IOWA Pork Producer Headlines

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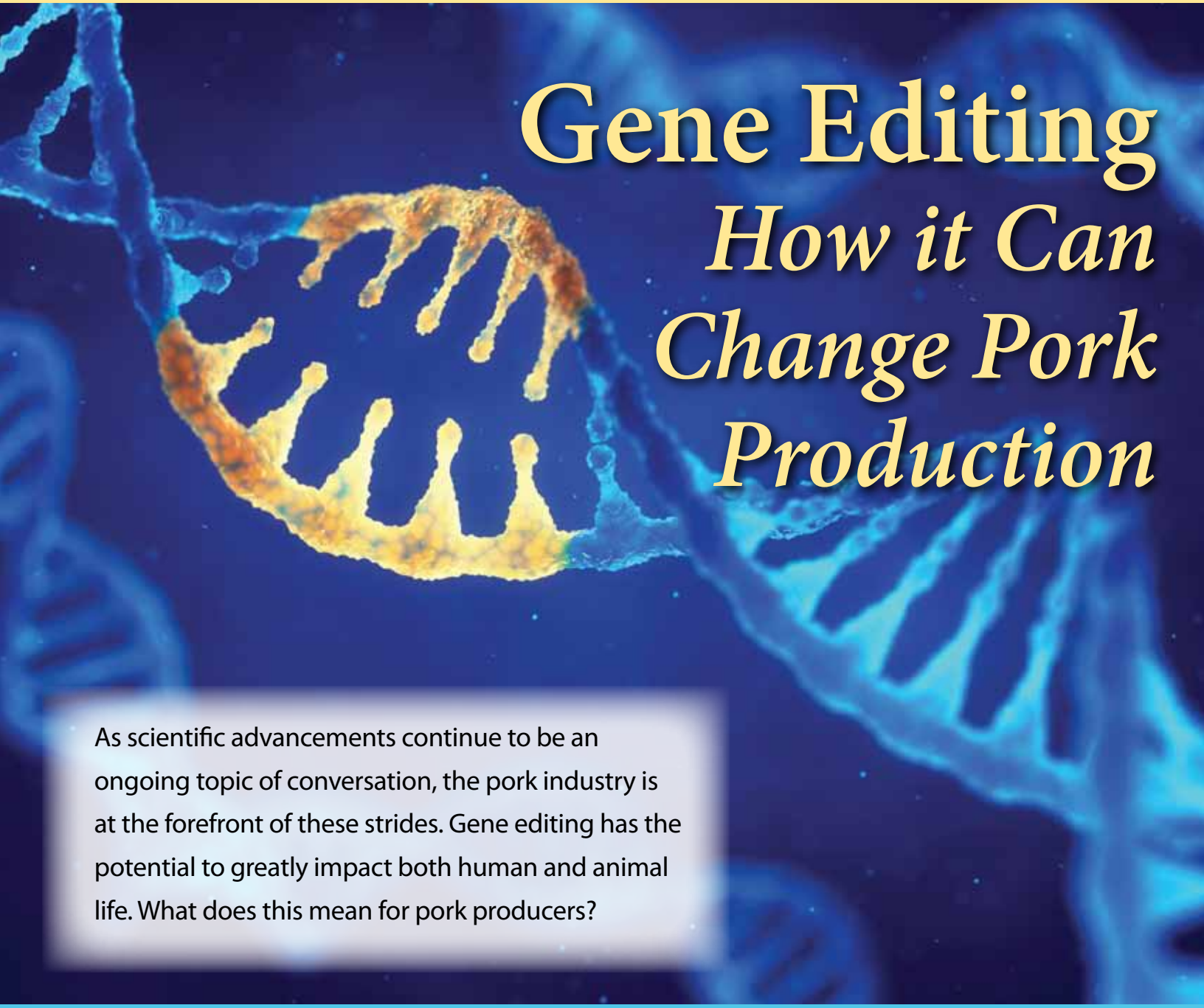

Gene Editing
How it Can Change Pork Production

As scientific advancements continue to be an ongoing topic of conversation, the pork industry is at the forefront of these strides. Gene editing has the potential to greatly impact both human and animal life. What does this mean for pork producers?

