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Interview with Kevin Tomaselli

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Kevin

…What can biotechnology do for the common man? Is that really the question, more or less? Okay, biotechnology really has a lot to offer to everyone in society, this is a scientific odyssey that began really about 20 years ago and was initially focused in the pharmaceutical, in the medicines field. And a whole industry sprang up in the late 70's with the focus using the power of modern biology, molecular biology, to create new medicines that can treat new diseases that have largely been unmet in the clinic and this industry from its pharmaceutical and medicine beginnings has spread into many other areas beyond medicine into the world of diagnostics, into the world or agriculture, and in the context of agriculture, I'm sure your aware of efforts to enhance the productivity of farmers, the modification of crop plants, of food plants, and even extending into the ornamental world of agriculture of flowers and decorative plants, so biotechnology today touches virtually everybody at some point in their lives.

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Every living organism is blueprinted by its DNA, all the genes that encode all of the working parts of the organism and what modern genetics has been able to do is to identify which genes lead to different traits in the organism and to isolate those pieces of DNA for the genes themselves and actually manipulate them. Move them from one organism to another, change them slightly, tweak the properties of that particular gene, and so in general, we can take DNA from a human organism for example and you can put it into a lowly bacteria, you use the bacteria as a machine for example to produce the protein in the case of the medicine, in the context of plant, you can take a plant gene, or even an insect gene, or in an extreme case, a human gene. And put that into another plant and you spell on that plant the properties that the plant doesn't normally have and if you wanted to, create in that plant you would have to go through a very lengthy process of breeding and then selecting the traits that you want. So what modern genetics does is really the same that breeders do and that is to alter the genetic makeup of

the plant but to do it in a very methodical way and a much more accelerated way so that you get to the endpoint, the desired trait, much faster than going through generation after generation of breeding and selecting, breeding and selecting. So it's really in the truest sense the natural way of producing the traits in a plant or a flower that you would like to have for the benefit of either the consumer or the farmer.

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The reason we would go through the process of engineering for example in plants, is there are many benefits that can accrue as a result of changing the properties of the plant. You can make the plant hardier, you could make the plant resistant to drought conditions or cold conditions, climate conditions. Essentially what you can do is you can help the farmer be more productive, so the hours spent and the amount of land dedicated to a particular crop, you could for example increase the yield or decrease the effect of pests or reduce the amount of insecticides that might have to be used in that plot of land, and we all know that insecticides in general, because they can kill insects, are generally nasty compounds. So there are a number of advantages that you might supply to the grower to make it easier for him to supply his crop, now from the consumer point of view, there may be also the benefits, the foods may last longer on the shelf, they may stay fresher, they may taste better, they may look better. In the case of ornamental plants, they may be more attractive, they may have colors that they normally wouldn't have, they might stay alive in a vase after they've been cut for longer. Imagine if you had a rose, when you gave your loved one a dozen roses on Valentine's Day instead of the roses being wilted in four or five days, there are still in beautiful bloom two weeks later. So it's really the types of qualities or traits the plants have, whether it be a crop or food plant or an ornamental plant as in the case of a rose.

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A very important phenomenon is cell death. If you think about it, in my body, in the amount of time it takes me to finish this sentence, probably tens of millions of cells have gone undergone cell death and it turns out that this is a very fundamental biological process and it's similar from humans all the way down to simple organisms like fruit flies, or a little worm or nematode, all the way down to plants. And there was a very surprising observation that was made that if you take genes that function in human

cells to control cell death, and put them, express them in plants that you bestow on the plants a resistance to cell death. Now what value is resistance to cell death in a plant? Well, if you think about it, plants are out in the wild and they're exposed to many nasty conditions, whether it's too much sun, not enough water, too cold, heat, nasty pests be they insects or fungi that get into the root so the plant needs all the defense it can muster, in order to survive and grow and become a food crop or an ornamental plant. Well, it turns out that if you make the plant more resistant to cell death by putting a human gene into the plant, and having it take part in the plant's biology if you will and the plant is much more resistant we have found in studies we have done and taken into the field, more resistant to a number of stresses, including drought, high salt content in the soil which is not good for plants. Cold stress, fungal bacterial possibly insect pests that attack the plant so we've been very pleased and surprised that this fundamental biological process which goes from humans all the way down to plants, can actually be manipulated and produce benefit for the plant which is then going to translate into benefit for the farmer, the grower of the plants, and ultimately, possibly to the consumer as well.

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So this was a surprising finding to us that the genes we work on for human medicine could have value for plants. And because we're a pharmaceutical company, we need to look at other opportunities for commercializing this surprising observation. So we've actually talked to a large number of companies that are focused on the agriculture business and there's been a tremendous amount of interest to in the possibility of using these genes to benefit plants both food plants and ornamental plants. And from the ornamental point of view, here in San Diego, we have a thriving ornamental plant business. Most of the poinsettias that we have in our homes during the holidays are produced up north of San Diego here in Encinitas at the Ecke Ranch, and we've spoken to, for example, Ruth Kobyashi, about the possibility of making these genes available to try to improve the poinsettia plants. Could they, for example, be more robust when you have them at home, could they last longer through the holidays, could they be made to grow more easily in the climate of Encinitas and make it easier for the grower. So we're very excited, but it will take a collaboration between Idun, which is a pharmaceutical company, and other companies like Ecke, for example who are focused on agricultural and

know everything you need to know about how to get the most out of a plant.

