Biotechnology Information Series

Principles of Biotechnology

Biotechnology Defined

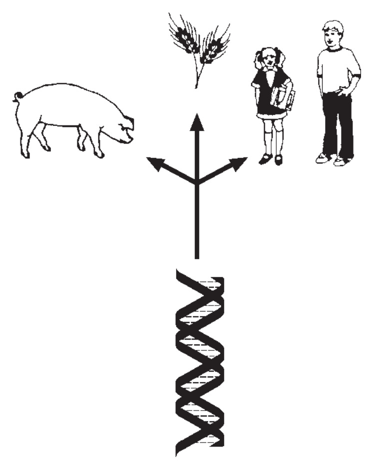
Biotechnology can be broadly defined as "using living organisms or their products for commercial purposes." As such, biotechnology has been practiced by human society since the beginning of recorded history in such activities as baking bread, brewing alcoholic beverages, or breeding food crops or domestic animals.

A narrower and more specific definition of biotechnology is "the commercial application of living organisms or their products, which involves the deliberate manipulation of their **DNA** molecules" (see glossary for definitions of bold-print words). This definition implies a set of laboratory techniques developed within the last 20 years that have been responsible for the tremendous scientific and commercial interest in biotechnology, the founding of many new companies, and the redirection of research efforts and financial resources among established companies and universities.

These laboratory techniques provide scientists with a spectacular vision of the design and function of living organisms, and provide technologists in many fields with the tools to implement exciting commercial applications.

Principles of Biology

All living organisms are composed of cells that contain a substance called DNA (deoxyribonucleic acid) in the **chromosomes**. (See Fig.1.) The structure of DNA molecules contains information that is used by cells as a "recipe" for the organism; that is, the characteristics of any living thing essentially are determined by the information in DNA. The "words" for the DNA recipe, called **genes**, are derived from a 4-letter alphabet (A, C, G, T) and usually contain between 1,000 and 100,000 letters. The entire recipe, called the **genome**, may contain between 4 million (simple bacteria) and 3 billion (human) letters or more.



All life is composed of cells that contain DNA.

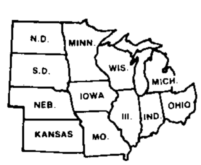
Figure 1

Except for the **sequence** and number of letters in each recipe, DNA from any organism is chemically and physically the same. One of the great scientific discoveries of biotechnology is that DNA from any organism will function if it is transferred into any other organism!

Using Biotechnology to Modify Plants and Animals

Combining DNA from different existing organisms (plants, animals, insects, bacteria, etc.) results in modified organisms with a combination of traits from the parents. The sharing of DNA information takes place naturally through sexual reproduction and has been exploited in plant and animal breeding programs for many years.

However, sexual reproduction can occur only between individuals of the same species. A Holstein cow can be mated with a Hereford bull because the two animals are different breeds of the same species, cattle. But trying to mate a cow with a horse, a different species of animal, would not be successful.



