HOW CAN CRISPR-CAS TECHNOLOGY ASSIST SMALL HOLDER FARMERS AROUND THE WORLD?

Panel Moderator: *Kevin Pixley*
October 18, 2017 – 2:45 p.m.

Introduction

Cynthia Milligan
Dean Emeritus, College of Business Administration, University of Nebraska-Lincoln and President and CEO of Wood Stieper Capital Group

And while they're leaving, if the CRISPR panel could come up and make themselves comfortable, and I think a chair will magically come for that panel.

So what is CRISPR as we talk about CRISPR-Cas technology? How can it assist the smallholder farmer around the world? As most of you know, CRISPR-Cas is a breakthrough in biology that helps farmers produce better and more food so that it can withstand ever-changing weather patterns, drought and diseases. These are genuine or genome editing techniques that are based on natural systems that have been used for centuries by farmers and as farmers have selected characteristics so that they can have higher yields and more nutrition in their food. So we are going to be talking about bringing this breakthrough technology that can safely improve yields for smallholder farmers.

And so I want to welcome to our panel here, Kevin Pixley, Neal Gutterson, and Nigel Taylor and Feng Zhang. And I want to say—welcome back to Iowa to Dr. Zhang who moved here and was here, as I understand it, during much of your middle school and high school years—and some of your teachers are in the audience. So we're very pleased to have you back. So I'm going to turn it over to Kevin Pixley, who is going to moderate this panel.

And we're going to be very efficient from now on for the rest of the afternoon. Now that Ambassador Quinn is gone, we'll do less on the introductions and look at them in your book, because then we'll have more time to hear their expertise that you came to hear about.

Panel Members

Kevin Pixley	Director of Genetic Resources Program, International Maize and Wheat Improvement Center
Neal Gutterson	Vice President of Research and Development, DuPont Pioneer
Nigel Taylor	Interim Director, Institute for International Crop Improvement, Donald Danforth Plant Science Center
Feng Zhang	Core Institute Member, Broad Institute

Kevin Pixley
Panel Moderator

Okay, well, thank you, and welcome to this panel discussion. I think we're going to have a really exciting time talking about how the technologies of CRISPR-Cas can be made to benefit smallholder farmers all around the world. So we're going to have a format where each of the panelists will have, oh, five or six minutes to make an opening statement.

We have a distinguished group, everything from the originators of the technology, Dr. Feng Zhang, to some of the corporate users and developers of varieties, to some of the non-for-profit groups working on crops for orphan crops for Africa, and of course myself, I'm Kevin Pixley. I'm the Director of the Genetic Resources program at CIMMYT, which is the International Maize and Wheat Improvement Center; and I'm based in Mexico, but I spent a large part of my career working in Southern and Eastern Africa on maize breeding.

So for me, these targeted genome editing technologies are probably the most exciting technology in genetics, of at least my lifetime. So at least today I have to say that. And I think there's a lot of optimism about what these technologies are going to achieve in terms of enhancing the efficiency of plant breeding but also in terms of enhancing food security and improving the state of smallholder farmers around the world.

But yet it's going to be at least a couple of decades before we really know whether this optimism has been validated and has been justified, so we're going to have to wait and see if we, all of us in this room and listening also online can help make this a reality for smallholder farmers around the world.

So we invite you spend a few minutes with us this afternoon, talking specifically about how it might benefit smallholder farmers. And you're going to briefly hear from us, and then we're going to give you the opportunity to ask us some questions as well.

But before I introduce our first speaker, we have a video, which I also have not yet seen, which is going to give us just a very brief introduction to what this CRISPR-Cas technology is all about. So if we could have the video, please.

VIDEO

The farmers from around the world face real challenges to producing food, because plants are under constant stress from factors like climate change, drought, disease and pests. These ever-evolving growing conditions, coupled with rapid population growth and changing diets, represent concerns about long-term food security and the preservation of our global environment. Agriculture must respond with timely solutions to these urgent needs. CRISPR-Cas, which stands for "Clustered, Regularly Interspaced Short Palindromic Repeats," is a breakthrough in biology with broad gene editing applications for plants, animals and humans. For agriculture, it offers a more efficient and targeted way to develop healthy seeds and help farmers produce more and better food with fewer resources. Based on a natural system, CRISPR-Cas gene editing technology can precisely improve a plant without incorporating DNA from another species. It's a continuation of what people have been doing since plants were first domesticated, selecting for characteristics such as higher yields, tolerance to drought, longer shelf life or better nutrition. Here's how CRISPR-Cas works.

