CRISPR Progress

What Does It Mean for the Veterinarians?

PEER REVIEWED

Since its inception in the early 80s, the genetically modified organism (GMO) has been mired in controversy. It has promised much: disease-resistance, more effective use of pesticides, longer shelf-lives for food and greater yields for farmers. Just as the debate on genetically modified organisms appears to be drawing to a close, with the US Senate issuing labelling rules and major food firms such as General Mills, Nestlé and Danone declaring some or all of their business to be becoming GMO-free, new technologies may be about to make the debate obsolete. Enter CRIPSR/Cas9.

What Is It?

If you don't know what CRISPR is, you aren't alone, but you'd probably better get on board. Chances are it will affect you in one way or another in the near future; particularly if you're involved in the field of veterinary medicine. CRISPR (clustered regularly-interspaced short palindromic repeats) as a technology is only three years old, but has existed in nature for thousands of years and its application to crops, animals and human medicine is about to change every aspect of life as we know it.

CRISPR is a revolutionary new way to edit genes that can do what traditional GMO techniques can do and so much more. What differentiates CRISPR from the many other forms of genetic modification is that by using the Cas9 enzyme, it mirrors a process which occurs in nature. CRISPR edits and rearranges genes, by cutting out part of the DNA that is damaged or unwanted, allowing the remaining DNA to be rearranged in a new way. CRISPR basically uses the same mechanisms living organisms use when repairing damaged DNA, snipping out unwanted fragments, replacing or reorganising what is left behind. Because this method is what occurs naturally, it is likely that CRISPR will not be subjected to the same levels of regulatory scrutiny that traditional GMO technology has been.

How CRISPR will Affect your Life

Consider the white button mushroom, the kind you find in the grocery store. Using the CRISPR/Cas9 method, a plant pathologist at Penn State University engineered it to be resistant to browning. This is a breakthrough from a biology standpoint, but also from a regulatory standpoint, for the US Department of Agriculture confirmed that the process does not require regulatory approval. A CRISPR edited corn variety (developed by DuPont Pioneer) quickly followed, and it also was not subjected to USDA regulations. While it is possible that the FDA or the EPA may elicit regulatory review, this technology certainly opens a door for the entire agricultural community.

How long before grocery aisles are stocked with CRISPR produce? And it's happening in other countries as well. The director of the Swiss Institute of Organic Farming has made a statement in favour of CRISPR, shocking many NGOs and lobby groups of organic agriculture. Even the Chinese government, renowned for their opposition to GMOs, are getting on board, indicating a willingness to embrace CRISPR in contrast with their antipathy toward the transgenic type.

So How Can CRISPR Succeed with Consumers where GMOs have Failed?

CRISPR has been receiving accolades in both science and technology circles. It was named the 2015 Breakthrough of the Year by *Science*, the journal of the American Association for the Advancement of Science, and in 2014 and 2016, it made MIT's list of the top 10 technologies. The development by scientists of a new way of editing the genes of plants and other living organisms through CRISPR avoids many of the pitfalls of transgenic GMOs. Despite approvals by the FDA and assurances of their safety, consumers have been concerned by traditional genetically modified organisms. These arise from the fact that the DNA introduced into the plant during the GMO process would never occur in nature (the DNA introduced often comes from different species, including insects, viruses and bacteria).

A variety of consumer groups, activists and scientists have expressed their mistrust of GMO technology, which has resulted in bans on planting (e.g., European Union) and introduction of labelling rules (USA). Many consumers in the US, China, and the EU distrust GMO products. Initial indications are that consumers accept CRISPR is a natural process.

What Could CRISPR/Cas9 Do?

The answer is almost anything. According to a deluge of scientific journal papers published in the last year, CRISPR could cure genetic defects and illnesses in people, such as cancer, Alzheimer's, cystic fibrosis, AIDS and more simply by snipping and removing DNA. Pending a final approval from the US FDA, the US National Institute of Health did approve the CRISPR technique for a human cancer treatment trial in June. Sichuan University's West China Hospital in Chengdu is testing the CRISPR method in lung cancer patients where traditional methods have failed. The Chinese have taken CRISPR a step further, however, including performing the editing technique on the genomes of human embryos, opening the debate over the ethics of gene editing and designer babies.

