Questions and Answers from Lemaux Talk

Question (?): If I'm not mistaken, there are some examples in which taking plants that have certain methylation pattems through seed again, you can change the methylation pattern. Have you seen that with the transformed plants that have altered methylation patterns?

Answer (LEMAUX): We are just now trying to take plants with methylated transformation events to the next generation. And we'll look at those. We've been in close contact with Ron Phillips who has done a lot of this work in maize. And they do see some changes, but many of those methylation changes are heritable. And our prediction is that most of the changes we see here in our own work are also going to be heritable. We're going to see them in the next generation. We will also continue to follow out these methylation through to the field material. So that when we see an impact in the field we can refer that back to a molecular change that we know occurred in that set of plants.

Question (R. OLDEMEYER) I'm from a different era. You indicated that a backcrossing technique would take too long. I would remind you that in five years a modern gene can be placed in (agronomically useful) sugarbeet, and cannot some of these transgenetic traits, after they're once discovered then isolated, be incorporated into the cultivars that you might want to use, rather than going through the process of transgenesis again?

Answer (LEMAUX): I used to work for a corn seed company. We use to have these arguments all the time. And now I have arguments with barley breeders. There are divergent views. Some breeders would say, just give me a transgene that expresses, I don't care what it's in-and I'll put it in to my favorite variety. And I think there is some value to doing that, but the closer we can come to delivering a transgene that's expressing well in something that is useful in the field, the less you're going to have to do introgression to get it in. The other thing is that some of the

problems that wea are encountering are not going to go away with crossing. So the methylation issue is probably not going to go away necessarily. And the somaclonal variation issue will be solved to a certain extent unless a variant is linked to the transgene.

Question: (R. OLDEMEYER) . I lived through the period and history of mutation genetics, so I'm a little concerned that you're trying to go too far. I don't know of any cultivars that were created directly just by shooting a bunch of gama rays in it.

Answer (LEMAUX): We're not looking to be able to deliver in the first generation something that's going to be identical to the cultivar that you started with. But, like I said, the closer you can come to that objective, the better off we're going to be.

DISCUSSION SESSION

KAFFKA: I've asked three people to think about some of the issues that were raised by previous speakers, and, perhaps, to suggest some ideas and thoughts of their own. Earlier this afternoon I suggested that we might want to think as well about what might be best for the American industry with respect to research, that is domestic research in this country, tapping the abundance of scientific talent that so far as I can tell is hardly touched at all with respect to the sugarbeet industry. We're going to start off again with Petty Lemaux. I've asked Peggy to be both a speaker and a panelist because Peggy has workedin industry; and now holds what may be a unique position in the United States. She's an Extension Specialist with a focus on molecular biology at the University of California at Berkeley, and works with scieintists throughout the UC system as a whole. Also participting are Bill Dolley, who is with Moribo and Crystal Seeds, and who does a number of things from classical plant breeding to some molecular work. Bill is a

knowlegeable scientist who is also is sensitive to the viewpoint of farmers. Lastly, Robert Lewellen will comment. He is one of the mainstays for the California industry in terms of generating new varieties and new germplasm, and one of the most knowledgable people in the world about the Beta genome and the history of classical breeding programs. I think each of these respondants will provide valuable reflections on this new and rapidly evolving technology.

PEGGY LEMAUX: I thought that J.R.Stander's talk (earlier in this symposium) was outstanding. It made many of the points that I think are important to make. Although my personal work invovles cereals, I talk with many different agricultural industries in California. And one of the important messages for any industry is that you really have to take a broad view when you're looking at molecular strategies. Certainly, we've seen evidence that we can do some things at the molecular level. I think J.R. Stander mentioned some that are currently more obvious. We'd done our homework to allow for these breakthroughs.

I haven't always worked in plants. Prior to working in plants I worked in mammalian systems. And there we've done a lot more homework, for a number of reasons. One is that we're dealing with a single organism, the human being, and trying to improve health care. But the second is that a lot more money has been put into basic research in the human system than in plants. When you think about it, we're dealing with lots of different plant species and lots of different pathogens. Because of this diveristy, we have to be very selective about what we do. We have to understand it. We can't just take any gene and put it in and hope that it works, because it probably won't. So, I think it's important to take the long view.

Now that I am working in a public sector institution, I think that we really have to form partnerships. Not just because we need them, but because industry needs them as well. Obviously, in industry, if you're working on a particular crop and you want to change some

agronomic property, you're not going to know all the basic biochemistry that you need to do that. You're going to have to depend on your partners in the public sector who can get money to do basic research. In the public sector we're going to depend on industry. In my position as a Cooperative Extension Specialist, I don't have the money or the resources to take things out into the field. So, I'm going to depend on industry to be a partner with me. But I think it's important to recognize that the relationship is not one-sided. I mean that as a public sector scientist I don't need industry more than they need me. And as Steve Kaffka pointed out in his presentation introducing this symposium, there are successful models for public-private consortia. To me that's the way we're going to solve big problems in agricultural biotechnology. And unless we do we're really not going to be able to make the kind of strides that we need to apply molecular techhniques. We're going to get some quick fixes, but others are going to take a lot longer because we're going to have to do a lot of homework to understand them. So, if you just look at particular biotechnology applications and say, for example, that we don't need herbicide resistant plants, or we don't need this particular application—that's taking a very narrow view. Biotechnology may not work for a particular application, but there are many different areas where this technology can come to play.