DNA is the instruction manual for the growth and development of all living organisms. In response to common internal and external stresses, breaks and repairs of DNA strands routinely happen through natural cellular processes. Over the past few decades, scientists have developed a deep understanding of the genetic and corresponding physical attributes within plants. With this knowledge, scientists can apply CRISPR-Cas to direct DNA breaks and repairs to create specific outcomes. The process is similar to how a copy editor proofs and revises an article. CRISPR-Cas reads the DNA of a particular plant. Then, based on how CRISPR-Cas is programmed, it finds a specific location in the genome and either deletes, edits or replaces targeted genetic sequences native to the plant to create a beneficial change.

CRISPR-Cas also delivers improved efficiency in healthy seed development. Using conventional plant breeding practices requires multiple cycles and years to develop a plant that grows well in certain environments. It is, for example, resistant to a certain disease. Working within the existing genetic diversity of the plant family, CRISPR-Cas incorporates identified characteristics, such as disease resistance directly in high-quality plants in as little as one to two cycles. This means we're able to reduce the total seed development timeline from an average of eight years to five years, while maintaining the same field-testing protocols.

CRISPR-Cas is one more tool available to develop sustainable agricultural solutions and improve farmers' ability to produce safe, abundant and healthy food for our dinner tables.

Kevin Pixley

Okay. Well, if you have any questions, you'll be able to ask our first panelist. Dr. Feng Zhang was one of the originators, or the originator of the technology. His original paper in science has, as of eight o'clock this morning, more than 5,000 citations. Feng Zhang is a Core Member of the Broad Institute of MIT and Harvard, and he's also the James and Patricia Professor in Neuro-Science at the McGovern Institute at MIT. He's a molecular biologist who has pioneered the development of genome editing tools based on CRISPR systems. He leverages the CRISPR mechanism and other methods to study molecular and complex human diseases, such as psychiatric and neurological diseases. And his long-term goal is to develop novel therapeutic strategies for disease treatment. Please, Professor Zhang.

Feng Zhang

Thank you for the introduction. First of all, it's really a pleasure to be back here in Iowa. I grew up here in Des Moines, went to middle school and high school here, and it's really good to be back. I got a chance to see my teachers, who are sitting in the back this morning. I'm very fortunate to have been a student in Iowa.

I'm also glad the video got the acronym out of the way—it's a mouthful. I was worried that I might actually mess it up, so it's good that it got it out of the way.

So CRISPR is what we call a gene editing system. And I'll tell you a little bit about how this system works and why it is so exciting. The genome for many organisms, both our genome and also many other organisms, have been completed, so we now know every single letter in the genome. The human genome, for example, has three billion letters in it. So if you think of this as a long document or a long book, when this document is in Microsoft Word, it's fairly easy to go in and make specific changes. You can open up your search function, type in the string, and they will take you to that location in the document, and they can backspace or delete and type to add in new letters into that genome.

Now, in the microscopic environment of the nucleus of a cell, that becomes a lot more challenging. How do you find a specific spot where the gene is to make the change when there's three billion letters in this entire, complicated genome?

The way the CRISPR-Cas system works is that you can program a protein called Cas9, and Cas9 is the equivalent of the search function. By giving it a short RNA that's 20 letters long—20 letters is enough to give you specificity within, say, a three-billion letter long genome—then this 20 base per RNA is the equivalent of a search string, and it'll work with the Cas9 protein together as a machine to then search along the DNA until where these 20 letters on the RNA matches the letters on the DNA. When that happens, Cas9 will get activated, and it will cut the DNA, make a severance, a double-stranded break. And you can think of this break as the equivalent of the cursor in Microsoft Word. So wherever you make the cut, that's where you can start to type to add any sequences, or you can delete sequences.

And so all this really made the gene editing approach a lot easier, because it's very easy to develop a 20-nucleotide long RNA and to give it to the cell. So, because of that, we now are able to study many genes, across the genome in any organism we want. And also we can study every single gene all at once to better understand biology. So for example, scientists are now able to do screens where they target every single gene, and then they see which gene, when you get rid of it or if you turn it on, a lot more can give rise to virus resistance or drug resistance or even drought resistance if this is done in a plant species.

So there's a lot of exciting opportunity to apply this technology in both human health and also in agriculture, and I'm really excited to be here and to participate in this panel.

Kevin Pixley

Okay, thank you very much. Our second panelist is Dr. Neal Gutterson. Neal is the global leader of Research and Development for the Agriculture Division of DowDuPont. He's responsible for leading all seeds and traits, crop protection, predictive agriculture and product development functions to create innovative agricultural products. Neal served as president, chief executive officer and board member of Mendel Biotechnology prior to joining DuPont Pioneer, and now he sits in CIMMYT's Board of Trustees where he is program committee chair.

Neal Gutterson

Thanks, Kevin, and again it's a pleasure to be here and share some thoughts with you about moving from the technology itself to the meaning of the technology, why it's important to us, broadly in agriculture and particularly with the focus on smallholder farmers. So you can see from the title, we think about this as bringing abundant potential to agriculture through this new technology.

