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The Insight in Genetic Engineering

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Abstract

Also known: biotechnology, gene splicing, recombinant DNA technology Anatomy or system affected: All Specialties and related fields: Alternative medicine, biochemistry, biotechnology, dermatology, embryology, ethics, forensic medicine, genetics, Pharmacology, preventive medicine.

Keywords: Genetic engineering • Gene cloning • Gene therapy • Recombinant Dna • Southern Blot

Introduction

Genetic engineering, recombinant DNA technology, and biotechnology — the buzz words you may have heard often on radio or TV, or read about in featured articles in newspapers or popular magazines. It is a set of techniques that are used to achieve one or more of three goals: to reveal the complex processes of how genes are inherited and expressed, to provide better understanding and effective treatment for various diseases, (particularly genetic disorders), and to generate economic benefits which include improved plants and animals for agriculture, and efficient production of valuable biopharmaceuticals. The characteristics of genetic engineering possess both vast promise and potential threat to human kind. It is an understatement to say that genetic engineering will revolutionize the medicine and agriculture in the 21st future. As this technology unleashes its power to impact our daily life, it will also bring challenges to our ethical system and religious beliefs [1].

Genetic Engineering and Human Health

Soon after the publication of the short essay by Crick and Watson on DNA structure (1953), research began to uncover the way by which DNA molecules can be cut and "spliced" back together. With the discovery of the first restriction endonuclease by Hamilton Smith et al. (1970), the real story of genetic engineering began to unfold the creation of the first engineered DNA molecule through splicing DNA fragments of two unrelated species together was made public in 1972. Soon followed were a whole array of recombinant DNA molecules, genetically modified bacteria, viruses, fungi, plants and animals. The debate over the issues of "tinkering with God" heated up and public outcry over genetic -spread. The birth of "Dolly", the first mammal ever cloned from an adult body engineering was wide cell, has elevated the debate over the impact of biological research to a new level. Furthermore, a number of genetically modified organisms (GM0s) have been commercially released since 1996.

Today, it is estimated that over 70% of US foods contain some ingredients from GMOs. Obviously, genetic engineering holds tremendous promise for medicine and human well-being. Medical applications of genetic engineering include diagnosis for genetic and other diseases; treatment for genetic disorders; regenerative medicine using pluripotent (stem) cells; production of safer and more effective vaccines, and pharmaceuticals; the prospect of curing genetic disorders through gene therapy; the list goes on. Owing to its potential to give humanity unprecedented power over life itself, the research and application of genetic engineering has generated much debate and controversy. Many human diseases, such as cystic fibrosis, Downs syndrome, fragile X syndrome, Huntington's disease, muscular dystrophy, sickle-cell anemia, Tay-Sachs disease, etc. are inherited. There are usually no conventional treatments for these disorders because they don't respond to antibiotics or other conventional drugs. Another area is the commercial production of vaccines and pharmaceuticals through genetic engineering, which has emerged as a rapidly developing field [2]. The potential of embryonic stem cells to become any cell/tissue/organ under adequate conditions holds enormous promise for regenerative medicine.

Prevention of Genetic Disorders

Although prevention may be achieved by avoiding these environmental factors that cause the abnormality, the most effective prevention, when possible, is to reduce the frequency of or eliminate entirely the harmful genes (mutations) from the general population. As more precise tools and procedures for manipulating individual genes are optimized, this will eventually become a reality. The prevention of genetic disorders at present is usually achieved by ascertaining those individuals in the population who are at risk of passing a serious genetic disorder to their offspring, offering them genetic counseling and prenatal screening followed with the selective

