Biotechnology: What It Can and Cannot Do

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Biotechnology: What it can and cannot do. This presentation won't be all "hype" or a sell job; it will be my perspective on what is possible. There are two goals. The first is to acquaint you with genetic engineering; what it is, how it's done, and what has been accomplished already. Second, I would like to explore those areas of particular interest to you and what may be possible to accomplish in the future with biotechnology.

Genetic Engineering

Genetic engineering is simply the alteration of the genetic makeup of any organism. It is important to dispel the myth that it is anything new. Mother Nature has used it for millions of years. In fact, evolution is simply genetic engineering applied to the formation of new types of organisms that compete more successfully in nature. Man has also used genetic engineering in a crude fashion for centuries. Almost all of the breeding programs for both plants and animals have been simply the application of crude genetic engineering methodologies to improve the different breeds that man has used in his various agricultural and industrial product formation.

The new methods of biotechnology and genetic engineering are vast improvements over past methodologies. We are now able to select exactly which new traits will be used. This results in the generation of plants and animals in a much faster fashion and, in fact, in a much better way. Thus, there should be less fear than there has been with conventional types of breeding programs, because it's impossible to define exactly what the new traits will be and what other traits will be carried along with the traits we are looking for.

In order to discuss genetic engineering, it is important to define three terms that are key players in the use of genetic engineering. These terms are "DNA," "RNA" and "proteins." These three form the basis for all of the work that is done in genetic engineering. They represent the flow of information that is used to generate or create an organism. These are the key players that must be altered in order to alter the organism, or parts of an organism.

DNA is the genetic blueprint for any living thing. This DNA contains all of the information that makes you "you" and me "me." This information is contained in segments called genes. There are roughly 100,000 different genes in humans and approximately that many in other types of large mammals. The DNA forms two complementary linear strands. These two strands then twist to form the famous double helix which contains all of the genetic information within an organism.

If DNA is a blueprint, then what role does RNA play? First, there is a need for building instructions as well as a blueprint. That blueprint is the RNA. Each different cell needs only about 10,000 different genes. Therefore, RNA is made only for those that are needed. RNA is a single-strand copy of DNA. All of the information that is in the DNA is still present, but in a form that can be utilized by the cell to form various kinds of proteins and other materials that are needed for the cell.

So, we have a blueprint and the instructions; the next thing we need, of course, is the materials. Those materials are, for most cells, predominantly protein. The information in the RNA is converted into the formation of various kinds of proteins. Proteins are the main components of living things. They are used for structure, for catalysis, as well as for almost all of the other functions that a cell performs. Proteins are made up of 20 different amino acids which are connected in a linear chain. This linear chain then folds into a three-dimensional structure which is the active form of the protein. These three-dimensional structures are very complex, and even today we don't really understand why and how the amino acids in the chain fold into this particular three-dimensional structure.

So, these are the main players in this drama. The goal of most genetic engineering is to put the genetic information into a cell or an organism that will result in the production of a desired protein. Nature does this by copying the double-stranded DNA into a single-stranded RNA. The single-stranded RNA is then converted into a linear protein sequence. The completed protein then folds up into its correct three-dimensional structure. For genetic engineering, we have to work in the reverse direction. We usually have a protein sequence which can be used with a computer data base to determine what should be the RNA sequence. That RNA sequence is then used to search for, to identify and, finally, to isolate the DNA codes for that protein. This presumably will result in whomever is doing the work becoming rich.

Once we have identified the gene that we are looking for, the work has only really just begun. The DNA in that gene must then be amplified and placed into some vector that we can use to alter a cell or an organism that we are interested in. In order to do this, we have to take the gene and insert it into a plasmid. A plasmid is simply like a mini-chromosome that bacteria carry, usually to create an antibiotic resistance for them. Using various kinds of splicing methodologies, it is possible to cut the plasmid, insert the gene we want and reinsert the plasmid back into the bacteria. This is then the cloned gene and can be used to multiply the plasmid many, many million-fold to get large quantities of the DNA for the gene we're interested in.