So I want to say at the beginning that CRISPR-Cas is a tool like many tools that could be used for many purposes. And for example it can be used to actually deliver a transgene to a particular location of the genome. In that case, you have a biotech product. What I want to talk about today is not that type of application but just the application set that we talk about as targeted breeding, a type of advance breeding. Pioneer has been in the business of breeding and providing improved genetics for our customers, our farmers, for over 90 years; and this tool for us is just part of the continued evolution of improved breeding systems.

So the new company, DowDuPont, our purpose is to enrich lives of farmers, of those who produce and those who consume, assuring progress for generations to come. So our purpose as an organization is very much aligned with the purpose, I think, of everyone in this room, whether it's a largeholder or a smallholder. And these are a set of the tools that we have available to us as a new company, and you can see it's a very rich set of tools for improving not just the seeds that we would deliver but also the tools that a farmer needs to ensure the realized value of those improved seeds.

Breeding has been the legacy within Pioneer, crop protection, of course. You'll see at the top, and I've circled CRISPR—that again is linked right below breeding, because for us it is part of the evolution of breeding systems. It's targeted breeding that's enabled by CRISPR-Cas technology. So how do we see using it, and how do we see this being broadly deployed?

So first of all, the technology is in general very easy to use. Having said that, I don't think it's as easy to engineer a rice plant or a weed plant that's going into your garage, and you might have read things like that. So it does take some skill and some capability, some knowledge of the genome, as Feng said. If you want to edit a text, you better understand the entire text that you're going to edit.

And for example, corn, roughly two and a half billion characteristics, compared to the human genome, about three billion; so these are pretty similar size. And so the crops are very variable in their sizes, but these are complex to edit. Nonetheless, you can see for us a series of crops that we work on, and you can see across the top a series of applications where we see real value to be able to use CRISPR in targeted breeding to edit these crops. And so you can see disease resistance is a very common problem in all these crops, crops around the world. We know a lot today about disease-resistance genes. And so it's the combination of what's important and what's feasible today that will direct some of our earliest applications of this technology. So disease resistance will be a key one for us, certainly improving yield and stable yield, tolerance to drought, and output traits. So certainly the ability to use this technology to improve nutrition, to develop fortified, biofortified crops, improved oil seeds and improved protein content, these are also really important applications that I think are relevant to farmers around the world and certainly to smallholder farmers as they can improve the profitability of their farms by improving the output value.

Now, we believe that there's a lot more applications that are interesting than just those, and so we've been working to partner over the last two to three years with a range of different organizations. And so the first of those relationships we announced with a view on enabling benefits to smallholder farmers was with Kevin's organization, CIMMYT where I do sit on the board of trustees. You can see on the left the result of infection by a devastating disease called maize lethal necrosis disease. It's a disease caused by two viruses together. There's no good treatments for that, other than genetic resistance. And CIMMYT recognized that, while they're developing their first-generation products for resistance for the regions you can see in the map where this is really an important problem, that we can ultimately accelerate the delivery of improved products that are really highly performing, high yielding and also resistant to that viral disease. And should the disease spread outside of Africa, we'll be poised to deliver solutions even faster. And so this is an example of the way we can see benefits coming and accruing to smallholder farmers in Africa as one example.

Now as I said, there are many different applications in a wide range of crops. There's only three on this picture. I 'm not going to go through those three particularly, but, in the case of spinach on the upper left, we know there are pretty easy ways to deliver improved disease resistance. And that could lead to the reduction of use of some pretty, not very pleasant pesticides that are currently used frequently to protect spinach from particular diseases.

And there are a wide range of other applications. I think for tomatoes, healthier tomatoes, more nutritious tomatoes, tomatoes with longer shelf life, just as an example—and I mentioned improved oil seed, you can see perhaps solutions even in trees that can be brought. So there's a wide range. There's an abundant potential of this in all the crops we can think of, I would say.

And so as we thought about what we want to do with this technology and how we could partner with people, we decided we need to open up what we do a bit more than we might have in the past, although we've had a very strong collaborative ethos and partnered with many people in many regions to solve smallholder farmer problems. But we believe we need to work together, private companies like ours, with the CG systems, with national organizations, to deliver benefits.

We announced yesterday a partnership with the Danforth to help improvement of cassava and some other products. That's the second in our alliance. And we recognized recently that, while we have certain really critical patent rights that one would need to have secured in order to bring a product to the market, whether it's a commercial market or a smallholder market, that the Broad where Feng works has another set of those patent rights that are important. And this morning we announced a joint licensing relationship to be able to create a much, much easier path and open up more democratic access to all interested parties for agriculture.