In this issue:

- What is Gene Editing?
- CRISPR
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Over the past two decades, scientists around the world have been working to develop a technology that has the potential to solve a wide range of challenges facing our society. This technology, called gene editing, has the power to significantly change the way food is produced through improved animal health, welfare and productivity.

What is Gene Editing?

Gene editing is a technology that allows for precise changes to be made to the deoxyribonucleic acid (DNA) of a cell. It involves adding, removing or replacing DNA bases at a specific location to change the characteristics of a cell or organism.

Gene editing is made up of two parts:

1) a nucleotide* that is capable of cutting DNA
2) a DNA-targeting sequence that is designed to guide the nucleotide to a specific sequence of DNA

After cutting the DNA at a specific sequence, the cell naturally repairs the cut and this is where scientists come in. After cutting the DNA, scientists can hijack the repair process to make desired changes to the DNA at that specific location in the genome.

Gene Editing Versus Other Methods

It is important to know the difference between gene editing and other methods like conventional breeding or transgene insertion (a form of genetic modification). Unlike transgene insertion, no DNA from other species is ever introduced into the DNA of a gene-edited organism. The genome is only changed by adding, cutting or specifically replacing the DNA that is already there.

For example, if a breeder wanted to breed a white Duroc pig instead of red, they could achieve this by cross-breeding with a white breed such as a Chester White. However, other characteristics such as meat quality would also be affected.

Gene editing, on the other hand, could be used to "switch out" the gene in Duroc that codes for red hair with the gene that codes for white hair in Chester White. In this case, all other desirable Duroc traits remain the same. This hypothetical example is used to highlight the fact that gene editing can be used in a variety of ways.

*Nucleotide: a compound consisting of a nucleoside linked to a phosphate group. Nucleotides form the basic structural unit of nucleic acids such as DNA and RNA

Diving Deeper into DNA

Deoxyribonucleic acid, more commonly known as DNA, is the most famous biological molecule on earth. This is because DNA holds a very important function to all forms of life.

DNA is the main carrier of genetic information and can be found in virtually every cell in an animal's body. DNA contains each animal's unique genetic code that makes them different from one another. Differences in genetic code explain why some animals grow more rapidly than others, are less susceptible to certain diseases and behave differently.

This two-stranded molecule has a shape referred to as a double helix and each length of DNA codes for a specific protein called a gene. Changing the DNA of an animal changes their genetic code, therefore changing the characteristics of that animal.

A Comparison of Crop and Livestock Improvement Methods

	Precision	Time to Achieve	Changes from Original Parental Genome	Requires Genetic Transformation	Requires Genetic and Molecular Understanding of the Trait
Genome Editing	High	Months	Targeted edit(s); often no other changes, though edits at locations with sequence similarity to the target(s) may occur	Sometimes	Yes
Conventional Breeding (Crosses)	High for the trait determinant (governed by selection; typically introgresses at the same genomic location as in the donor); other donor DNA that introgresses is determined at random	Years	Introgressed gene and closely linked sequences from donor parent; after backcrossing, ~5% other donor DNA distributed at random through the genome	No	No
Random Mutagenesis	None	Months; with extensive backcrossing, years	Many and random; with extensive backcrossing, ~95% identical to parent	Sometimes	No
Conventional Genetic Engineering (Transgene Insertion)	None	Months to a few years	Presence of transgene; interruption of native DNA sequence with transgene	Yes	Yes

Council for Agricultural Science and Technology (CAST). 2018. Genome Editing in Agriculture: Methods, Applications, and Governance—A Paper in the series on The Need for Agricultural Innovation to Sustainably Feed the World by 2050. Issue Paper 60. CAST, Ames, Iowa.

CRISPR

There are multiple targeting sequences that can be used for genome editing purposes, but perhaps the most popular and widely known technique is a system called CRISPR, which stands for Clustered Regularly Interspaced Short Palindromic Repeats. CRISPR is a naturally occurring gene-editing system in bacteria that scientists have discovered and are able to utilize in making desired changes to the DNA of humans, plants and animals.

During the CRISPR process, an RNA-guided (RNA is ribonucleic acid) enzyme called Cas9 searches for the desired DNA sequence in the genome and, when it finds a match, cuts the DNA at that spot. Once the DNA is cut, researchers use the cell's own DNA repair machinery to make changes to the DNA by replacing an existing segment with a customized DNA sequence or deleting a portion of the DNA.