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Accomplishments to Date

What has new genetic engineering accomplished to date? First of all, we can look at medically important products. Remember that most of these medically important products are proteins. The first product on the market of major significance has been human growth hormone. It is important to note that it really has not been much of a money-maker for the company involved. It is also important to recognize that this particular product came at a very critical time for a number of people who were using human growth hormone because of dwarfism. This is because the human growth hormone they had been using was isolated from human cadaver pituitaries, and it was found that some of the material used previously was contaminated with a slow virus that caused the inevitable death of some of the patients who were using that particular material. So, the human growth hormone now available is not only cheaper because it's much less expensive to produce; but it is also much safer, because it can be verified to be free of any contaminating viruses.

The first medically important product that has significant monetary value has just reached the market. This particular product is called tissue plasminogen activator (TPA). TPA dissolves blood clots that form in heart attacks and various kinds of strokes. Unlike many of the current products used to dissolve these clots, TPA does not attack other tissues. So, although it is twice as expensive, it is also much more specific and, therefore, in many cases may be easier to use. This is particularly true for EMT's and those people who would treat patients very early in the heart attack situation before they actually reach the hospital. The advantage of TPA is that it can be used intravenously without worries about damage done to other tissues and can be used by EMT's very early on.

Altered Organisms

Another area of genetic engineering that is beginning to have a major effect is in what one would have to describe as altered organisms. We will take a look at four different types of altered organisms which have been created by genetic engineering. The first of these is the creation of specific bacteria for toxic waste degradation.

Early work demonstrated that it was possible to create a species of bacteria that were altered such that they would destroy certain kinds of petroleum waste. Clearly this was a minor use and has not yet been exploited commercially, or even practically. A recent publication has demonstrated the creation of a bacteria for which a specific toxic waste degradation pathway has been generated. This particular bacteria was created through the use of borrowed genes from several different bacteria, all of which could partially degrade certain kinds of chemicals, particularly PCBs. Unfortunately, none of these bacteria could completely degrade the toxic waste; therefore, eventually the bacteria would die before the complete detoxification of the PCBs was accomplished. What these scientists did was take each one of these separate genes from the various bacteria and put them into a single bacteria. So, it is now possible for this bacteria to completely degrade into various nontoxic compounds, the PCBs, and in the process to use those compounds for growth. Thus the bacteria is self-limiting; after the toxic waste is completely degraded, the bacteria no longer have a food supply and therefore stop growing.

A second and potentially very useful creation of altered organisms has been the generation of herbicide-resistant plants. These herbicide-resistant plants are specifically created by putting in a gene that can do one of two things to a herbicide. The first is that you can put in a protein that is actually resistant to the herbicide itself to replace the normal protein; therefore, the herbicide does does not affect the plant. The second method is to put in a protein that will specifically degrade the herbicide before it has a chance to affect the plant. Current research has generated plants in both categories which are resistant to a number of different herbicides. The plants are able to resist at least two to four times the normal amount of herbicide put onto the plant during agriculture operation. Many plants falling into this category are in the process of small field trials. It would be expected within the next few years, barring any unforeseen problems, that these plants will become available on a commercial basis to the farmers in this country.

A recent publication in the journal *Science* has demonstrated the ability to create and alter the plant in a very different and very unique way. These investigators introduced the protein luci ferase from fireflies that generates the light in those insects. The protein was genetically engineered into the plants to demonstrate that it was possible to show that very different kinds of proteins can still be expressed in the plants. Although this particular demonstration on the surface would not appear to be particularly useful, in fact it may be very useful. Because of the ease of detecting the expression of protein, it may be used as a marker to demonstrate where other kinds of proteins are being made. This is still one of the major problems of genetic engineering to be able to genetically engineer the organism to produce the protein in the right cell type.

The next example I would like to present is one that is much more closely aligned with this particular conference. That is the generation of animals that contain an extra copy of the growth hormone gene. This has been accomplished very successfully in rats, and to some extent in mice. It has also been tried in a wide variety of other animals with varying amounts of success. Rats and mice have been very successfully transformed using genetically-engineered growth hormone genes inserted into the genome.

The results with beef, sheep and pigs have been much more ambiguous. It appears that it is possible to successfully insert those genes into the animal; but whether the gene will have an effect on the animal's growth has yet to be clearly shown. There are certain animals, among the many animals where this has been attempted, for which it has been successful. Unfortunately, the ability to control the expression of the growth hormone gene, and therefore be able to regulate the growth of the animal, has been much less successful. In fact, in sheep today it is not clear that anybody has been able to successfully demonstrate the growth hormone gene having an effect on regulated growth. This points out a very important fact; just getting the gene into the animal is not sufficient. In fact, the most important part will be to control the expression of the protein such that it is expressed in the right tissues and also expressed at the right time to cause the desired effect.