And so the couple of instances so far are part of our journey to find new ways and really complement, you know, Feng and the leaders of the Broad for working with us on bringing a single way to get access to this new and really important technology to serve the developing world. So thank you very much.

Kevin Pixley

Thank you, Neal. Now we're going to hear from Dr. Nigel Taylor. Nigel is the Dorothy J. King Distinguished Investigator at the Donald Danforth Plant Science Center. He currently serves as Interim Director of the Institute for International Crop Improvement and is principal investigator of the Virus Resistant Cassava for Africa project. His experience is mainly on tissue culture and the genetic transformation technologies required to deliver genetically improved cassava to famers in East and West Africa. He's a native of Scotland, as you're going to soon hear. And if you look at his recent publications, you'll see frequently the words, "cassava," "Africa," and "smallholder farmers." So, please, Nigel.

Nigel Taylor

I'm going to stand up, because I'm pretty happy to stand and move around. Thank you. So, yeah, thank you, and thank you for the introductions from the other speakers. That makes it easy for me. So what I'm going to do is I'm going to give you a little bit of a feeling for how I see the opportunities but also the challenges of bringing CRISPR-Cas technology to benefit smallholder farmers. And I'm talking mostly about the orphan crops. We saw on the list from Neal the commodity crops like maize and soy and canola and wheat. I am very interested in the orphan crops and what can CRISPR-Cas do to completely… I think it's going to change things significantly. And these are the crops, importantly, that missed out on the Green Revolution. And unfortunately, to date they have also missed out on GM technologies. They have not been deployed. We are working on that, but we're way behind for some reasons that we might get into. We must make sure that we don't miss out on the CRISPR-Cas revolution as well. So they have been neglected today, but the exciting thing about them is they have huge potential, because they have not undergone the improvement, for example, that maize has gone through or rice has gone through.

And so I'm just going to give you a few examples of our work in cassava. We are using CRISPR-Cas technology in cassava right now, and we're making progress. I'm showing you here cassava brown streak disease. That's a virus disease that's epidemic in East Africa, now in Central, so Central Africa, and by all accounts, the guys tell us, this is going to get to West Africa and is going to hit Nigeria. Nigeria is the largest cassava-producing country in the world. There will be a food security issue when it gets there.

So we've been using… Now this is… Most of you are not familiar. This is a farmer holding… He's broken open the [inaudible], and you can see the brown streaks. You can't eat these, you can't sell them, you can't feed them to the animal—it's a complete loss.

On the panel on the left, that is a plant in our greenhouse that has not been edited. The storage roots are damaged; you can see that on the right. And we've gone and we used CRISPR-Cas technology to edit two genes, and these are by the romantic name of EIF4E genes. We edited two of those, and now that means that the virus cannot replicate properly in the plant. So we're seeing very little disease there, and the viral load is completely reduced.

So this is a type of an example of how we could use this technology in cassava and for brown streak disease—for bacterial disease as well. My colleague. Becky Bart, who I think is in the audience, she's working on this as well. And what we would do here… This has already been shown in rice to be effective. CRISPR-Cas, you modify what's called the sweet 10 gene and the promoter of the sweet 10 gene, the bacteria can no longer recognize that, and it cannot replicate and it cannot cause disease. So we're using CRISPR-Cas technology there as well.

A very, very exciting thing that we was not to do is we would like to bring the green revolution to Teff by producing semi-dwarf Teff, and we can do this by CRISPR-Cas. We know exactly the gene and the sequence. We have the sequence in Teff. We know how to do this. We just have to go ahead and do it. There are no naturally occurring dwarf Teff varieties known to the breeders, so the breeders can't do this. But we can use CRISPR-Cas technology. We can go in, we can modify that gene, and we can make dwarf Teff. And that would be like almost spreading the Green Revolution to Teff—a very exciting possible application.

So what I've mentioned to you is knocking out one or two genes at a time or modifying one or two genes, and we actually have to think bigger than that. And those of you who have been maybe following this, you would see a group in Spain. They, in one experiment, knocked out 35 genes, 35 of the 45 genes that make gluten in wheat. And that is incredible to me, absolutely incredible. They're going to go back now and knock out the remaining 45. So we have to think big here as well. So this means we can actually go after metabolic pathways. Neal touched on that as well. So we really should think big. We're already targeting five genes in cassava that control flowering. So if we can do this, then the breeders will be able to manage this. Flowering is a problem in cassava, some varieties. But really we can think about using CRISPR-Cas to take out anti-nutrients, for example, in sorghum and maize, cassava post-harvest deterioration, a very complex physiological response. But with CRISPR-Cas, we can target multiple genes, several pathways. And we could probably do it at the same time in one shot or two shots. So this is just some examples of the type of things that we can do.

