the intended part of the immune system, while the grafted gene initiates the necessary immune response," said Lucina Galina, DVM, PhD, director of swine technical services, Zoetis.

'Natural form'

When PCV2 first became a problem in US swine herds, scientists looked at taking the immunogenic capsid gene from PCV2 — often referred to as ORF2 — and cloning it into the backbone of nonpathogenic PCV type 1 to produce a live chimeric vaccine for PCV2. They also knew that a live chimeric vaccine like this would not revert to virulence[2] because

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LUCINA GALINA, DVM, PHD

the backbone is an avirulent virus. In fact, the ability to design viruses with this safety feature is the main reason why the chimeric approach is increasingly being used in human and animal vaccinology.

In time, inactivated and subunit PCV2 vaccines provided a relatively simpler, faster path to vaccine development. Still, researchers continued to be intrigued by the chimeric-vaccine concept, even when formulating inactivated PCV2 vaccines.

Because they thought it would produce a better path to protection than the commonly used subunit technology, Zoetis scientists chose the chimeric approach when developing its line of PCV2 vaccines. The company's latest PCV2 vaccine — Fostera Gold PCV MH — contains two chimeric PCV1-PCV2 viruses to provide broader coverage against the PCV2 viruses currently circulating.

"Although the benefit of non-reversion no longer applies to a killed vaccine, we still felt it made more sense to present an antigen in the natural form of a whole virus," Galina reasoned. "It's a more natural way for the immune system to see an antigen. Both might present the same protein, but only the whole virus has it in context."

Cell proteins

For most vaccines, manufacturers grow viruses in cell culture. Components of the growth medium, including proteins from disintegrated cells, are typically present in the final product.

With PCV vaccine production, the chimeric PCV viruses are grown in a pig-cell line. As a result, the pig's immune system remains neutral, interacting with cell proteins as an extension of itself and doesn't generate an unnecessary immune response. Furthermore, the virus particles are brought together by the protein-building machinery of a pig cell, which mimics the process in a natural infection.

Alternatively, some PCV2 vaccine manufacturers use baculovirus-derived capsid protein, typically described as "killed baculovirus vector" on product labels. The starting point for these products is also a genetically modified virus — in this case, an insect baculovirus containing the PCV2 ORF2 gene. With this approach, the PCV2 capsid protein produced by the modified virus becomes the antigen in the vaccine instead of the complete virus particle.

"The insect virus is then grown in an insect-cell line, and its proteins are assembled by insect-cell ribosomes, which may introduce subtle differences in the final structure compared to mammalian-cell assembly," Galina explained.

What counts

She acknowledged that many of the arguments about the preferred form for a PCV2 antigen are theoretical. What counts in the end is the safety and efficacy of a vaccine observed in the field.

"Whether it's the vaccine's chimeric virus antigens or the MetaStim® adjuvant, the safety and efficacy of Fostera Gold PCV MH have been convincingly demonstrated against PCV2a, 2b and 2d — the leading genotypes affecting US herds,"[3,4] Galina said.

[1] Fenner and White's Medical Virology, 5. 2016. Chapter 11. Vaccines and Vaccination. Pages 155-167. Elsevier.

[2] Chimeric DNA Vaccine. Avens Publishing Group. Accessed February 13, 2018.

[3] Iowa State University Veterinary Diagnostic Laboratory. 2017 PCV2 genotype isolation.

[4] Data on file, Study Report No. 16PRG BIO-01-01, Zoetis LLC.

For more information on chimeric vaccines and the benefits of Fostera Gold PCV MH, contact lucina.galina@zoetis.com or your Zoetis representative.

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