Disease Detection

Another very important area where genetic engineering will play a role is the detection of certain kinds of diseases. These diseases tend to be viral in nature because viruses are much more difficult to detect. This method of detection will be based on the ability to detect the presence of specific DNA segments that can only be found in the virus. In fact, new technology using various kinds of DNA amplification techniques suggests that it may be possible to find one viral particle in up to a million different kinds of cells. Thus, our ability to detect the presence of viruses in meat and in other kinds of tissue will be vastly increased. This will also allow the early detection of various viral diseases before the animals are either imported into this country or before new animals are introduced into other herds, where the disease could then spread.

The detection of genetic diseases will also be an important use of genetic engineering/biotechnology kinds of techniques. Genetic diseases such as muscular dystrophy, cystic fibrosis, sickle-cell hemoglobin, Huntington disease and TaySach's disease are all possibilities for the use of genetic engineering methodologies to detect altered genes in people who either have the disease or are carriers. This methodology will easily be extended to other kinds of animals, particularly farm animals; and instead of looking for defective genes, what may be more important to do is to be able to find genes that carry certain kinds of desired traits. This will allow much easier access in breeding programs to information as to which animals have the desired traits at the genetic level and may allow for a rapid improvement through traditional breeding methods if it is found that genetic engineering methods are insufficient to generate the trait that is desired.

These are just a few of the thousands of projects worldwide which are going on using biotechnology/genetic engineering techniques to change the genetic makeup of various kinds of organisms.

Areas of Particular Interest

Finally, let us look at areas of interest to this particular conference. I see a number of areas where biotechnology can and probably will have an impact in the field of meat science. These particular areas include: 1) gene markers, 2) ruminant bacteria, 3) fermentation, 4) preservation methods, 5) processing methods, 6) alteration of fat/lean ratios, 7) composition of lipids, and 8) different muscle fiber types.

In the area of gene markers, the methodology will certainly follow the expression of certain kinds of genes in various kinds of tissues. These types of markers will become increasingly important as we explore in greater detail the factors that go into the generation of different meat characteristics.

The role of ruminant bacteria is certainly one that is worthy of exploration and is now being studied in a number of different areas. The possibility of genetically engineering bacteria to generate specific products in the ruminant is one that allows the mind to run somewhat wild. It would be hoped that one could influence a number of different characteristics of the meat if one could affect the various types of input from the ruminant through the blood to the various kinds of cells. Although there still remains somewhat of an area of fantasy, it certainly is likely that effects can be created by genetically altering the bacteria in the ruminant to create certain kinds of products that will then be utilized by the cells.

The area of fermentation is another one that appears to be right for the use of genetic engineering. It certainly is feasible and it is extremely likely that bacteria can be genetically engineered to produce certain kinds of either flavor enhancers or other types of compounds that will create new types of meat products. This would appear to be particularly attractive for various kinds of processed meats, where the wide variety of flavor enhancers could be naturally produced in the meat during fermentations.

The use of naturally-occurring preservatives is also an area in which I would expect to see a number of advances being made in the next few years. Again, it is possible to genetically alter bacteria to create various kinds of preservatives in the meat, during either fermentation or other types of processing mechanisms. This would allow for naturally-occurring preservatives that would prevent spoilage and yet be the kinds of preservatives that one would expect to be very acceptable to the vast majority of the population.

Effects of genetic engineering and biotechnology on processing of meat is one that requires a bit more speculation. But again, it is not inconceivable that the various kinds of processing enzymes and other types of effects can be created in a much cheaper fashion through genetic engineering than is currently done. An example of this and other types of processing is the creation of genetically-engineered renin in the processing of cheese. Thus, it is likely that various kinds of processing can be done in a much cheaper and possibly in an entirely different fashion in meat, as we explore further the use of various kinds of genetically-engineered or genetically-altered enzymes and bacteria.

The last three areas are much more speculative, in terms of the actual effect that one could see on meat and various kinds of meat products. The first area of altering the fat-to-lean ratio in various kinds of meat products is an interesting aspect that probably will involve a much more complex kind of genetic engineering than is currently available in most types of genetically-altered organisms. One could speculate, however, that the ratio of fat to lean could be altered by various kinds of effects on cells in terms of the regulation of expression of certain kinds of genes, rather than the actual creation of new or different types of gene products. Thus as we begin to understand the actual regulation of gene expression, it may be possible to regulate and alter that expression to alter the various kinds of fat and lean ratios in meat.