CRISPR is different from other forms of gene editing due to its simplicity and efficiency. CRISPR/Cas9 is smaller and easier to use than other methods and, most importantly, far more precise. One of CRISPR's greatest advantages is that it can be used to introduce, or remove, a number of different genes at one time.

Benny Mote, Assistant Professor and Swine Extension Specialist at the University of Nebraska-Lincoln, explains CRISPR as being a very in-depth, precise process. "While gene editing using CRISPR/Cas9 has made tremendous technological advances over previous revising procedures, the gene editing process requires keen knowledge of not only the function of the gene edit being studied, but also requires a comprehensive understanding of how a revision in as little as one base will produce a different amino acid and thus affect protein shape and function," says Mote.

Gene editing is a technology that has spurred a growing interest in agriculture, specifically the swine industry, due to its ability to make rapid improvements in several genes that affect swine health, welfare and production efficiencies. For years, agriculturalists have been using selective breeding techniques to make genetic improvements to plants and animals, which can take years to accomplish. With gene editing, these improvements can be done more quickly and with greater precision.

Disease Resistance

The main opportunity gene editing presents for the swine industry is disease resistance. As many pork producers know, one of the most devastating diseases for pigs and producers is Porcine Reproductive and Respiratory Syndrome, or PRRS. This virus, first recognized in the United States in the mid-1980s, can affect pigs of all ages. Each year it affects roughly 10 percent of U.S. herds making it one of the most economically devastating diseases in the industry.

Once this disease enters a herd, it spreads rapidly and typically results in significant mortality and morbidity and ultimately economic losses. There is currently no effective cure for the PRRS virus. The pork industry has tried to vaccinate against PRRS, to varying degrees of success, but PRRS rapidly mutates, thus proving to be a difficult virus to eradicate. Therefore, vaccines may only work for a period of time and, like selective breeding, developing a new vaccine is a timely process.

Through gene editing, resistance to PRRS can and has been achieved. In addition to decreasing PRRS cases, gene editing also has the power to decrease susceptibility to other viral diseases in swine such as African swine fever, foot and mouth disease, porcine epidemic diarrhea virus, and bovine tuberculosis.

Decreasing the amount of disease outbreaks on pig farms would:

1) Alleviate animal suffering
2) Reduce the need for antibiotic usage
3) Improve production efficiency including reducing carbon footprint
4) Help farmers continue to produce a safe product

Other Gene-Editing Opportunities

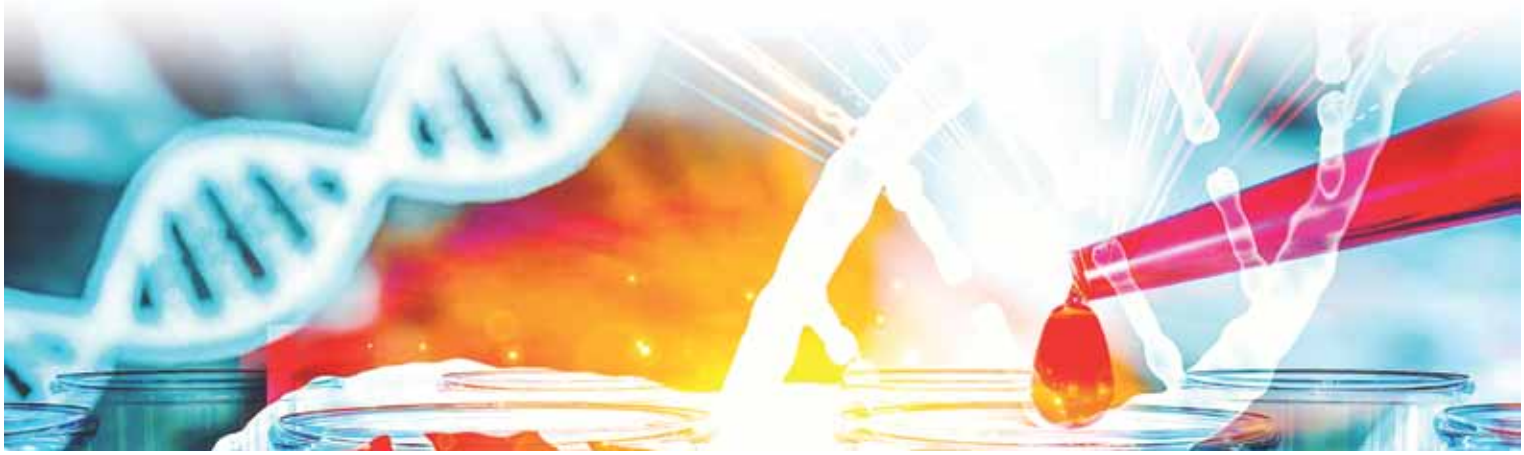
If you are wondering what else gene editing can do, scientists are looking beyond disease resistance applications.

