Research Looks at Genetic Factors in Vaccine Response

by ***Heather Smith Thomas***

Cattle producers often assume that vaccinated animals all develop a good immune response. In reality some individuals build strong immunity, and a few have no response at all — with others falling somewhere in between.

Many factors enter into vaccination response. Animals that are sick, nutritionally stressed or suffering from other types of stress (such as weaning and/or bad weather) may build less-than-optimum immunity. Young calves that still have maternal antibodies (passive transfer of immunity from colostrum) may not respond to certain types of vaccine.

There is yet another factor that plays a role in whether or not the animal can mount response to vaccination. Genetics may determine a certain animal's capability to respond. Research at South Dakota State University (SDSU) is currently looking into the genetics of cattle immunity.

This research is led by Michael Gonda, animal and range science assistant professor.

"We are finding that some cattle respond better to vaccine than others," Gonda says. "Vaccine response is a polygenic trait, which means it is controlled by a number of different genes. We now have evidence that this is a heritable trait and are trying to find out how or what genes are involved in determining the animal's individual vaccine response — whether it's a high response, average or a low to non-response.

"There's a segment of every vaccinated population that does not respond at all to the vaccine. These animals lack the capability to respond, mainly because they don't have the genes to do so. The purpose of our project is to find those genes," he explains.

The project

The researchers are collecting a large number of individual samples from calves (individual phenotypes) and documenting their responses to a vaccination. "We have been sampling calves for two years here, from research herds at SDSU at locations in eastern South Dakota, as well as several outlying research stations in western South Dakota," Gonda says.

The researchers are vaccinating all the calves with the same vaccine. They have been using Pyramid 5, which is now being sold by Boehringer Ingelheim Vetmedica Inc. (BIVI). For the past year and a half, BIVI has been providing vaccine free of charge for the project. Pyramid 5 is a combination BVD (bovine viral diarrhea) 1 & 2-IBR (infectious bovine rhinotracheitis) -PI_3 (parainfluenza-3 virus) -BRSV (bovine respiratory syncytial virus).

"We've been looking at the calves' response to the BVD portion of the vaccine. Vaccine response is measured by the antibodies produced, utilizing an ELISA (enzyme-linked immunosorbent assay) test, checking the calves 20 to 30 days after vaccination," Gonda explains. This check gives researchers a good indication of how well the individual calf responded to the vaccine.

For this study, the researchers only used calves that had never been vaccinated against this particular pathogen. Using unvaccinated calves gives the researchers a better picture of the calves' true response, because they do not already have antibodies from vaccine.

"There are some complications," Gonda explains. "Often, when these calves are being vaccinated, they still have maternal antibodies they gained from colostrum. This can be an issue in the younger calves and is one of the challenges we have to work through with this study. So we get a blood sample at the time of vaccination to determine what their maternal antibody concentration was at that time. This can be used as our baseline."

The calves being tested are not yet weaned, varying in age from 4 to 6 months. This is the age when producers want to protect them against calfhood illness or help prepare them for weaning stress by starting to build immunities against respiratory diseases; so it's a good time to know if they will make a good response to vaccination.

The results

"Right now we are still in the process of collecting samples, banking them and running antibody assays — determining each individual's vaccine response. We have done some preliminary analyses and found that for each of the calves, the sire is associated with that calf's response to BVD vaccine." Thus there is strong evidence for a genetic component to vaccine response.

The herds being tested have a variety of genetics. Some are purebred Angus, and some are predominantly Angus with other breeds and mixes represented. One herd is crossbred. It will be interesting to see if there's stronger immune response in crossbred calves due to heterosis.

"This is one area we want to investigate in the future. We have not yet looked at heterosis in our beef calf samples, but we do have results from earlier work with dairy herds. We have already compared vaccine response between purebred Holsteins, purebred Jerseys and crossbreds of those two breeds — in collaboration with faculty at North Carolina State University, where we've been working closely with Dr. Christian Maltecca."

In the SDSU project with beef calves, the DNA from these calves has been banked. "One of the things we want to do is run all the DNA samples on the 50K SNP (single nucleotide polymorphism) chip and see if any of those SNP on that SNP chip are associated with vaccine response," Gonda explains. "This SNP chip allows scientists to capture a large percentage of genetic variation in the bovine genome. By using this SNP chip, we can identify

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regions of the bovine genome that are associated with vaccine response. Once we identify these regions, we can look for genes in these genomic regions and test to see if these genes are associated with vaccine response. This approach allows us to look at most of the bovine genome at once, as opposed to just one or two genes at a time."

The future

At this point, samples have been collected from more than 800 calves, but Gonda hopes to eventually have about 1,000 for the genetic studies.

"We are close to getting a large enough sample size to work with," he says. "Right now we are searching for enough funding to continue our research. We're still able to do some work, thanks to funding from our Agricultural Experiment Station here in South Dakota, but we won't be able to run the 50K SNP chip without additional funding. To do that, we would probably have to go to USDA (U.S. Department of Agriculture) or organizations and commodity groups to see if they would fully or partially fund our experiments.

"If we gain funding, we'd probably be able to identify genomic regions that affect vaccine response, at least preliminarily, within the next two years. When doing anything with genetic markers, you need to confirm the initial association you find — confirming it in an independent population. Research can often get a lot of associations that may look like they are true, the first time, but the second time around you realize they may not be that accurate. You don't want to be marketing a DNA test or any markers that are not truly associated with vaccine response and healthier calves. Research has to be slow in order to be careful," Gonda adds.

Today genetics companies sell DNA tests for specific uses. "Most of these tests work very well, but others are less certain," Gonda explains. "I hope that people don't get frustrated and give up on DNA testing because of a few glitches. The tests for genetic defects are very accurate, but some of the tests the beef industry is starting to utilize, such as economically important traits like marbling, are a different story. Some of those tests work well and some don't."

At SDSU another study regarding vaccine response is being done with Ben Holland, feedlot specialist. This study is looking at what the correlation is between the individual primary vaccine response (which is what researchers are measuring in young calves) and what researchers are seeing after the calves are weaned and placed in the feedlot.

In the study, calves are exposed to a PI animal (persistently infected with BVD) and then tested to see the correlation between morbidity and mortality (when exposed to that PI animal) and their primary vaccine response. This test will add some challenges — exposure to the pathogen — to the study.

"We can measure the primary vaccine response — the immune response — but with this additional study, we can determine whether it really protects them when they get to the feedlot. This is one of the things we want to find out," Gonda says.

The results of this genetic research may be helpful to cattle producers in the future as they seek to select animals that will be more likely to stay healthy. "There are two major implications that could come from this research. The first is that it could lead to development of a DNA test for animals that respond more strongly to vaccines, and this would enable us to select healthier animals," Gonda says.

"The second thing it will be useful for is helping immunologists and veterinarians design and develop better vaccines. If we can better understand how genetics plays a role in vaccine response, hopefully this will help researchers develop vaccines that are more effective for the entire population of animals.

"This research may also benefit other species and add to our understanding of vaccine response in humans as well. A genetic component for response to BVD vaccine would probably also determine vaccination response to other vaccines or disease challenges," Gonda explains. **HW**

If this research is successful, a producer could select for calves who are more likely to respond well to vaccines.