One partiuclar application that I always like to talk about is the use of a crop to make novel compounds, not what it naturally does, but a synthesis pathway from a different species. This is something we cannot do without biotechnology. We can't keep using non-renewable resources to make everything needed in modern societies. For example, we can make biodegradable plastics in plants, industrial oils, and a lot of other things. And I think this is one need in agriculture that we're going to enter into with the advent of these genetic engineering technologies. So I really think it's important that we all keep an open mind.

Public acceptance and regulatory issues have been mentioned by Chris Wozniak in his presentation. My views differ from Chris'. Here in the United States, public acceptance will not be a big issue. I think once people see these products in the marketplace, they see their value. It will really become transparent. It will not be an issue anymore. People in Europe are struggling much more with these issues. Green Peace has been more successful with its anti-biotechnolgy campaign there. One reason why public opposition has not occurred in the United States to the same extent because we've been very pro-active here in the United States. Scientists, cooperative extension specialists, and public interest groups have been telling people about these technologies and helping them understand them more thoroughly. An equivalent effort has not been made in Europe, so public will take longer. In the end if people see a value, either in their pocketbook or an environmental value,opposition to biotechnology will become less of an issue. regulatory issues will also be left by the public to the appropriate sector. Regulations in the United States started out being very rigorous and tight. I think they're easing and I think that as we get more experience working with these plants, this trend will continue. So I think the regulatory issues will go away.

The issue that most concerns me, particularly in application to crops in California, is intellectual property. This is a new issue for agriculturalists who really haven't been confronted with the limitations assocaited with rapidly increasing patent restricitions before. They're not really familiar with what's going on. A lot of the intellectual property is being held by companies. Both the public and the private sector need to recognize that we need to work together to be able to use these pivotal technologies to more efficiently develop new products. I hope that we can all work together to use this technology to its fullest.

DOLEY: First of all I'd like to thank Steve for inviting me to participate in the panel here. It's quite a timely topic that we're dealing with with the introduction of Roundup Ready® and Liberty Link® sugarbeets into the official testing system this year. So, there's a lot of new issues that face not only the plant breeders and sugar companies, but the farmers as well. I'm not a molecular biologist, but I do spend a lot of time thinking about applications of molecular biology in plant breeding and what it means to our business both as a seed business and as a sugar business. It's very exciting to have these new tools available. And that's what I think of them, as new tools. Extremely powerful new tools. Not only of great use to plant breeders but also to plant physiologists and plant pathologists. One of the benefits, aside from coming out with new varieties, is the speed and the rate of acquisition of basic knowledge. We're learning things so much faster about biology than we did in the past, it's kind of mind boggling where it will lead us. Even though today's crops look pretty much like they did 50 years ago, it's difficult to predict what our crops will look like 50 years from now. There are two aspects to molecular biology that I find very exciting and positive for progress in crop agriculture. One is its use as a tool in the way we're going to understand things such as host- pathogen interactions. Also understanding how sugar gets accumulated in the root and being able to manipulate that. Those are potentially quite exciting breakthroughs.

With all due respect to the views of Dr. Ken Fry of Iowa State, (quoted by J.R. Stander earlier during the symposium) that the primary gene pool for crop improvement will always remain the conventional gene pool, I somewhat disagree and I think that one of the big breakthroughs made possible by biotechnology is that we now have a universal gene pool. The genes of all crops are now shared and there are no minor crops any longer. And this is a big boone to crops like sugarbeets and other minor crops which have not had a big research base to

develop biotech traits. But when someone develops a trait for corn and it can work in beets, it's a big plus for the beet industry. Another interesting consideration from a breeding aspect is that if we can come up with some effective transgenes to control diseases, particularly fungi in this country, we may end up with some base germplasm which is essentially immune to fungi and allow plant breeders to essentially breed just for productivity—yield and sugar per acre. That will allow production of sugar per acre to go up at a much more rapid rate because we'll only be working on the one primary trait of interest and not all the accessory traits that really do slow breeding down.

While I'm very excited about these positive aspects of biotechnology, there are also some potential negative aspects. At what cost to the farmer and to the consumer will these improvements come to us? As Peggy Lemaux just mentioned, the important aspect of intellectual property rights has not been satisfactorily resolved. Anyone who has been looking into this area realizes that there is, literally, a mine field of intellectual property rights associated with these germplasms, whether it involves constructs or genes or lines. So there are patents on promoters and patents on coding sequences and patents on transformation technologies and patents on whole genotypes based on utility patents. And from discussions at this meeting, it appears that this intellectual property issue, the cobweb of intellectual property that's out there is already beginning to stifle basic research in the public arena. Anyone in the private sector must be aware, if they are in research, of the value of basic research, particularly that done in the public sector, which the private industry can't afford to do themselves, and where they really count on the public sector. In the long run it's going to hurt everybody if public sector research can't go forward because it is encumbered with intellectual property issues. So that's an issue I'd like to hear comments from as we get into the discussion here from people in the public and private

sector. How we can rectify this situation and allow research to go on without so many intellectual property obstacles.