Examples of other benefits from gene-edited pigs:

1) **Eliminating the need for tail docking.** Genetically engineering pigs to be born without tails improves animal welfare and reduces the chance of an injury or infection.
2) **Eliminating the need for surgical castration in male pigs.** Genetically engineering pigs to remain in a pre-puberty state improves animal welfare, increases pork quality attributes, and decreases aggression in male pigs by providing an alternative to surgical castration.
3) **Turning fat cells into energy and heat in piglets.** This improves animal welfare by allowing pigs to better withstand cold stress as well as utilizing feed stuffs more efficiently.

Gene editing is being used in other food animals such as goats, sheep and cattle. On all these animals, editing out the myostatin gene has allowed for increased muscling in meat production. Gene editing has also produced polled dairy cattle, or dairy cattle born without horns, which improves animal welfare and labor efficiency by eliminating the need to physically dehorn calves.

Gene editing technology in human medicine has tremendous potential to change the future of the medical field forever. Gene editing has been used to modify human blood cells that are then put back into the body to treat conditions including leukemia and AIDS, and has the potential to treat genetic conditions such as sickle cell anemia, Parkinson's Disease and muscular dystrophy.



Barriers to Approval

Consumer Acceptance

As with all new technology, gene editing faces some societal barriers to approval before being used in the market-place. One of these barriers will likely be consumer acceptance of the technology. In general, the public has misconceptions about genetically modified organisms as a result of successful misinformation campaigns and gene editing could fall into the same category if we do not share the correct information.

Mike Paustian, a pork producer from eastern Iowa and Vice President of Producer Services for the IPPA Board of Directors, recently attended the 2018 CRISPRcon conference in Boston where he participated in discussions regarding consumer acceptance of the technology.

"We might only have one chance to successfully introduce gene-edited animals to consumers. If it goes badly and becomes vilified as we have seen happen to GMOs, it is possible that we could lose our ability to use the technology in the future. I think one of the ways we can help address these concerns is by highlighting how gene-edited animals will benefit consumers, not just farmers," says Paustian.

One organization looking at gene editing from a consumer perspective is the Center for Food Integrity. According to Charlie Arnot, Chief Executive Officer of the Center for Food Integrity, it is important for producers to understand that consumers look at this topic through a different lens. Arnot provides three tips for producers to consider when having a conversation about gene editing with a consumer:

1) **Start the conversation by outlining the consumer and social benefits of this technology.** Instead of laying out how this technology will benefit producers, find out what information is relevant to the consumer and what they care about. For example, instead of talking about increased labor efficiency and decreased cost, explain how gene editing can improve animal welfare, promote sustainability, and reduce the cases of premature animal death.

2) **Relate gene editing to practices already being used in agriculture.** For decades, agriculturalists have been using conventional breeding techniques to achieve desired characteristics in plants and animals. Now, we can use this same kind of technology to do so in a more precise way. Being able to relate gene editing to techniques we are already using will make the technology appear less concerning to a consumer.

3) **Relate gene editing in agriculture to gene editing in human medicine.** As previously mentioned, consumers are most interested in the benefits they will receive from new technology. When talking about disease resistance in pigs, explain that gene editing also has the potential to prevent human diseases.

"Even though we are likely years away from having gene-edited pigs on our farms, we need to begin participating in discussions about gene editing now in order to lay the groundwork for future acceptance of this technology."