And another really interesting thing that's happening, and this I'll show you. These are examples in tomato, but this is also being done right now in the laboratory of Joyce Van Eck of the BTI. And they're taking this technology, and they're working on golden berry, which is cape gooseberry. It's only a semi-domesticated crop, but they're going to use CRISPR-Cas to increase the branching, to make the fruits larger, to improve the plant habits so it's easier to cultivate. So we can imagine also during this for orphan crops in Africa. And I'm not just talking about the staples. You can be thinking about the legumes and the fruits and the vegetables, which really have undergone very little improvement. We could bring CRISPR-Cas and fast track the domestication of these crops.

So those are some of the exciting potentials, and of course we could talk much more about them. But there are definitely challenges. And I'm sure those of you who have been around for a while, and I actually came to the World Food Prize in 1999, and people were saying what GM is going to deliver and how it was going to revolutionize smallholder farmers. And of course that has not panned out the way that people had said. So, but there are some challenges, and we have to be aware of them. We will have to develop the technology for the target crops. We will have to develop the economic platforms. We have to specifically develop the tissue culture systems. The type of thing that I work on is delivering the CRISPR tools so we can do this. We must train African scientists, for example; they must be part of this as well, and we are doing that. We would love to do more of it.

I've underlined regulatory, because this is really a big question is how will the products of CRISPR-Cas technology… How will these new crops be regulated? That is not clear right now. So we must engage and train the regulators, work with the stakeholders. And very, very important is that the African scientists and others around the world must be part of this conversation right now. This technology is moving so fast that we must not be left behind again. We really don't, mustn't have that. So communication and education also about this new technology is essential.

Kevin Pixley

Okay, thank you very much Nigel. Now, long before I was asked to be the moderator for this panel, I had been asked to speak about what CRISPR-Cas technologies will be able to, and can and will, achieve for smallholder farmers. So before I do that, I thought it would be really necessary to talk a little bit more about what we mean, what we intend, what we desire in terms of impact. And I think that probably 99% of us in this room would agree with a shared vision where what we really want is sustainable agriculture. And we want sustainable agriculture that provides food and nutrition security for all, while enabling biodiversity conservation. And I think we would also agree that poverty alleviation and improved livelihoods for farmers are also part of our shared vision.

So starting from this shared vision of what we all aspire to, we see CRISPR-Cas as one technology that can contribute to achieving this. So how might it contribute?

Well, it certain could accelerate. We've already seen it accelerate in the breeding process. And what we intend to do at CIMMYT is to emphasize challenges to smallholder farmers—some of the things that Nigel was mentioning.

These technologies can also reduce the risk of investing in technology for farmers and not only investing in seed, but if their varieties are more resilient to maize lethal necrosis or the cassava brown streak, then they might also invest in fertilizer or other technologies.

These technologies of CRISPR-Cas might also reduce the cost of investing in this technology, because it is less expensive perhaps than some alternatives. And I think Nigel's examples of lodging-resistant T eff is something that might not happen if it were much more complex and much more costly technology required to achieve it. And one of my favorites is really that CRISPR-Cas may help us to close the technology gap between those technologies that are available to the resource-rich and resource-poor farmers of the world.

So the only example that I'm going to tell you a little bit about that we're preparing to and beginning to work with at CIMMYT is resistance to maize lethal necrosis. As Neal mentioned, we're working with DowDuPont Pioneer on this project. The resistance is conferred by, or largely conferred by a gene on chromosome 6; and what we will need to do, because it's inherited in a recessive form, is we'll have to convert the susceptible allele to resistant allele in all parents of a variety that we would then make available to farmers.

So in Africa, Eastern Africa where this disease is the greatest concern at the moment, most hybrids in use are three-way crosses, which means that we would need to then convert all three parents, inbred parents of a hybrid, from susceptible to resistant allele. And this can be done quite quickly once we have in place the methods using CRISPR-Cas. The good news also is that in Africa successful hybrids typically have a long commercial life. So once we've converted some of the popular hybrids, they might have a fairly long success rate and a fairly long contribution to farmers in Africa.

So what would come next? We could also work on rust-resistant wheat, various nutritional qualities; and probably my favorite one would be Striga-resistant maize where we might be able to knock out the stimulant for Striga attachment on maize plants.

So that would be some of the possibilities that would see coming along, in addition to many of those mentioned by Nigel.

Of course, I think as was suggested by Nigel as well, we cannot assume that these technologies will reach smallholder farmers. At this point, I believe if I ask my mother, she wouldn't even know what CRISPR-Cas is or probably has never heard of it. So public opinion is largely unformed, and it's largely uninformed about CRISPR-Cas. And the regulatory framework is largely undefined, which is a great opportunity for us to help form it in a way that will make these technologies available to smallholder farmers.