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abortion of affected fetuses. Genetic counseling is the process of communicating information gained through classic genetic studies and contemporary research to those individuals who are themselves at risk or have a high likelihood of passing defects to their offspring. During counseling, information about the disease itself - its severity and prognosis, whether or not there are effective therapies, and the risks of recurrence is generally presented. For those couples who find the risks unacceptably high, counseling may also include discussions of contraceptive methods, adoption, prenatal diagnosis, possible abortion and artificial insemination by a donor, etc. Even though the final decision must still rest with the couple themselves, the significant increase in the accuracy of risk assessment made possible with genetic technology makes it easier for parents to make well-informed decisions. To these couples who find the burden of having an affected child unbearable, prenatal diagnosis may solve their dilemma. Prenatal screening could be performed for a variety of genetic disorders. It requires samples of fetal cells or chemicals produced by the fetus through either amniocentesis or chorionic villus sampling. After sampling, several analyses could be performed. First, biochemical analysis is used to determine the concentration of chemicals in the sample and therefore diagnose whether a particular fetus is deficient or low in enzymes that facilitate specific biological reactions. Next, analysis of the chromosomes of the fetal cells can show if all the chromosomes are present, and whether or not there are any structural abnormalities in any of them. Finally, the most effective means is to detect the defective genes through recombinant DNA techniques. This has become possible with the rapid increase of DNA copies through a technique called PCR, which can produce virtually unlimited copies of a specific gene or DNA fragment, starting with as little as a single copy. Routine prenatal diagnosis is being performed to screen the fetus for Down syndrome, Huntington's disease, sickle-cell anemia, and Tay-Sachs disease. Procedures are being developed for prenatal diagnosis of more and more severe genetic disorders. Thus, an effective roadblock to the passing of defective genes from one generation to another in the population is possible [3].

Treatment of Diseases and Genetic

Disorders Genetic engineering may be used for direct treatments of diseases or genetic disorders through various means, including the production of possible vaccines for AIDS, treatment for various cancers, synthesis of biopharmaceuticals for a variety of metabolic, growth, and development diseases, etc. In general, biosynthesis is a process where gene coding for a particular product is isolated, cloned into another organism (mostly bacteria), and later expressed in that organism (host). By cultivating host organism, large quantities of the gene products can be harvested and purified. A few examples will illustrate the useful features of biosynthesis. Insulin is essential for the treatment of insulin-dependent diabetes, the most severe form of diabetes. Historically, insulin was obtained from a beef or pig pancreas. Two problems exist for the traditional supply of insulin. First, large quantities of the pancreas are needed to extract enough insulin for continuous treatment of one patient. Second, insulin so obtained is not chemically identical to human insulin, hence some patients may produce antibodies which can seriously interfere with the treatment. Human insulin produced through genetic engineering is quite effective yet without any side-effects. It has been produced commercially and made available to patients since 1982. Another successful story in biosynthesis is the production of human growth hormone (HGH), which is used in the treatment of children with growth retardation called pituitary dwarfism. The successful biosynthesis of HGH is important due to several reasons. The conventional source of HGH was human pituitary glands removed at autopsy, which only exist in brain and liver. Each child afflicted with pituitary dwarfism needs twice-a-week injections until the age of 20. Such a treatment regime requires over a thousand pituitaries. It's obvious that autopsy supply could hardly keep up with the demand. Furthermore, due to a small amount of virus contamination in the extracted HGH, many children receiving treatment developed virus related diseases. Other biopharmaceuticals under development or in pre-clinical or clinical trials through genetic engineering include anti-cancer drugs, anti-aging agents, and a possible vaccine for AIDS, malaria, etc. Broadly speaking, three types of gene therapy exist, germ line therapy, enhancement gene therapy, and somatic gene therapy. Alt gene therapy trials currently underway or in the pipeline are restricted to the somatic cells as targets for gene transfer. The germ line therapy involves the introduction of novel genes into germ cells such as egg/early embryo. Although it has the potential for correcting defective genes once for all, germ line gene therapy is highly controversial and currently banned by many countries. The enhancement gene therapy, through which human potential might be enhanced for some desired traits, raises an even greater ethical dilemma. Both germ line and enhancement gene therapy has been banned based on the unresolved ethical issues surrounding them [4]. Somatic gene therapy is designed to introduce functional gene(s) to body cells, which enable the body to perform normal functions thus providing temporary correction for genetic abnormalities. The cloned human gene is first transferred into a viral vector, which is used to infect white blood cells removed from the patient. The transferred (normal) gene is then inserted into a chromosome and becomes active. After growth to enhance their numbers under sterile conditions, the cells are re-implanted into the patient, where they produce a gene product that is missing in the untreated patient, allowing the individual to function normally. Several disorders are currently being treated with this technique, including Severe Combined Immunodeficiency (SOD). Individuals with SCID have no functional immune system and usually die from infections that would be minor in normal people. Gene therapy is also being used or tested as a treatment for cystic fibrosis, skin cancer, breast cancer, brain cancer, and AIDS. However, most of these treatments are only partially successful, yet prohibitively expensive. Over a 10- year period, more than 4000 people were treated through gene therapy. Unfortunately, most of these trials were failures that led to a loss of confidence in gene therapy. The major reasons for these failures have been attributed to inefficient vectors. In the future, as more efficient vectors are engineered, gene therapy is expected to be a common method for treating a large number of genetic disorders [5]. Genetic Engineering in Agriculture, Forensics and Environmental Science As the use of genetic engineering expands rapidly, it's hard to generate an exhaustive list of all possible applications. However, there are at least three other areas worth noting — forensic, environmental, and agricultural applications. Although these three areas are not directly related to medicine, they certainly have profound impacts on human well-being. There are numerous ways that genetic engineering may be used to benefit agriculture and food production. First, the production of vaccines and the application of methods for transferring genes for commercially important traits such

