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Genetic Engineering -A Summary Review

Editor's Note: Some groups have argued that genetic engineering is "wrong" and is "doing the work of god," but most scientists believe that genetic engineering is essential to help future biological, medical and agricultural discoveries. In this month's column, a review is presented with the help of 'Wikipedia' encyclopedia.

Genetic engineering, genetic modification (GM) and gene splicing are terms for the process of manipulating genes, generally implying that the process is outside the organism's natural reproductive process. It involves the isolation, manipulation and reintroduction of DNA into cells or model organisms, usually to express a protein. The aim is to introduce new characteristics or attributes physiologically or physically, such as making a crop resistant to a herbicide, introducing a novel trait, or producing a new protein or enzyme, along with altering the organism to produce more of certain traits. Examples can include the production of human insulin through the use of modified bacteria, the production of erythropoietin in Chinese Hamster Ovary cells, and the production of new types of experimental mice such as the OncoMouse (cancer mouse) for research, through genetic modification.

Since a protein is specified by a segment of DNA called a gene, future versions of that protein can be modified by changing the gene's underlying DNA. One way to do this is to isolate the piece of DNA containing the gene, precisely cut the gene out, and then reintroduce (splice) the gene into a different DNA segment. Daniel Nathans and Hamilton Smith received the 1978 Nobel Prize in physiology or medicine for their isolation of restriction endonucleases, which are able to cut DNA at specific sites. Together with ligase, which can join fragments of DNA together, restriction enzymes formed the initial basis of recombinant DNA technology.One of the best known applications of genetic engineering is the creation of genetically modified organisms (GMOs). There are potentially momentous biotechnological applications of GM, for example oral vaccines produced naturally in fruit, at very low cost.

Genetic Engineering and Research

Although there has been a tremendous revolution in the biological sciences in the past twenty years, there is still a great deal that remains to be discovered. The completion of the sequencing of the human genome, as well as the genomes of most agriculturally and scientifically important plants and animals, has increased the possibilities of genetic research immeasurably. Expedient and inexpensive access to comprehensive genetic data has become a reality with billions of sequenced nucleotides already online and annotated.

Now that the rapid sequencing of arbitrarily large genomes has become a simple, if not trivial affair, a much greater challenge will be elucidating function of the extraordinarily complex web of interacting proteins, dubbed the proteome, that constitutes and powers all living things. Genetic modification permits alteration of the primary structure of proteins and has therefore become a powerful tool in analyzing structure-function relationships in protein research. The use of the term "genetic engineering" to describe the experimental genetic modification of whole organisms, however, suggests a level of precision and an understanding of developmental biological principles beyond what has been achieved. Nonetheless, research progress has been made using a wide variety of techniques, including:

Loss of function, such as in a knockout experiment, in which an organism is engineered to lack the activity of one or more genes. This allows the experimenter to analyze the defects caused by this mutation, and can be considerably useful in unearthing the function of a gene. It is used especially frequently in developmental biology. A knockout experiment involves the creation and manipulation of a DNA construct in vitro, which, in a simple knockout, consists of a copy of the desired gene which has been slightly altered such as to cripple its function. The construct is then taken up by embryonic stem cells, where the engineered copy of the gene replaces the organism's own gene. These stem cells are injected into blastocysts, which are implanted into surrogate mothers. Another method, useful in organisms such as Drosophila (fruit fly), is to induce mutations in a large population and then screen the progeny for the desired mutation. A similar process can be used in both plants and prokaryotes.

Gain of function experiments, the logical counterpart of knockouts. These are sometimes performed in conjunction with knockout experiments to more finely establish the function of the desired gene. The process is much the same as that in knockout engineering, except that the construct is designed to increase the function of the gene, usually by providing extra copies of the gene or inducing synthesis of the protein more frequently. 'Tracking' experiments seek to gain information about the localization and interaction of the desired protein. One way to do this is to replace the wild-type gene with a 'fusion' gene, which is a juxtaposition of the wild-type gene with a reporting element such as Green Fluorescent Protein (GFP) that will allow easy visualization of the products of the genetic modification. While this is a useful technique, the manipulation can destroy the function of the gene, creating secondary effects and possibly calling into question the results of the experiment. More sophisticated techniques are now in development that can track protein products without mitigating their function, such as the addition of small sequences which will serve as binding motifs to monoclonal antibodies. SJ