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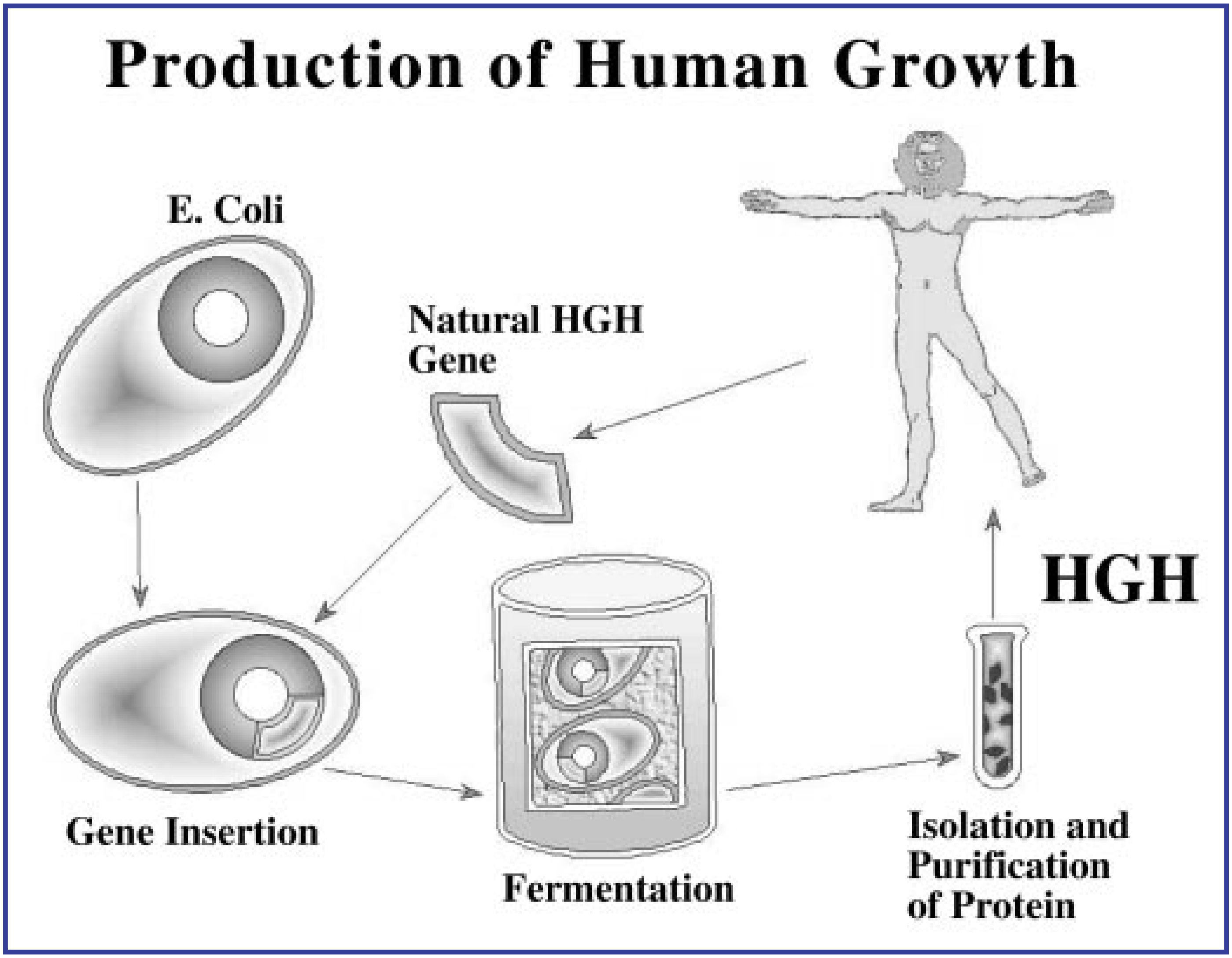


Figure 2

What's new since 1972 is that scientists have been able to identify the specific DNA genes for many desirable traits and transfer only those genes, usually carried on a **plasmid** or virus, into another organism. This process is called **genetic engineering** and the transfer of DNA is accomplished using either direct injection or the **Agrobacterium**, **electroporation**, or **particle gun transformation** techniques. It provides a method to transfer DNA between any living cells—plant, animal, insect, bacterial, etc. Virtually any desirable trait found in nature can, in principle, be transferred into any chosen organism. An organism modified by genetic engineering is called **transgenic.**

Products of Genetic Engineering

Specific applications of genetic engineering are abundant and increasing rapidly in number. Genetic engineering is being used in the production of pharmaceuticals, gene therapy, and the development of transgenic plants and animals.

1) Pharmaceuticals

Human drugs such as insulin for diabetics, growth hormone for individuals with pituitary dwarfism, and tissue plasminogen activator for heart attack victims, as well as animal drugs like the growth hormones, bovine or porcine somatotropin, are being produced by the fermentation of transgenic bacteria that have received the appropriate human, cow, or pig gene. (See Fig. 2.)

2) Gene Therapy

The first clinical gene therapy is underway to correct an enzyme deficiency called ADA in children. Bone marrow cells are removed, defective DNA in bone marrow cells is supplemented with a copy of normal DNA, and the repaired cells are then returned to the patient's body.

3) Transgenic Plants

Transgenic plants that are more tolerant of herbicides, resistant to insect or viral pests, or express modified versions of fruit or flowers have been grown and tested in outdoor test plots since 1987. The genes for these traits have been

delivered to the plants from other unrelated plants, bacteria, or viruses by genetic engineering techniques.
(See Fig. 3.)

4) Transgenic Animals

Presently, most transgenic animals are designed to assist researchers in the diagnosis and treatment of human diseases. Several companies have designed and are testing transgenic mammals that produce important pharmaceuticals in the animal's milk. Products such as insulin, growth hormone, and tissue plasminogen activator that are currently produced by fermentation of transgenic bacteria may soon be obtained by milking transgenic cows, sheep, or goats.

Using Biotechnology in Diagnostic Applications

Since each living creature is unique, each has a unique DNA recipe. Individuals within any given species, breed, or hybrid line can usually be identified by minor differences in their DNA sequences—as few as one difference in a million letters can be detected! Using the techniques of **DNA fingerprinting** and **PCR** (polymerase chain reaction) scientists can diagnose viral, bacterial, or fungal infections, distinguish between closely related individuals, or map the locations of specific genes along the vast length of the DNA molecules in the cells.