as milk yield, butterfat, and a higher proportion of lean meat are likely to benefit animal husbandry. For example, the bovine growth hormone produced through genetic engineering has been used since late 1980's to boost milk production by a cow. A mutant form of the myostatin gene, nick-named "Schwarzenegger gene" has been identified and found to cause heavy muscling after this gene was introduced into mice, and later the Belgian Blue bull. This marks the first step toward breeding cows and meat animals with lower fat and a higher proportion of lean meat. Other examples of using genetic engineering in animal husbandry include hormones for faster growth rate in poultry, production of recombinant human proteins in the milk of livestock, etc. Second, genetic engineering is expected to dramatically alter the conventional approaches of developing new strains of crops through breeding. The technology allows transferring genes for nitrogen fixation; improving photosynthesis (and therefore yield); resistance to pests, pathogens, and herbicides; and tolerance to frost, drought, increased salinity; and improved nutritional value and consumer acceptability. Genetically engineered tobacco plants have been grown to produce protein Phaseolin, which is naturally synthesized by soybean and other legume crops. The first genetically engineered potato was approved for human consumption by US government in 1995 and by Canada in 1996 .The New leaf Potato developed by corporate giant Monsanto (St. Louis, MO), carries a gene from the bacterium Bacillus thuringiensis. This gene produces a protein toxic to the Colorado potato beetle, an insect that causes substantial loss of the crop if left uncontrolled. The production of this protein by potato plants equips them with resistance to beetles, hence alleviates crop loss, saves cost on pesticides, and reduces the risk of environmental contamination. Antiviral genes have been successfully transferred and expressed into cotton, and the release of new cotton strains with resistance to multiple viruses is just a matter of time. At least five transgenic corn strains with resistance to herbicide or pathogens have been developed and commercially produced by US farmers by 2002. Some genes coding tolerance to drought, and to sub-freezing temperatures have been cloned and transferred into or among crop plants, some of which have already made a great impact on agriculture in developing countries. Initial effort has been made to replace chemical fertilizers with more environment-friendly bio-fertilizers. Secondary metabolites produced naturally by plants have also been purified and used as bio-pesticides. Shortly, we will see more grain, produce, milk and meat that are produced by animal or plants which have been genetically engineered one way or another. DNA fingerprints from samples collected at the crime scene provide strong evidence in trials thus help solving many violent crimes. DNA can easily be isolated from a tissue left at a crime scene, a splattering of blood, a hair sample, or even skin left under a victim's fingernails. Nowadays, a variety of techniques can be used routinely to determine the probability of matching between sample DNA and that of a suspect. DNA fingerprints are also useful in parenthood disputes, settling disputes over who owns the right to certain property, studying the genealogy of various species. The metabolism of microorganisms can be altered through genetic engineering, which enables them to absorb and degrade waste/hazardous material from the environment. The growth rate and metabolic capabilities of microorganisms offer great potential for coping with some environmental problems. Sewage plants can use engineered bacteria to degrade many organic compounds into non-toxic substances. Microbes may be engineered to detoxify specific toxic wastes in waste dumps or oil spills. Many bacteria can extract heavy metals (lead, copper, etc.) from their surroundings and incorporate them into compounds that are recoverable, thus serving to clean these toxic heavy metals from the environment. There are many more such applications yet to be tested and discovered.

