NEWS IN FOCUS

XI-JUN YIN

These meaty pigs could become the first genetically engineered animals to be approved for human consumption.

GENE EDITING

Super-muscly pigs created by small genetic tweak

Researchers hope the genetically engineered animals will speed past regulators.

BY DAVID CYRANOSKI

Belgian Blue cattle are hulking animals that provide unusually large amounts of prized, lean cuts of beef, the result of decades of selective breeding. Now, a team of scientists from South Korea and China says that it has created the porcine equivalent using a much faster method.

These 'double-muscled' pigs are made by disrupting, or editing, a single gene — a change that is much less dramatic than those made in conventional genetic modification, in which genes from one species are transplanted into another. As a result, their creators hope that regulators will take a lenient stance towards the pigs — and that the breed could be among the first genetically engineered animals to be approved for human consumption.

Jin-Soo Kim, a molecular biologist at Seoul National University who is leading the work, argues that his gene edits merely speed up a process that could, at least in principle, occur through a more natural route. "We could do this through breeding," he says, "but then it would take decades."

No genetically engineered animal has been approved for human consumption anywhere in the world, owing to fears of negative environmental and health effects. Fast-growing transgenic Atlantic salmon have languished in regulatory limbo for 20 years with the ▶

US Food and Drug Administration (see *Nature* **497,** 17–18; 2013).

Kim and his colleagues are part of a growing band of researchers who hope that gene editing, which can be used to disable — or knock out — a single gene, will avoid this. Reports of gene-editing applications in agriculture include the creation of hornless cattle. (Horns make the animals difficult to handle and are currently burned off in a painful procedure.) Researchers have also engineered pigs that are immune to African swine fever virus.

Key to creating the double-muscled pigs is a mutation in the myostatin gene (*MSTN*). *MSTN* inhibits the growth of muscle cells, keeping muscle size in check. But in some cattle, dogs and humans, *MSTN* is disrupted and the muscle cells proliferate, creating an abnormal bulk of muscle fibres.

To introduce this mutation in pigs, Kim used a gene-editing technology called a TALEN, which consists of a DNA-cutting enzyme attached to a DNA-binding protein. The protein guides the cutting enzyme to a specific gene inside cells, in this case in *MSTN*, which it then cuts. The cell's natural repair system stitches the DNA back together, but some base pairs are often deleted or added in the process, rendering the gene dysfunctional.

The team edited pig fetal cells. After selecting one edited cell in which TALEN had knocked out both copies of the *MSTN* gene, Kim's collaborator Xi-jun Yin, an animal-cloning researcher at Yanbian University in Yanji, China, transferred it to an egg cell, and created 32 cloned piglets.

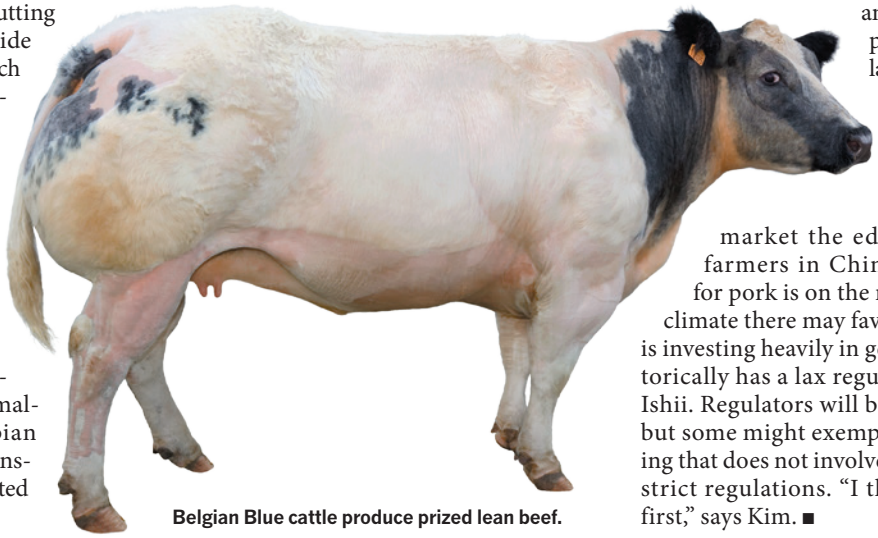
Kim and his team have not yet published their results. However, photographs of the pigs "show the typical phenotype" of double-muscled animals, says Heiner Niemann, a pioneer in the use of gene-editing tools in pigs who is at the Friedrich Loeffler Institute in Neustadt, Germany. In particular, he notes, they have the pronounced rear muscles that are typical of such animals.

Yin says that preliminary investigations, show that the pigs provide many of the double-muscled cow's benefits — such as leaner meat and a higher yield of meat per animal. However, they also share some of its problems. Birthing difficulties result from the piglets' large size, for instance. And only 13 of the 32 lived to 8 months old. Of these, two are still alive, says Yin, and only one is considered healthy.

Rather than trying to create meat from such pigs, Kim and Yin plan to use them to supply sperm that would be sold to farmers for breeding with normal pigs. The resulting offspring, with one disrupted *MSTN* gene and one normal one, would be healthier, albeit less muscly, they say; the team is now doing the same experiment with another, newer gene-editing technology called CRISPR/Cas9. Last September, researchers reported using a different method of gene editing to develop new breeds of double-muscled cows and double-muscled sheep (C. Proudfoot *et al. Transg. Res.* **24,** 147–153; 2015).

Because gene editing is a relatively new phenomenon, countries have only just started to consider how to regulate it in agricultural plants and animals. There are some signs that government agencies will view it more leniently than they do conventional forms of genetic modification: regulators in the United States and Germany have already declared that a few gene-edited crops fall outside of their purview because no new DNA has been incorporated into the genome. But Tetsuya Ishii, who studies international biotechnology regulation at the Hokkaido University in Sapporo, Japan, and who has done an international comparison on GM regulations, says that gene editing will raise increasing alarm as it progresses in animals.

Kim hopes to market the edited pig sperm to farmers in China, where demand for pork is on the rise. The regulatory climate there may favour his plan. China is investing heavily in gene editing and historically has a lax regulatory system, says Ishii. Regulators will be cautious, he says, but some might exempt genetic engineering that does not involve gene transfer from strict regulations. "I think China will go first," says Kim. ■



CLAUDIUS THIRIET/PHOTONONSTOP/CORBIS

Belgian Blue cattle produce prized lean beef.

FUNDING

How an Oregon cancer institute raised a billion dollars

Gains from two-year fund-raising frenzy will aid the early detection of tumours.

BY HEIDI LEDFORD

Cancer researcher Brian Druker had no idea that a fund-raising gala would change his life. On 20 September 2013, armed with a speech that his wife had written for him, he waited patiently to be introduced by Philip Knight, the billionaire co-founder of sportswear brand Nike.

Knight was a friend and benefactor; a few years earlier, he and his wife Penny had donated US$100 million to the cancer centre that Druker directs at Oregon Health & Science University (OHSU) in Portland. But nothing had prepared Druker for what happened next. "Penny and I will donate $500 million to OHSU, if it is matched in pledges within two years in a fund-raising campaign," Knight said, drawing gasps of surprise from the audience. "If the campaign raises $499 million, we are relieved of our pledge," he added. Druker turned in shock to his wife. "What do I do now?," he asked.

So began a frantic two-year scramble at the