GENETICALLY MODIFIED ORGANISM

Genetic engineering - was made possible through a series of scientific advances including the discovery of DNA and the creation of the first recombinant bacteria in 1973, i.e., E .coli expressing a salmonella gene. This led to concerns in the scientific community about potential risks from genetic engineering.

A genetically modified organism (GMO) or genetically engineered organism (GEO) is an organism (plant or animal) whose genetic material has been altered using genetic engineering techniques. These modifications are generally used to benefit medicine or food production. There is controversy about these techniques, as there are fears of tampering with an organism's evolution, and the long-term irreversible effects that could come from that tampering.

The general principle of producing a GMO is to add a lot of genetic material into an organism's genome to generate new traits. These techniques, generally known as recombinant DNA technology, use DNA molecules from different sources, which are combined into one molecule to create a new set of genes. This DNA is then transferred into an organism, giving it modified or novel genes. Transgenic organisms, a subset of GMOs, are organisms which have inserted DNA that originated in a different species.

Genetically modified bacteria were the first organisms to be modified in the laboratory, due to their simple genetics. These organisms are now used for several purposes, and are particularly important in producing large amounts of pure human proteins for use in medicine.The first example of this occurred in 1978 when Herbert Boyer working at a University of California laboratory took a version of the human insulin gene and inserted into the bacterium *Escherichia coli* to produce synthetic "human" insulin.The drug industry has made good use of this discovery in its quest to cure diabetes. Similar bacteria have been used to produce clotting factors to treat haemophilia, and human growth hormone to treat various forms of dwarfism. These recombinant proteins are safer than the products they replaced, since the older products were purified from cadavers and could transmit diseases. Indeed the human-derived proteins caused many cases of AIDS and hepatitis C in haemophilliacs and Creutzfeldt-Jakob disease from human growth hormone.

For instance, the bacteria which cause tooth decay are called *Streptococcus mutans*. These bacteria consume leftover sugars in the mouth, producing lactic acid that corrodes tooth enamel and ultimately causes cavities. Scientists have recently modified *Streptococcus mutans* to produce no lactic acid. These transgenic bacteria, if properly colonized in a person's mouth, could reduce the formation of cavities. Transgenic microbes have also been used in recent research to kill or hinder tumors, and to fight Crohn's disease. Genetically modified bacteria are also used in some soils to facilitate crop growth, and can also produce chemicals which are toxic to crop pests.

<u>Moving Genes between Species—how to do……</u>

- The process by which scientists introduce new genetic material into a microorganism is called ***molecular or gene cloning or genetic engineering***.
- It involves the isolation of DNA from a source other than the microorganism itself. Source organisms span the world of living things, from microbes to plants to animals, including humans. Scientists obtain source DNA in several different ways: by **disrupting cells** of the target microbe (or plant or animal) and **fragmenting it into small pieces**, by **synthesizing it from an RNA template using an enzyme called reverse transcriptase**, or by knowing the specific gene sequence and synthesizing it directly in the laboratory.
- Once obtained, the pieces of DNA are inserted into a small genetic component that has the ability to make copies of itself (replicate) independently from the microbial genome. This self-replicating unit is called a cloning vector. Although these genetic elements exist naturally in the form of **plasmids** and bacterial viruses, many of the ones used today have been altered to improve their properties for transferring genes. **Restriction enzymes**, which nick the donor DNA and the cloning vector at specific sites, and DNA ligase, which attaches the donor DNA to the cloning vector, allow the source genes of interest to be inserted into the cloning vector without disrupting its ability to replicate.
- The next step in the process is the introduction of the cloning vector with its segment of new DNA into a living cell. Bacteria have the ability to transport DNA into their cells in a process called transformation, and this ability is commonly exploited to achieve this goal. Getting the DNA into the cell, however, is only the beginning. No transformation is 100 percent efficient, and so the bacteria that receive the gene(s) of interest must be separated from those that did not. One of the best studied and most commonly used cloning vectors, pBR322, is especially useful for this purpose, as it contains several genes for antibiotic resistance. Hence, any cell transformed with DNA containing pBR322 will be antibiotic resistant, and thus can be isolated from similar cells that have not be so transformed by merely growing them in the presence of the appropriate drugs. All that remains is to identify bacteria that are producing the product of the desired gene(s), and cloning is a success.