Identifying Organisms

By using **RFLP** technology (restriction fragment length polymorphism), DNA fingerprints can be generated. Any individual organism can be uniquely identified by its DNA fingerprint. Consequently, this fingerprint can be used to determine family relationships in paternity litigation, match organ donors with recipients in transplant programs, connect suspects with DNA evidence left at the scene of a crime (in the form of hair or body fluids), or serve as a pedigree for seed or livestock breeds. (See Fig. 4.)

Identifying Genes

One important aspect of genetic engineering projects is to

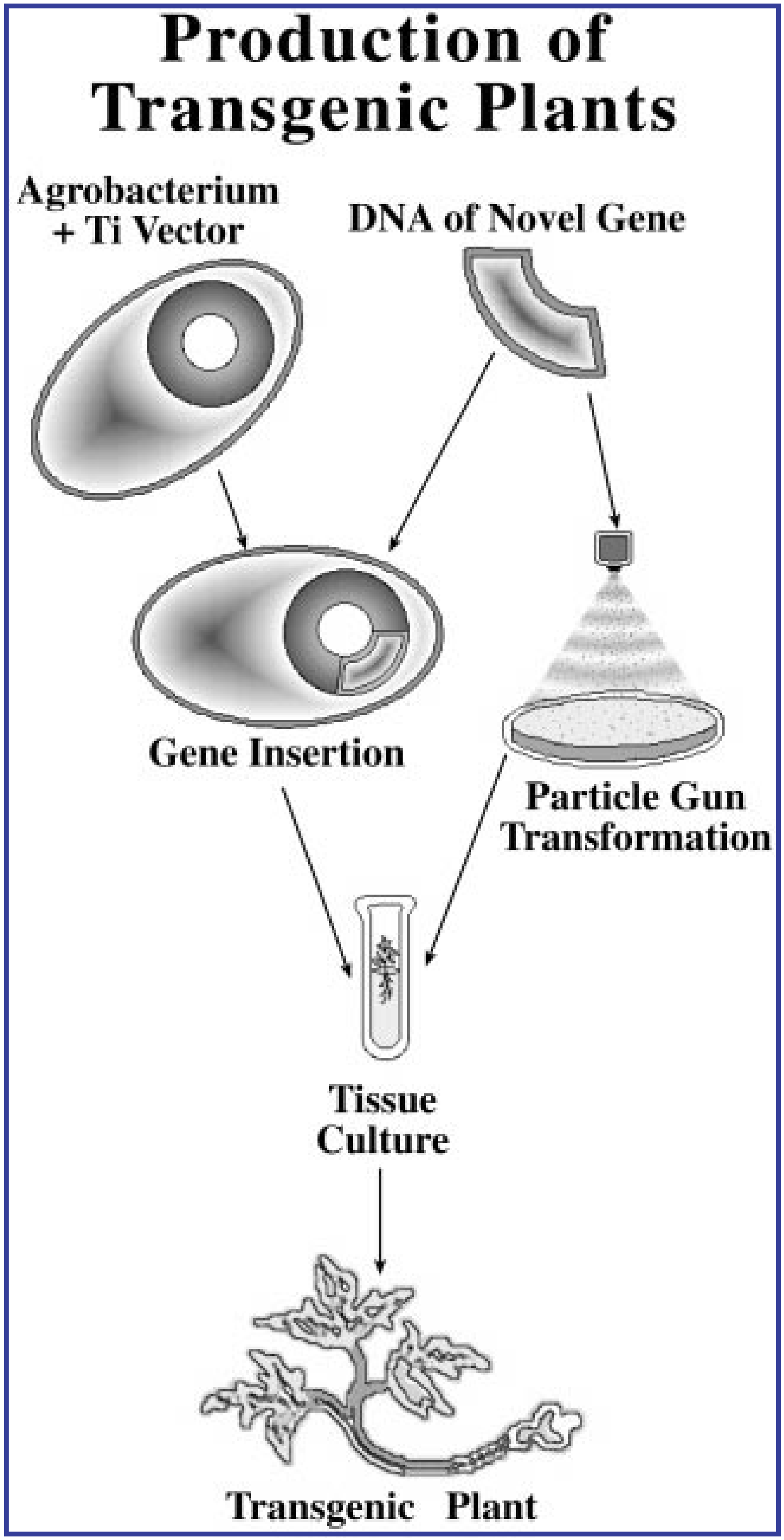


Figure 3

identify the DNA gene that controls a particular trait. In the same way that a visitor might use the state, city, street, and house number to locate a friend's house, genetic engineers use **genetic "maps"** to locate genes. The genetic maps are generated by statistical analyses, PCR, RFLP, and DNA sequencing. Maps are being developed for humans, mice, swine, cattle, corn, wheat, and other plants or animals with commercial or research importance.