I think if CRISPR-Cas technology, and I put it in parentheses, because if any advanced and beneficial technology does not reach smallholder farmers, then we risk really increasing that technology lag and decreasing the competitiveness of smallholder farmers and further then enhancing the poverty cycle that of course we're all working to alleviate.

So how can we as a scientific community help to ensure that the technological options or the technological prospects and optimism about CRISPR-Cas does have positive impact on smallholder farmers? I think we need to begin by recognizing and respecting the sovereignty of every country to decide if and when and how they're going to use this technology. I think we have a great responsibility to provide accurate, complete and trustworthy information to the public and to the regulatory process. We also, of course, need to implement excellent safety and stewardship in our research of CRISPR-Cas and other advanced technologies.

I think we also have a role—and part of it is like this one—to advocate for equity in the access to the possible benefits of this and other technologies. So at CIMMYT we work to keep or to try to secure or obtain access to CRISPR-Cas, put it and bring it into the public domain so that it can benefit smallholder farmers. And of course we need to offer capacity development in the effective use of this technology.

So of course eventually I worked with CIMMYT, and your mission statement is "Maize and wheat science for improved livelihoods." And we work on everything from agronomy to socioeconomics to value chains, and of course we do a lot of plant breeding. And within our toolbox of plant breeding, we are beginning to use CRISPR-Cas. We know that it's not going to be a magic bullet, as no technology will be, but we also think it's unethical to dismiss any technology without responsibly considering its possible contributions.

Q&A Session

Kevin So as I said, I'm wearing two hats this afternoon. I think we've done a reasonable time of managing our time, so we will invite questions from the audience. But before I do that, I tried to prepare one question for each of our speakers, and I'd like to start with Nigel.

I know that one of the things that will help the public in general to accept this and other technologies is a success that actually benefits consumers; it benefits society in general. So what do you think in Africa might be the first success using CRISPR-Cas to deliver products to consumers?

Nigel I think the Teff example is a really good one, and I think because it's technologically simple to do, and I think it's very visible, very visual. So I think that would be the top of my list. I mean, when we get into disease resistance, for example, with cassava, that's a harder one and you have to do multiple locational field trials, and it takes longer. So to keep my answer succinct, I would go with the Teff. I want to start that next week.

Kevin We look forward to it, eating more Teff at the table.

Nigel Well, and I take that opportunity to say as well that the collaborative agreement we now have with DowDuPont is going to be a really important component of that. So we could take this on ourselves and go with it, but it would be challenging. But with the expertise that is available through this collaboration…, I believe that we can…, and the excellent technology, that we will now be able to take and adopt Teff, I believe we can do this really quickly.

Kevin I see that we have one person at the microphone. I'll come to you in just a moment, but if anybody else has a question, please begin to approach the microphones. And in the meantime, Neal, you talk about using this technology for genome editing and targeted breeding. What do you think is going to be its impact on genetic diversity?

Neal Well, thanks, Kevin. You know, I think the issue of genetic diversity is an important one, that we retain diversity in our cropping systems. We've invested a lot as a community in germplasm banks that have…, whether it's potato or rice or wheat or maize. And we tap into that diversity, and I think the [inaudible] is a good example when a problem arises or there's a new target to be addressed. But when you take an elite variety and then take a very foreign, unrelated variety and try to bring in the value of that trait, it can really slow down the breeding process. And so by being able to actually go in and interrogate in the germplasm banks, find particular genes that deliver that particular outcome and just swap in the right allele into that elite variety, directly into the elite variety, we can actually get much greater use of the diversity that exists in all our germplasm banks. So I think if you look forward to the next few years, if things look well, the value of our germplasm banks will actually be greatly enhanced by the use of CRISPR-Cas targeted breeding technology. I think it's really exciting.

Kevin And, Feng, you work mostly in CRISPR-Cas applications for human diseases. I'm wondering if in your community you face similar discussions about how these technologies can reach the intended public and what you might be able to tell us you've learned from those discussions that might inform us.

Feng Certainly. So CRISPR is a very broad technology. There is application in human health; in basic science research, in the agriculture. And so in all the applications related to human health, there are a lot of discussions about how do we think about translating this into therapeutics, or how do we turn this into a way so that we can very rapidly understand the disease mechanisms so that we can develop drugs based on understanding the disease and then going after the root cause. And so there's a lot of discussion around that.

And one of the important things from some of those discussions really has been the recognition that CRISPR is such a fundamentally important tool. And because it's so broadly reaching, it's important to make sure that it's accessible, the technology is usable by researchers around the world who want to use this to advance their understanding of biology and human health and also agriculture. And so that's why we're really excited to have the opportunity to work with DuPont Pioneer to reach this agreement to really make the intellectual property for the CRISPR technology openly accessible to any agricultural application, so that as many people as possible can benefit from the positive use and also the broad potential of the technology. And the same is happening in the research area as well. And we've been trying to provide sort of nonexclusive licenses to many different parties, whoever wants to use this to be able to advance the understanding of biology, advancement of human health. And I think that's really one of the things that the whole field is recognizing as the important thing to do.

