COPY. REPLACE. DELETE

What is gene editing, and what's its potential?

by Miranda Reiman, senior associate editor

The very first genetically modified organism (GMO) was approved in the United States during the Reagan administration, and in 2022 scientists are now studying ways to make gene editing applicable and scalable for animal agriculture.

Clare Gill, professor of animal genomics with Texas A&M University, is one of those researchers. She presented the topic at the National Angus Convention & Trade Show in Fort Worth, Texas, in November.

"Remember where we are today with genomic-enhanced expected progeny differences (EPDs) selection seems to have flown by, but it's been 20 years of effort to get to where we are today," she said. "I expect it's going to be 20 years before we really see gene editing be a norm."

Gill is confident it will become commonplace, mostly because of the problems the technology could solve for cattlemen in the future. Yet, it's not all a clear-cut path. Understanding how gene editing works helps point to some of the hurdles.

HOW DOES IT WORK?

Gene editing is both as simple and as complicated as it sounds. At its base, it's purely taking a nucleotide (or several) and replacing or deleting it.

"We can knock out a piece of the DNA or we can put new DNA in," Gill said.

That works through a process first discovered in bacteria. To ward off viral attacks, bacteria often use a nuclease enzyme called Cas to cut up DNA. That protein pairs naturally with two RNAs, one is a tracer, or helper. The other is CRISPR (clustered regularly interspaced short palindromic repeats) that works like a homing beacon to find specific DNA in a cell.

Once that's all paired together, the "molecular scissors," or the Cas protein, goes to work.

"It's going to chop the DNA at a very precise site," Gill said. "What that allows researchers to do is then take advantage of every cell's DNA repair function."

The system that uses CRISPR and the Cas protein takes advantage of the cell's natural process.

"The CRISPR-Cas9 complex has a half-life of about 24 hours, and eventually it's gone," she said. "Then the only thing that's left is the nucleotide change that was made, and that could be a naturally occurring mutation. So, it's equivalent to natural mutations without having to crossbreed. Introducing the polled mutation from Angus into other breeds is an example."

WHAT COULD IT BE USED FOR?

From the very first cattle genome sequencing in the early 2000s to today, the cattle community has learned there are at least 84 million single-nucleotide polymorphisms (SNPs), or 84 million places in the genome that vary in sequence and another 2.5 million natural small additions and deletions.

"It could be something completely new, but most of the current opportunities are taking advantage of the tremendous diversity in cattle as a species," she said.

Imagine wanting a trait from another breed, but you don't want to start with a 50-50 cross to get it.

"You just want that one little piece of DNA. You can do it now," Gill said.

Breed associations, private companies and individuals are currently weighing what a future with gene-edited animals could look like. Today there are only two commercially available genetically modified animals: GalSafe pigs and AquAdvantage salmon, though neither were made by gene editing.

Gill gave hypothetical examples of how gene editing could be used to aid in:

- eliminating specific genetic defects;
- introduce disease resistance; and
- improving animal welfare or efficiency traits.

"One of the opportunities for gene editing is to introduce precisely some edits that would advance the breed, without changing any of the other background of those elite bulls and

dams that are contributing to genetic advances in your breed," Gill said.

TRADITION OF TEAMWORK

Technology companies and associations already have a history of working together by incorporating genomic data into the long-established EPDs.

"I can use a SNP chip, but you need the information from that SNP chip in an easy way that you can make selection decisions quickly, and that collaboration has resulted in transforming that information into something you can use," Gill notes.

The technology works best when it has live animal data to pair with it.

"Whether you're using genomic selection, whether you as an organization do begin to use gene editing, always, always, always continue to monitor your phenotype, collect measurements," she said. "Look at the animals and make those recordings."

POSSIBILITIES AND PRECAUTIONS

Still, for all the opportunities, there's a heap of challenges, too.

The technology still needs honing, so it's viable and economical on a larger scale. Today, edits are made by cloning cells and replacing the nuclei of harvested eggs before implanting them into recipient cows.

All three points in that process could benefit from improvements and efficiencies — the success rate of *in vitro* fertilization (IVF), of the actual gene edits and when transferring the nuclei.

Gill is certain researchers will find solutions, but it will take larger discussions to get at questions that range from best practices for maintaining genetic diversity to being certain there are not unintended consequences.

Then, once the industry decides, there's still the government oversight quandary.

"Right now there are some regulatory barriers that are impending innovation on the animal side of the food supply chain with relationship to gene editing," Gill said.

CLARE GILL

USDA, the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) are all involved in different parts of biotechnology approvals.

Even though consumers regularly eat GMO grains, fruits and vegetables, and many gene edits in plants are exempt from regulations, gene edited animals cannot enter the food chain without a permit, even when the genetic matter is already naturally present in the bovine species.

"That's what's stifling a lot of gene editing research in food animals the United States and preventing innovations in this field," she said.

"You as an association have a framework in place to take advantage of this when approvals begin to come through," she noted, reading from the policy adopted in September 2021. "It has to be an approved edit, it has to be beneficial to the breed, the progeny still have to be parent-verified and then remember you have to track the progeny."

Gene editing is not coming, it's been here, Gill said. However, applications for the Angus breeder? Those are still on the horizon. AJ

Editor's note: To learn more about the Association's current gene-editing policy, refer to the Breeder's Reference Guide online at www.angus.org/pub/brg.pdf.

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