I work in the seed business, but I also work for a sugar company. Our sugar company happens to be a cooperative, so we have a somewhat unique perspective when it comes to sugarbeet farmers. Our mission as employees of the company is to maximize the growers' returns per acre. And we can do that by increasing the productivity of their land, but also by reducing the inputs that they use to produce a crop of beets. We look at the cost of seed, the cost of chemicals, the cost of fuel, and whatever, as inputs to be reduced; anytime we have an opportunity to try to influence their cost we try to do so. In contrast to other business organizations, we may be trying to force the cost of something down as opposed to up. One of the reasons we stay in the seed business is to have some influence over the cost of seed. And one of the fears that I have with all the intellectual property restricitions involved now is that the co-op and the growers are going to lose some control of seed costs, because new variety development will fall into the hands of a few large companies that have all that intellectual property in their hands. So my question to the group, is where are we going as an industry? Where do we want biotechnology to take us and do we want it to take us there or would we like to tell it where we want it to take us? Thank you.

LEWELLEN: My concern is with intellectual property rights. Where does somebody in a public breeding program fit into this? I will never be a molecular biologist but I'm very enthusiastic about the products of molecular biology. I think that as these genes become available they're going to be very useful to all crops, but particularly sugarbeets in enhancing our productivity, eliminating diseases, and protecting the environment. I have 30 years invested in a conventional

breeding program based upon population improvements. One of the tenants of that program is that we ingress genetic variability. There have been only two places to obtain genetic variability: within the crop species itself and then from the species you could outcross *Beta vulgaris* with. So that in sugarbeet that would be all of the genus *Beta*. In contrast, one of the things that's usually given as an advantage of molecular biology transformation technology is that this will give us additional genetic variability. My concern is when, in a public sector breeding program, should we start utilizing some of these genes from biotechnology? When, for instance, do I start incorporating a gene or genes for herbicide resistance and virus resistance? Right now there is not cause for a great deal of concern. In sugarbeet, we are considering very few new genes and these genes can be very quickly moved individually into commercial breeding lines. But 10 years from now, we probably will have hundreds or thousands of new genes, each requiring, if handled separately, an individual backcrossing program. As a population breeder, somebody that works in population improvement, I think we are going to have to handle some of these new genes as quantitative traits. And that means we're going to have to put them into populations and have them in many forms, or have them in segregates in our population. So that as we pull more advanced material (parental lines and their parental lines) out of our breeding programs, (particularly for use by the commercial breeders), that these lines have combinations of new transgenes that are useful. So I guess my concern is more along the lines of intellectual property rights. What will the problems be with patents, what will the problems be with patent infringements, and who besides the very large companies who own the patents, really will be able to use these genes?

OPEN DISCUSSION AND COMMENT

CHRIS WOZNIAK:. Just for the sake of correction I wanted to mention something Peggy said. I don't feel that public perception or negative public perception will influence the arrival of commercial transgenic sugarbeets in the U.S. However, I do feel that will be the case in several countries in the EEU. However, I expect what I call noise, in both the U.S. and in other countries and I'll give you a few examples that are about to occur or have occurred. This past year one of the environmental groups held one of their meetings on top of a transgenic plot. And, of course, trampled it to death. Recently, or actually in the very near future, there is a conference going on in the state of Nebraska to consider separate labeling for transgenic products that would hopefully mark any product that has any bit of food, fiber, whatever, that came from a transgenic plant. In addition, I know people in the seed sales business and in co-op's who have been contacted directly by Green Peace, for example, with what I call propaganda, asking them not to promote the sale of any transgenic seeds. In this case, largely corn and soy beans in that arena. But, all in all, through that noise, I do think that we will see transgenic sugarbeets by 1998.

PEGGY LEMAUX: Public acceptance is something I could talk about for an hour. I think it's important to remember that this is not the first controversy in the history of agriculture and food. There have been a lot of controversies. And there are always people who object. There have been studies analyzing public acceptance. Both in the United States and Europe. And far and away the vast majority of people are not troubled by plant biotechnology. There is a core percentage (about 10%) of the people in the United States who have serious problems with genetic engineering. They're the same people who are concerned about fluoridating the water and a number of different issues like that. Those people are going to keep their mind set. And that's OK. That's their business and they're certainly entitled to their views. But the vast majority of people, about 60% in these polls, really are reasonably enthusiastic about

biotechnology. The other 30% remain ambivalent. They're waiting. And I think those are the people who are going to gradually become supportive as useful products come out. The profile in Europe is not grossly different from that in the United States. The same polls have been done there. Results are going to be published very soon in *Nature/Biotechnology*. In some countries there is a severe problem. There it will probably take a while to get over public reaction, and maybe they won't ever.

Labeling is another interesting issue that has been brought up off and on by different groups. I think here in the United States, because we have fairly strong governmental agencies that the public trusts, like the Food and Drug Administration, that have taken a pretty strong stand, that labeling will also become a non-issue.