It may not be long before clients are asking about

designer pets too. From a veterinary standpoint, CRISPR is already well on its way. China has taken the lead to produce novelty animals such as beagles with twice the muscle mass, leading to an animal with better stamina and endurance. This particular attribute could easily segue into the horse world as well. Other possibilities include adaptations wherein labs have better hips, or pugs' respiratory issues are alleviated. While it hasn't been noted that the beagles or any other CRISPR creations have been bred, it is possibly only a matter of time.

Discussions revolving around disease resistance in production animals are also under consideration, by making animals' immune cells capable of resisting critical viral diseases such as African swine flu, avian influenza for poultry or foot-and-mouth disease for cattle, greatly reducing the need for antibiotics or other therapeutics. These type of uses may be more easily accepted by the general public than gene alterations for physical attributes. From a crop perspective, this could create higher productivity or yields, possibly lower pollution (cows that produce less methane), increased profit margins (animals that require less food). The possibilities are endless.

CRISPR could also solve many of our intractable global health problems, such as malaria, West Nile virus and Lyme disease. It could change the genes of insects, such as mosquitoes and ticks, making them more susceptible to insecticides. This could help make vaccines more targeted and effective. As vaccines are currently produced using the whites of eggs, this can potentially cause allergic reactions for those with egg allergies. Scientists even now are attempting to alter the gene that causes this reaction.

It could also help feed our planet. Plant genes (e.g., wheat, corn, canola) can be edited to improve disease resistance, or resist the application of specific pesticides. This could greatly increase a farmer's yield. This is significant given projections that the human population will exceed 9 billion people by 2050, with much of the growth in the middle class and thus bringing higher demand for meat, milk and eggs. Indeed, from a consumer perspective, CRISPR is a game changer. It will alter the grocery store or online delivery experience by offering new food choices in a manner that thus far has been shown to be more accepted by the government, requiring no labelling regulations. This makes it consumer-friendly in a way GMOs have never been.

On the other end of the scale is the opportunity it offers for human health. We may be on the verge of curing some of the most evasive diseases known to man, potentially saving millions of lives. But how far is too far? That is where the debate will go next.

What is the Business Perspective for CRISPR/Cas9?

A CRISPR organism costs 1percent of a GMO one and can be conducted in a tenth of the time. If it is consumer acceptable, who can be against it?

Agriculture and human health create billions of dollars of new businesses every year. It may seem wrong to assess CRISPR from this angle, but it is clearly a game changer and as such has the opportunity to create monumental investment opportunities. It passes the 'smell test' that GMOs failed in the minds of many consumers the minute they heard that the DNA of plants was being mated with those of viruses, bacteria and insects. That didn't sound good, and made it easy to characterise the results as 'Frankenfoods'. Combined with confusing labelling, it had the potential to kill a product even before it got started. In food, the need to label, even when obscured by numbers or codes, affects consumer acceptance and in turn the potential for market success.

For veterinarians there are three specific takeaways:

1. CRISPR can be used in animals, specifically companion animals, to remove genetic defects and enhance certain traits.
2. Gene editing through CRISPR is a more consumer-friendly technique to get crops and farm animals with greater disease resistance and productivity with enhanced nutritional traits.
3. The CRISPR technology can be used in vaccine production, reducing allergenic effects when the vaccines are produced in eggs and potentially speeding up the design of new vaccines.

The implications of designer animals, consumer-friendly agricultural production and superior vaccination techniques all could be just over the horizon. Undoubtedly much of this brings up ethical questions and questions in regulatory decision-making, but the speed of development of the technology, particularly in countries such as China, is now moving forward so quickly that even with some forms of restrictions and agreements, we will soon see CRISPR cause tectonic shifts in the way the world produces food.

CRISPR is here to stay. Will CRISPR succeed where GMOs failed? Probably. If the cost, speed and power of CRISPR/Cas9 technology is not enough to cause the demise of transgenic organisms as we know them, then the power of proactive consumers (prosumers) and the burden of regulation surely will.

Aidan Connolly is the chief innovation officer and vice president of corporate accounts at Alltech. Connolly is responsible for the commercialisation of Alltech's global research, in addition to corporate account strategy within the company. Connolly is an adjunct professor of marketing at University College Dublin and China Agricultural University. He is an executive board member of the International Feed Industry Federation, the National Chicken Council and the National Turkey Federation. He is also a former board member of the European Union Association of Specialty Feed Ingredients and their Mixtures and the International Food and Agribusiness Management Association. Connolly is responsible for the highly anticipated Alltech Global Feed Survey, which is released annually.