An area that has undergone some intense speculation in recent months is that of the composition of lipids present in various kinds of meat products. There certainly has been a lot of "hype" about omega fatty acids and the possibility of creating meat products that are much higher in omega fatty acids. This also would appear to be a fairly complex process and one that is worthy of significant study. Whether it will be possible to easily alter the omega fatty acid composition of meat remains to be seen. There are a number of ways of suggesting that this can be done either through altering the intake the animal has of fatty acids, or by actually altering the enzyme ratios that generate the various fatty acids in the tissues themselves.

Finally, it may be possible to alter the actual fiber type that is found in a certain type of muscle tissue. Whether this will be useful in terms of altering the characteristics of meat or meat products remains to be seen. This is certainly another area that has been speculated on and which may be worthy of pursuit. This is true because if it requires an alteration only in the regulation of various kinds of gene products, this allows for a much easier approach using genetic engineering than the use of specifically-altered genetic information in the cells and in the fibers.

Summary

In summary then, it seems to me that genetic engineering and biotechnology in the future are likely to have a major role to play in the perspectives and in the actual products that the meat industry will be providing to the American and world consumer. The speed with which this takes place would appear to be clearly dependent on the adoption of these methods by people who are actually working in this field and by the formation of useful collaborations with people who work with meat and meat products and with those people who have been applying the genetic engineering and biotechnology methods to other types of problems. Hopefully, these collaborations will lead to an increased utilization and an increased acceptance of red meat products by the American consumer.

Discussion

D. Anderson: Do you see any problems with society accepting this technology and if you do, what might be some of the ways of overcoming their concern?

R. Lewis: It turns out that I had an opportunity, if you call it that, to participate in a debate with Jerry Rifken which was held in this same room several months ago. Frankly, I think that there is some resistance on the part of the public. But I think a lot of it has to do with the inability of ourselves or the companies producing the material to present the concepts of biotechnology in a palatable fashion. Even if you choose the methodology correctly and approach the population in the correct manner, I think you still are going to have people who don't want to see things change; but I think it shouldn't be difficult to convince regulatory agencies what you're producing is better, safer and possibly cheaper than what's currently available. I think those are the kinds of things that eventually will sell the population.

D. Kropf: A lot of us are interested in sport activities like basketball and can visualize unscrupulous coaches creating the kind of players that they want to create or families creating sons, lets say, with certain physical dimensions. Do you think this will happen, what are the limitations and what will be some of the undesirable consequences?

Lewis: I think the best analogy I can make is the current drug being used for skin treatments. It's a vitamin A derivative. I happen to know a lot about it because Hoffman-LaRoche is the company that produces it. It is very clear that people are using it who shouldn't be, particularly, pregnant women. There are prohibitions against using it in pregnant women and doctors simply are not doing their job. It seems to me the use of growth hormones is the same way. What they have done in other countries is restrict the ability to prescribe this drug to certain doctors in certain major medical centers. It may be that growth hormone would have to be regulated the same way. To my knowledge, growth hormone has been available for 2½ years now; I know of no cases that have become public where people have used it unscrupulously. The thing I think one would have to be somewhat concerned about is that there are other physical effects. That is, its ability to augment growth is combined with other kinds of effects. I guess that if parents desire that for their children, it will be somewhat difficult to legislate against it. It seems to me the way you do it is to restrict the number of doctors who can prescribe it.

C. Calkins: Would you help us define the word "biotechnology"? You gave us some feeling for the definition of genetic engineering. I think there is some sense in the population that the word is being used in a broader and broader sense to incorporate more and more programs. Do you have your own definition of the term that you could share with us?

Lewis: To me, biotechnology is simply the use of methods that have been developed in the last 20 years applied to biological problems; this includes genetic engineering, monoclonal antibody techniques and those kinds of things. Biotechnology is clearly a catch word. Therefore it's like a lot of words, it's abused. That is why I stuck with what I call "genetic engineering" because it defines it for me a little more tightly. We are really looking at the movement of and the effects on genes rather than looking at biotechnology as a much broader kind of approach.