- The introduction of human genes into bacteria has several complicating wrinkles that make cloning them even more challenging. For example, a bacterial gene codes for a protein from start to finish in one long string of **nucleotides**, whereas human cells have stretches of noncoding nucleotides called introns within their genes. Bacteria do not have the same ability as human cells to remove these introns when producing proteins from the gene, and if the introns are not removed, the intended protein cannot be produced. This, along with other complications, has been overcome using many of the tools of genetic engineering.

Uses of GMOs

Examples of GMOs are highly diverse, and include transgenic (genetically modified by recombinant DNA methods) animals such as mice, fish, transgenic plants, or various microbes, such as fungi and bacteria. The generation and use of GMOs has many reasons, chief among them are their use in research that addresses fundamental or applied questions in biology or medicine, for the production of pharmaceuticals and industrial enzymes, and for direct, and often controversial, applications aimed at improving human health (e.g., gene therapy) or agriculture (e.g., golden rice). The term "genetically modified organism" does not always imply, but can include, targeted insertions of genes from one into another species. For example, a gene from a jellyfish, encoding a fluorescent protein called GFP, can be physically linked and thus co-expressed with mammalian genes to identify the location of the protein encoded by the GFP-tagged gene in the mammalian cell. These and other methods are useful and indispensable tools for biologists in many areas of research, including those that study the mechanisms of human and other diseases or fundamental biological processes in eukaryotic or prokaryotic cells.

Transgenic microbes

Bacteria were the first organisms to be modified in the laboratory, due to their simple genetics. These organisms are now used in a variety of tasks, and are particularly important in producing large amounts of pure human proteins for use in medicine.

Bacteria-synthesized transgenic products

- Insulin
- Interferon
- Hepatitis B vaccine
- Tissue plasminogen activator
- Human growth hormone
- **Ice-minus bacteria**

Did you know that this is a is a nickname given to a variant of the common bacterium *Pseudomonas syringae* (*P. syringae*). This strain of *P. syringae* lacks the ability to produce a certain surface protein, usually found on wild-type *P. syringae*. The "ice-plus" protein (In a protein, "Ice nucleation-active" protein) found on the outer bacterial cell wall acts as the nucleating centers for ice crystals. This facilitates ice formation, hence the designation "ice-plus." The ice-minus variant of *P. syringae* is a mutant, lacking the gene responsible for ice-nucleating surface protein production. This lack of surface protein provides a less favorable environment for ice formation. Both strains of *P. syringae* occur naturally, but recombinant DNA technology has allowed for the synthetic removal or alteration of specific genes, enabling the creation of the ice-minus strain. Modifying *P. syringae* may have unexpected consequences for climate. A study has shown that its ice nucleating proteins may play an important part in causing ice crystals to form in clouds. If humans increase the frequency of bacteria lacking these proteins then it may affect rainfall

Commercial Applications

- Transgenic microbes have many commercial and practical applications, including the production of mammalian products. A company called Genentech was among the earliest and most successful commercial enterprises to use genetically engineered bacteria to produce human proteins. Their first product was human insulin produced by genetically engineered *Escherichia coli*. A variety of other human **hormones**, blood proteins, and immune modulators are now produced in a similar fashion, in addition to vaccines for such infectious agents as hepatitis B virus and measles.
- Another promising application of genetically engineered microbes is in environmental cleanup, or biomediation. Scientists have discovered many naturally occurring genes that code for enzymes that degrade toxic wastes and wastewater pollutants in bacteria. Examples include genes for degrading chlorinated pesticides, chlorobenzenes, naphthalene, toluene, anilines, and various hydrocarbons. Researchers are using molecular cloning to introduce these genes from several different microbes into a single microbe, creating "super microbes" with the ability to degrade multiple contaminants.
- Ananda Chakrabarty created one of the first microbes of this nature in the early 1970s. He introduced genes from several different bacteria into a strain of *Burkholderia cepacia*, giving it the ability to degrade toxic compounds found in