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I think biotechnology has a big role to play in the future of San Diego. We're fortunate that San Diego has become a hotbed for many types of technology including biotechnology. Ten years ago, most of the biotechnology was really concentrated in two places and in fact, two very desirable places to live. San Francisco and Boston, and here in beautiful San Diego, and we're lucky now that this has become a hotbed for biotechnology. A lot of companies are getting started here. In the last five years, the number of companies has grown to approximately 200 companies, there's a lot of venture capital interest in starting companies in biotechnology. There's a great university environment, UCSD, Salk Institute, Scripps research, San Diego State, a lot of academic science going on here and this is an outlet, the biotech community, the creation of new companies to commercialize the inventions and discoveries in all of these academic labs, it's perfectly natural that San Diego has become a biotechnology hot spot.

Biotechnology brings a whole diversity of job types. For example, in our company at Idun, we have research scientists, chemists, analytical people, we have business functions within the companies, the finance, accounting, shipping and receiving. We have the communication aspects of companies. There's a real diversity of job types in biotechnology, it's not just a bunch of scientists huddled around an experiment, but it's all the components that go into a real company, real people, many different types of jobs, and this will create a lot of opportunities for the residents of the San Diego community.

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Genetic modification of organisms, including plants is front page news in many cases. There are a lot of issues that go into producing safe and effective alternatives for farmers and consumers and the emphasis should really be on safety. I can tell you that in the human pharmaceutical, human medicines, the food and drug administration which has the overall responsibility for that, places as much if not more emphasis on the safety of the products so that we don't have that thalidomide story that we had in the

sixties. So safety is the most important aspect of new medicine discovery. And the same should be true with plants, and the introduction of genetically modified plants into the world definitely does come with issues that need to be addressed. Would they grow out of control, would they actually have some traits that aren't beneficial, they're actually detrimental, and consequently there has to be a diligence, a scientific diligence, in the production of these new commodities, these genetically modified plants. And I think that essentially we're on a learning curve, that five years ago the processes were not all that well worked out for determining the safety and the long term safety of genetically modified organisms. And people would say look I am worried about this, I'm concerned about this and I want to know that it's not only going to be safe today but it's gonna be safe five years from now. And the scientific community listens to these concerns. Scientists aren't just concerned with the almighty dollar, they want there products to be safe and effective. And so now we're coming up the learning curve, we've heard the concerns and now people are responding. Processes are being put in place, they're looking very carefully and scientifically I would stress at issues of safety.

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Some people might take the position that it's unnatural for a human gene to be anywhere else but in humans. Let alone in a plant. But in fact, even in nature, genes jump from organism to organism, they're actually natural genetic mechanism where a gene of an insect might work it's way into the genome or the DNA of a plant. Or a gene of a virus might become part of the human gene or vice versa. Essentially a virus has stolen all of their genes from the organisms that they infect, whether their humans or animals or plants. So gene swapping is not an unnatural thing, therefore it should be no surprise that human intelligence should be able to understand how to do that more efficiently and to the benefit of mankind going forward. So I personally don't see anything unnatural about moving genes from one place to another. As long as they're safe and beneficial because nature does that anyhow.

Long term risks are indeed difficult to judge. And so it really becomes a risk benefit issue. The same is true in pharmaceuticals, in medicines, if you have a grave disease that gives you a fifty percent chance of dying within the next thirty days. You would have no qualms about taking the medicines that is gonna decrease that risk substantially but is going to increase the risk

of you getting cancer ten years from now. That's a risk benefit. And for you, the patient, you'd much rather be alive and face the increase risk of cancer later. The same is true in the context of genetically modified organisms, for example plants. How are we going to know what will happen ten or twenty years from now? The fact is that we can't, until ten or twenty years have elapsed. We can model what might happen, we can show that the product is safe in the near term, we can take safeguards to prevent the unlikely from happening, so in human medicines it becomes a risk benefit analysis. Is there enough food supply to support the world's population out twenty years from now? And if the answer is no, that's a tremendous risk. So if there are ways we can increase the output or the productivity of food crop production to meet that very important demand, that's where risk benefit comes in.

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I think it would be very important to harness the benefits that biotechnology can create. Because there is at least a possibility that things can spread and go out of control so there has to be diligence again and I stress scientific diligence, not emotional diligence, in understanding what the risks are and putting up the safeguards. We don't want America's indigenous corn that might have a certain type of value to become forever and irreversibly contaminated with a corn trait that might be beneficial in another crop of corn. So there has to be barriers that can limit the presence or the spread of genetic modifications and that certainly is something of high concern that people should be paying attention to and should be diligent about.

I think the beauty of science in general and biotechnology in particular is the unexpected, there's so much we don't know, so even though today in 2002 we've sequenced the entire human genome, we know that thirty thousand protein molecules the actual years and wheel and pulleys that function in our bodies exist. We don't know how they relate to each other in every aspect. So that means that there's a lot unknown and a lot to be discovered. And it's the unexpected, for example, it was completely unexpected that these human genes that function in cell death in our bodies could function in a plant cell to also control cell death and bestow on that plant disease resistance or drought resistance, heat resistance, cold resistance, very unexpected finding and that I think is really where the excitement and the power of biotechnology is.

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