Perspective and Prospects

Since the discovery of the double-helical structure of DNA by Francis Crick and James Watson in 1953, human curiosity regarding this amazing molecule has propelled the advancement of biological sciences in an unprecedented fashion. The first successful experiment in genetic engineering was described In 1972 when DNA fragments from two different organisms were joined together to produce a biologically functional hybrid DNA molecule. The next milestone came in 1975 when Dr. Edward Southern introduced a technique which has many applications and proved invaluable for subsequent development of genetic engineering. This technique, Southern blotting, is used to identify an articular of thousands of different genes or DNA fragments. Later, the automated gene or DNA fragment from transcriptase and PCR further improve our capabilities in studying and manipulating DNA molecules and genes they carried. Using this technique the first prenatal diagnosis of genetic disease was made in 1976 for thalassemia, a genetic disorder cause by the absence of globin genes. This represented monumental step forward in the use of genetically tools in the medical fields. It paved the way for the later development in which the mutation in many genes could be detected in early pregnancy. Three years later, insulin was first synthesized through genetic engineering. In 1982, The commercial production of genetically engineered human insulin became a reality. The first complete human genetic map was published in 1993, and various new techniques in DNA fingerprinting and the isolation of specific genes were developed, trials of gene therapy also begun in 1990, first with SCID. Also, an increasing number of pharmaceuticals are being produced through genetic engineering. Two versions of the draft copy of the human genome were published in 2001, launching off the genomic revolution. In 21st century, genetic engineering will continue to offer more benefits in medicine and in agriculture in ways we have never dreamed of before. In retrospect, genetic engineering presents a mixed blessing of invaluable benefits and dilemmas that science and technology have always offered to humankind. There are those who would like to restrict the uses of genetic engineering and who might prefer that such technology had never been developed. Others feel that the benefits far outweigh the possible risks and that any potential threat can easily be overcome through government regulation and/or legislation. Others do not take sides on the debate in general but are greatly concerned with some specific applications [6]. Obviously, the power of genetic engineering demands a new set of decisions, both ethical and economical, by individuals, government and the entire society. Considerable concern was expressed by both scientists and the general public regarding possible biohazards from genetic engineering. What do we do if engineered organisms prove resistant to all known antibiotics or carry cancer genes which might spread throughout the community? What if a genetically engineered plant becomes an uncontrollable super weed? Would these kinds of risks outweigh the potential benefits? On the other hand, others argue that the risk has been exaggerated, and therefore do not want to impose limits on research. Genetic engineering has also generated legal issues concerning intellectual properties and patents for different aspects of the technology. Much controversy is unsettled

due to the differences in perception of patent and the pitfall of the existing patent law. Even more controversial are many ethical issues. Perhaps the most obvious ethical issue surrounding genetic engineering is the objection to some applications that are considered socially undesirable and morally wrong. Take bovine growth hormone as an example, some vigorously opposed its use in boosting milk production for two main reasons. First, the recombinant hormone may change the composition of the milk. However, this view has been dismissed by experts from National Institute of Health and Food and Drug Administration after a thorough study. Second, many dairy farmers fear that greater milk production per cow will drive prices down even further and put some small farmers out of business. Numerous aspects of the application of genetic engineering to humans also present ethical challenges. For couples who both carry a defective gene and have an appreciable chance of having an affected child, should they refrain entirely from having children of their own? For genetic disorders caused by chromosomal abnormalities, such as Tay-Sachs disease, prenatal diagnosis can detect the defect in a fetus with great precision. The question then becomes, should the fetus be aborted if the screening result is positive? Should screening tests of infants for genetic disorders be required? If so, would such a requirement infringe the rights of the individual by the government? Perhaps the greatest concern of all is the possibility to design or clone a human being through genetic engineering. Some of these concerns are genuine and expressed with good intentions. The debate over ethical, legal, and social implications of genetic engineering should help to formulate and optimizing public policy and laws regarding the technology. Research and applications of genetic engineering should proceed with caution and humility.

Conclusion

Genetic engineering is to reveal the complex processes of how genes are inherited and expressed, to provide better understanding and effective treatment for various diseases, (particularly genetic disorders), and to generate economic benefits which include improved plants and animals for agriculture, and efficient production of valuable biopharmaceuticals.

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