petroleum. This microbe offered a potential alternative to skimming and absorbing spilled oil. Chakrabarty's genetically modified bacterium has never been used, however, due to public concerns about the release of genetically engineered microbes into the environment. The microbe did, on the other hand, play an important role in establishing the biotechnology industry. The U.S. Patent Office granted Chakrabarty the first patent ever for the construction and use of a genetically engineered bacterium. This established a precedent allowing biotechnology companies to protect their "inventions" in the same way chemical and pharmaceutical companies have done in the past.

In addition to bacteria being used for producing proteins, genetically modified viruses allow gene therapy. Gene therapy is a relatively new idea in medicine. A virus reproduces by injecting its own genetic material into an existing cell. That cell then follows the instructions in this genetic material and produces more viruses. In medicine this process is adapted to deliver a gene that could cure disease into human cells. Although gene therapy is still relatively new, it has had some successes. It has been used to treat genetic disorders such as severe combined immunodeficiency, and treatments are being developed for a range of other incurable diseases, such as cystic fibrosis, sickle cell anemia, and muscular dystrophy.

Genetically modified bacteria are also used in agriculture to facilitate crop growth, and can also produce chemicals which are toxic to crop pests.

Transgenic animals

Transgenic animals are used as experimental models to perform phenotypic tests with genes whose function is unknown or to generate animals that are susceptible to certain compounds or stresses for testing in biomedical research. Other applications include the production of human hormones, such as insulin. Frequently used in genetic research are transgenic fruit flies (*Drosophila melanogaster*) as genetic models to study the effects of genetic changes on development. Transgenic mice are often used to study cellular and tissue-specific responses to disease.

Transgenic plants

Transgenic plants have been developed for various purposes. Most of transgenic plants were created for research purposes and were not intended for eventual commercialization. From these few which have reached the market the most common transgenic traits include 1) resistance to pests or herbicides, 2) improved product shelflife.

In the near future crops with improved nutritional value and with resitance to harsh environmental conditions might reach the marketplace. Since the first commercial cultivation of GM plants in 1996, GM plants tolerant to the herbicides glufosinate or glyphosate, and producing the Bt toxin, an insecticide, have dominated the agriculutral seed market for corn and other crops (soybean, cotton). Recently, a new generation of GM plants promising benefits for consumers and industry purposes is entering the market. Whenever GM plants are grown on open fields without containment there are risks that the modification will escape into the general environment. Most countries require biosafety studies prior to the approval of a new GM plant release, usually followed by a monitoring programme to detect environmental impacts. Especially in Europe, the coexistence of GM plants with conventional and organic crops has raised many concerns. Since there is separate legislation for GM crops and a high demand from consumers for the freedom of choice between GM and non-GM foods, measures are required to separate foods and feed produced from GMO plants from conventional and organic foods. European research programmes such as Co-Extra, Transcontainer and SIGMEA are investigating appropriate tools and rules.

Controversy over GMOs

The use of GMOs has sparked significant controversy in many areas. Some groups or individuals see the generation and use of GMO as intolerable meddling with biological states or processes that have naturally evolved over long periods of time (although many crops and animals have been modified by humans via unnatural selection over the last several thousand years), while others are concerned about the limitations of modern science to fully comprehend all of the potential negative ramifications of genetic manipulation.

While some groups advocate the complete prohibition of GMOs, others call for mandatory labeling of genetically modified food or other products. Other controversies include the definition of patent and property pertaining to products of genetic engineering and the possibility of unforeseen local and global effects as a result of transgenic organisms proliferating. The basic ethical issues involved in genetic research are discussed in the article on genetic engineering.