Mike Paustian
Iowa Pork Producer and IPPA Board Member

Regulation

With a technology like gene editing, there is no doubt that regulation will play a huge role in the future availability of this technology. There are ongoing discussions about whether the United States Department of Agriculture (USDA) or Food and Drug Administration (FDA) should oversee regulation, but currently the FDA's Center for Veterinary Medicine is responsible for evaluating the safety and effectiveness of gene-edited animals, while the USDA oversees gene-edited crops.

The FDA has updated the framework of their opinion on gene-edited animals under the FDA Draft Guidance 187 and, under this draft guidance, the FDA looks at gene-edited animals under the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act. Under this framework, each specific genome edit is considered a separate new animal drug subject to new animal drug approval requirements.

Several people in the swine industry are concerned about this framework and feel there are potential complications to treating gene-edited animals the same as a new animal drug. For example, with this framework, it is possible that every sow farm with genetically engineered animals could be classified as a drug manufacturing facility. Another concern is that under this framework, any meat harvested from a gene-edited animal could be subject to a GMO label.

Dr. Dan Kovich, Assistant Director of Science and Technology for the National Pork Producers Council, feels that gene-edited animals should be regulated the same as gene-edited plants, which are regulated by the USDA.

"We feel that the current approach to regulation of gene-edited animals under the FDA is going to kill the promise of this opportunity. We feel strongly that gene-edited animals should be regulated by the USDA under the Animal Health Protection Act, similar to how gene-edited plants are regulated by the USDA under the Plant Protection Act," says Dr. Kovich.

Currently, the administration is looking at this issue and the FDA is revising their draft guidance. The timing of this revision is unknown and there is no information on what the revisions will look like. The USDA is also revising the regulations on the plant side. "We expect the revisions of gene-edited plants under the USDA's Plant and Protection Act to be pro-innovative and reasonable, and we just want the same thing for animals," says Dr. Kovich.

"We can only hope that the government agencies that provide regulation oversight of gene-edited animals will soon give clear guidance for a path forward for approved use of gene editing in animals. We should hold those agencies to basing those regulations on scientific merit and data, not on unrooted fears of the unknown," says swine specialist Benny Mote.