Kevin Thank you very much. All right, we have just over 12 minutes for questions from the audience, and so I'm going to ask you to briefly state who you are and then your question as succinctly as possible. And we'll take, I think, three questions in a row, and then we'll have the panel answer those questions before returning for more questions. And I'd like to start with the young lady over here on my right.

Q Thanks for calling me. My name is Dorothy Masinde. I teach at the Iowa State University, and my field is sociology and international development. And in Uganda we work with small-scale farmers in deep, rural villages of Uganda. This is a good technology that can help Africa and Uganda in particular. I'm wondering. Are you talking to the eventual users of this technology and making this, translating everything into a language that the people, we work with, who are the politicians, who are going to be a roadblock to you transferring this technology to the people and using a language they're going to be able to understand so that they don't fight you back. Having social scientists in the research station is good, but you need to work with the people who are working on the ground, we start understanding what this is all about, so that when you bring this technology, we don't fight you back; we are sociologists and we are waiting for you.

Kevin Thank you very much. Let's take a question from the gentleman on my left.

Q I'm Dr. Alan Koslow. I'm a community activist, and I also do international medical missions, and I'm actually here at this, covering this for one of the local newspapers as a columnist. And my question, first to Nigel, is how long and how expensive was it to do that change in cassava. And, Zhang, is it more difficult to know which gene and what the gene does, or is it more difficult to make the change in the gene?

Kevin Okay, thank you, and let's take more question before we go to answers.

Q I am Juliana Rwelamira, managing director for Sasakawa Africa Association, and we work with the smallholder farmers of Africa, Sub-Saharan Africa mainly. My question is to ask whether the benefits of this very important technology will benefit the post-harvest activity. For example, African farmers are not only faced with production diseases, but in storage they lose the crop to aflatoxins; they cannot use what they have stored for eating or for sale in the market, because the quality has gone down. I think since you are still in the breeding stage, maybe you consider that area as well.

Kevin Okay, thank you very much. We'll come back for more questions, but let's hear from the panel as some answers. Maybe, Nigel, would you like to start the specific questions on cassava.

Nigel I'd like to answer the first question if I can. So, and I can't see the lady that asked the question, but hi, there. So specifically, I showed you the flowering in cassava. That was done by a Ugandan scientist working in our lab, and he did that whole thing—five genes to improve flowering in cassava. So I think it's really important that, for example, Ugandan scientists are doing this and understand the technology and then are able to go back and talk about it. So to answer your question directly, no, we are not talking to the end users about this technology, not yet. We are talking to the National Agricultural Research System and the guys at NaCRRI, Namulonge, that we collaborate with, our partners there. But you are absolutely correct—we must start to do that. This is all very new. Everything I told you about, we've only done… We published our first paper last week on CRISPR-Cas technology in cassava. The flowering is new. Everything is really new to us as well. But that's why I put at the end—communication is really important.

Kevin Neal would like to follow up on that one—right?

Neal Let me add a comment to that before you come to the other cassava part of the question. You're absolutely right. A couple of things are really important here, I think. First of all, languages does matter—right?—the words we use, what resonates with people. We may think we're saying something, but someone hears something else. Something might be frightening to someone and to us it's comfortable. So we think a lot about the right language, how to talk about the technology, how to talk about the products, talk about the benefits, and put that in some context that's meaningful. So we spend a lot of time listening to people, holding stakeholder conversations around the world on many continents to start to truly understand, to share, but to truly listen and understand what people feel about the technology as well and products of the technology.

The last comment about that is that ultimately it's about trust. I mean, we need to get to a point of a trusted relationship with the end user, so we are talking to the end user.

I mentioned the company's focus on farmers but also on the end consumer. And we know that today, and someone said it, you know, the farmer may want technology, but if the consumer doesn't want the product, the farmer has no technology to get access to. So we know that's an important part of it. And I think it's an interesting catch-22. At some level there's a tendency to hold back and not use the technology, let it play out. But I think if people, like folks in this room, see it as a really important technology that can bring value and begin to use it, then I think there's a greater chance to build trust, because inherently I think the world will look in this room and probably look at me and think I'm the last person to be trusted, whether that's right or wrong, because I come from a big, multinational company.

Kevin Okay, let's tackle question number 2, which is about how long and expensive the work on cassava was.

Nigel Specifically do you mean, for example, the brown streak disease?

Q Right. Just for an example—if you want to do a change in the plant, how much time in the lab is best and how much money and human resources is invested? You know, it's including [inaudible].

Nigel Right. So the first time you do something, it's really hard, and it takes longer, but we're past that now into… So we could go… We're going to… We added to two of the genes for the brown streak resistance. We're going to edit now the remaining five. That'll take us about five, five or six months to get the plants. We know exactly what we're going to do. We start it, five or six months to get the plants. I have not costed it out, so I can't answer that question right now. I could probably make an estimate for you, and we can talk afterwards. It is not crazy expensive.

Kevin Okay, anybody have an answer to the question about post-harvest? Anybody aware of targets on post-harvest?

Neal Yeah, there's certainly… There's no question that people have looked at ripening kind of issues, which lead to senescence—right?—and decay. And so there's a lot of interest in reducing waste by addressing those kinds of issues for produce. There's no question. And the specific targets on a crop-by-crop basis and types of challenges need to be a deeper conversation to be had. But certainly it's an area of great interest as well.

Kevin We certainly recognize the value and the importance of targets on post-harvest, and I'm not aware of anybody working on it now, but that doesn't mean it's not happening. And I wouldn't be surprised to hear from somebody in this room that, yeah, we're working on that in one of our crops.

So thanks for those questions. I see we have lots of questions, and we have four more minutes, so we'll start on the left, and then we'll take a couple questions from the right. And I'm sorry we may not have time for all the questions this afternoon.

Q My name is Massolin Egden, and I come from Tuskegee University. I have a question and a comment. Nigel, I was hoping to hear cassava, because it benefits everybody in Africa. Teff is kind of limited to a [inaudible] in a way, although it's gaining momentum, would be a vegetarian industry in America. My question is—we are all excited about CRISPR. At Tuskegee we have utilized it to edit the [inaudible] and the [inaudible] gene in sweet potato, a hexaploid crop. We are all excited, but I think we are going to make the same mistake we made with the transgenic era. We have to start to talk to the public, to educate, to have education. I know you have touched on it a little bit, but we have to have another strategy. You know, as scientists, I can see it, but as a layperson, how do I see it? I've been told a lot of opportunities going to benefit the farmer, going to do that. We need an integrated and a sustainable education now, not talking among us scientists but make sure that we don't make the mistake of non-acceptance and perception that we have with the transgenic era.

Kevin Okay, thank you, thank you very much. I think we'll only have time for one more question, so apologies to everyone else who would like to, but you can approach us afterwards if you have time. And let's just take one more question, and then we'll get some answers, and we need to wrap up.

Q First of all, thank you for accepting my question. I am Erin May, a fifth generation Kansas farmer. My research for the Global Youth Institute… I was accepted to come here from Kansas, and my research was on plant science in Ethiopia utilizing CRISPR. My question is—Some people are anti-technology or they're uninformed of technology. How can we give them positive reinforcements of the use of CRISPR while telling them what the negative repercussions and effects might be, giving them a positive aspect?

Kevin Okay, thank you. Maybe, Feng, would you like to try to answer these questions?

Feng Sure, I'll try, and please feel free to jump in. I think both the questions are a little related, which sort of underscore the importance of communication and they underscore the importance of getting the right information, getting the public to really understand what a technology is about, what the strength of the technology is, where we are, and then what are the challenges that remain that we have to solve with the technology. And so I think, as the whole community of scientists as well as policymakers and application scientists and developers, farmers, as a community together, I think we all have a responsibility to get sufficient information and get the right information so that people have a full understanding of what the technology is. We face this not only in agriculture but very much so in therapeutic applications as well, applications of technology for treating diseases at different stages. So it's not the easy thing to do, but I think if we all do our part and we try to communicate things in a clear and responsible way, that will pave a long way for what we're trying to do.

Please feel free to add to that.

Neal No. I think that's key. I think we need to certainly start by focusing on the really meaningful benefits. You know, you think about therapeutics, and you get the benefit of a life-saving application. No one's going to question… People will then question what the risks are, but you've got to get interest in the benefits, and I think the same thing is true for agriculture. What are the really compelling benefits? And there are a number. And then we need to talk honestly about what the risks are. So, you know, whether it's on websites that provide information or other kinds of dialogues, we helped sponsor an event called "CRISPR Con" a couple of months ago, brought together many, many different voices about the issues that might concern people about the products of this technology coming to the market. So we need to have those events continued.

Kevin And I'm afraid time is up. It’s really… We’ve consumed our time, and I think we’re going to have to cede the podium to someone else, but I'd really like to thank everyone for the excellent questions, for your attention, for your interest in this exciting technology, and let’s thank the speakers one more time.

Cynthia Milligan

That was very interesting. The potential, I think we would all say to you all, is very exciting, and the speed is breathtaking.