Commercialization

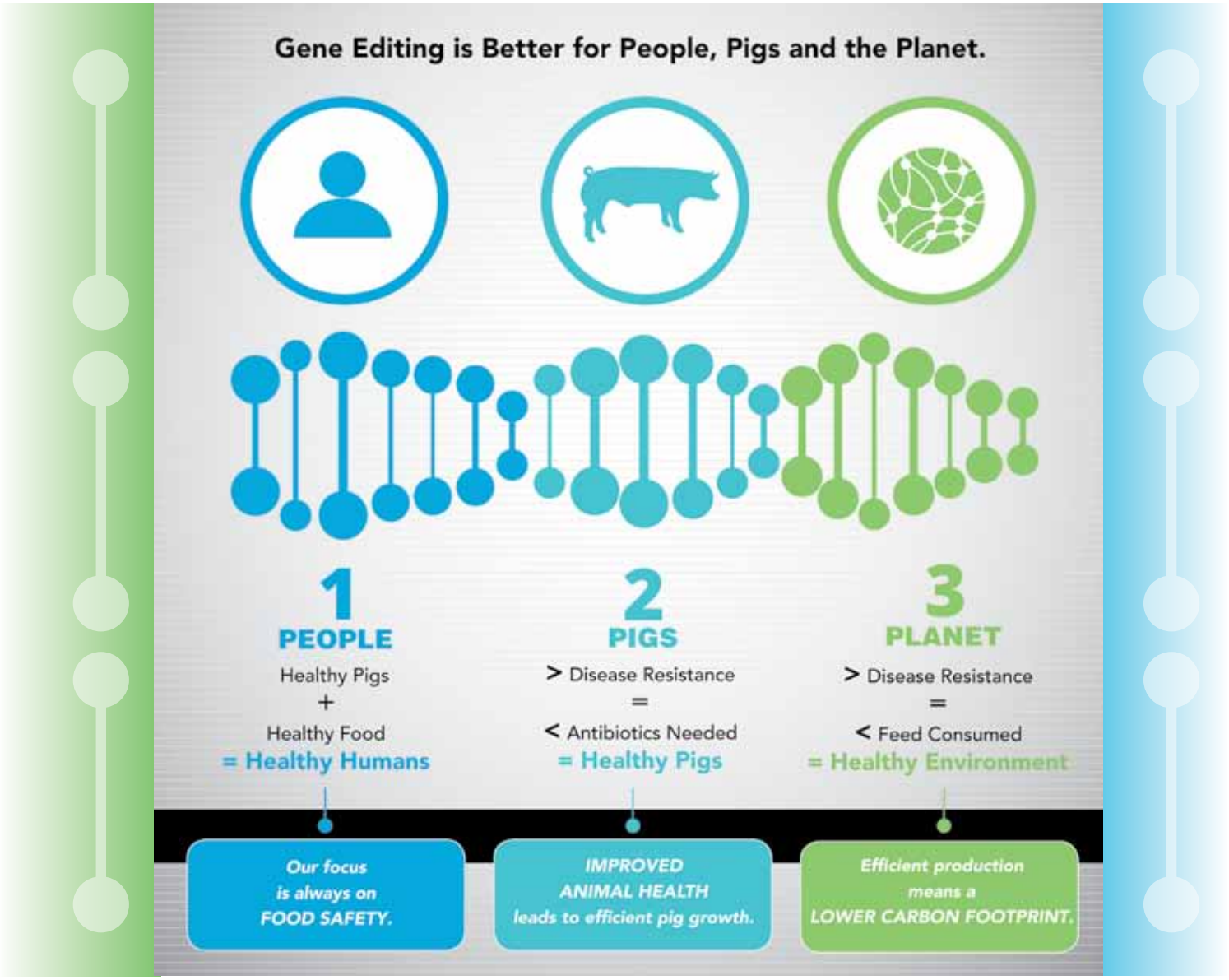
Another barrier to approval is finding a way to make this technology available on a commercial level. Organisms are composed of millions of cells, making it nearly impossible to edit the same gene in every single cell of a human, a crop, or a pig. Most of the changes introduced with gene editing are in somatic cells, or non-reproductive cells. Therefore, the changes made to somatic cells would not be passed down to future generations. Changes need to be made to genes in egg or sperm-cells, or the cells of an embryo, to be passed from one generation to the next in a species, a process that is still being researched.

"Ultimately the biggest hurdle will likely be getting the genetic changes that have been made using gene editing sufficiently disbursed so that they can be applied in a commercial setting. This is no small feat and something that genetic suppliers are currently considering so that when gene-edited animals pass regulatory barriers, they are prepared," says Dr. Chris Hostetler, Director of Animal Science at the National Pork Board.

"Like all technologies, this technology may not be adopted by all pork producers because it does not fit into their business model or their production system. However, it is a very powerful tool that can be utilized by swine genetics companies to provide pork producers with specific genotypes."

"Soon, producers will have the opportunity to use this technology to further improvements in animal health, welfare and production efficiencies that ultimately improve the way we manage pigs."

Dr. Chris Hostetler
Director of Animal Science, National Pork Board



Graphic credit: National Pork Board

What This Means for Producers

What does all this mean for you and your farm? Although you cannot take advantage of this technology yet, you are an extremely important part of the conversation around public acceptance and understanding of gene editing. Taking advantages of opportunities like attending a CRISPR conference, engaging with key stakeholders and becoming more educated on the topic is a huge contribution toward getting this technology approved for farmers to use.

When having these conversations, remember the three main tips:

1) Start the conversation by outlining the consumer and social benefits of this technology.
2) Relate gene editing to practices already being used in agriculture.
3) Relate gene editing in agriculture to gene editing in human medicine.

Conclusion

Overall, gene editing has the potential to solve a wide range of challenges facing agriculture today. There are several ways that this technology could improve the swine industry, but most of the changes will likely be seen in the areas of disease resistance, swine welfare and production efficiency. While the regulatory steps of approving this technology are being determined, it is important for pork producers to be informed about the possibilities of this technology so they can engage key stakeholders and consumers that play an active role in acceptance of this technology.

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Mission Statement

The Iowa Pork Producers Association is an industry inclusive organization whose mission is to provide a unified voice to promote and educate for a sustainable, socially responsible, profitable and globally competitive pork industry.

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