Diagnosing Infectious Diseases and Genetic Disorders

Diagnosis of infectious diseases is a profound application of the new DNA technology. Tuberculosis, AIDS, papillomavirus, and many other infectious diseases, in addition to the inherited disorders like cystic fibrosis or sickle cell anemia, are diagnosed within hours by the PCR technique rather than days or weeks by traditional methods. The greatly increased sensitivity and speed of the PCR technique, as compared with traditional methods, allows earlier intervention and treatment. PCR assays will soon be available to diagnose diseases of crops and livestock.

Summary

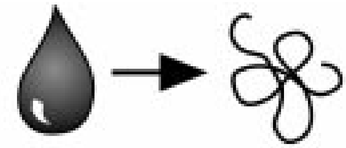
1) **All living organisms are composed of cells that contain the molecule DNA.** The chemical structure of DNA contains information, based on a 4-letter **genetic code**, that cells use as a "recipe for life." The functional units of information, the "words" of the recipe, are called genes.

2) **DNA from all living organisms is the same, except for the sequence and number of letters in the "recipe."** Therefore, traits can be transferred from one organism into another by transferring the DNA genes for those traits. This transfer process is called "genetic engineering" and the organisms that are produced are called "transgenic."

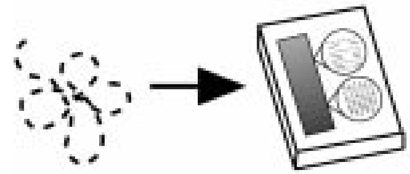
3) **Organisms can be uniquely identified by their DNA sequences.** Though the DNA of all organisms is chemically and physically the same, the DNA "recipe" (sequence and number of letters) is unique to each individual. These different sequences account for the diversity of life observed in nature and are the basis for using DNA "fingerprints" to distinguish

THE PROCESS OF DNA FINGERPRINTING

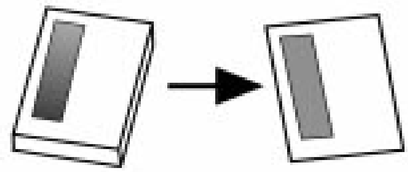
1. The process begins with a blood or cell sample from which the DNA is extracted.



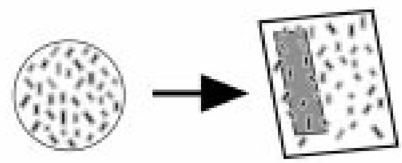
2. The DNA is cut into fragments using a restriction enzyme. The fragments are then separated into bands by electrophoresis through an agarose gel.



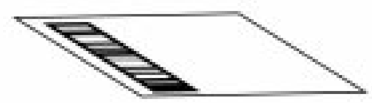
3. The DNA band pattern is transferred to a nylon membrane.



4. A radioactive DNA probe is introduced. The DNA probe binds to specific DNA sequqences on the nylon membrane.



5. The excess probe material is washed away leving the unique DNA band pattern.



6. The radioactive DNA pattern is transferred to X-ray film by direct exposure. When developed, the resultant visible pattern is the DNA FINGERPRINT.

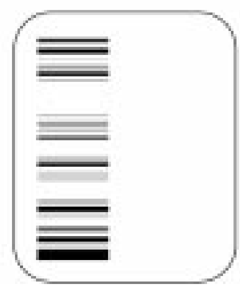


Figure 4

between any two individuals, breeds, hybrids, species, etc. They are also the basis of diagnosis of viral, bacterial, or fungal diseases using PCR technology.

Glossary

Agrobacterium—a natural bacterium that can be used to transfer DNA genes into broadleaf plants, such as tobacco, tomato, or soybean.

Chromosome—a cellular structure comprised of a long, folded DNA molecule and protein.

DNA—deoxyribonucleic acid, the substance within cells that carries the "recipe" for the organism and is inherited by offspring from parents.

DNA fingerprinting—cutting a DNA chromosome with restriction enzymes and separating the pieces by **electrophoresis** to generate a unique pattern, the "fingerprint" for each species, breed, hybrid, or individual, depending on which enzymes and **probes** are used.

Electrophoresis—a lab technique for determining DNA fragment sizes by separating them in a gel placed in an electric field.

Electroporation—using an electric shock to transfer DNA into the cells of an organism; one of several procedures called transformation.

Gene—a functional unit of DNA, one "word" in the DNA recipe.

Genetic code—the information contained in DNA molecules that scientists describe on the basis of a 4-letter alphabet (A, C, G, and T).

Genetic engineering—the process of transferring DNA from one organism into another that results in a genetic modification; the production of a transgenic organism.

Genetic map—the locations of specific genes along a chromosome marked with probes.

Genome—the entire DNA "recipe" for an organism, found in every cell of that organism.

Mutation—a change of one of the "letters" in the DNA "recipe" caused by chemicals, ultraviolet light, X-rays, or natural processes.

Particle gun—a gun that shoots DNA into the cells of an organism; the most versatile of a series of procedures called transformation.

PCR—polymerase chain reaction, which rapidly duplicates specific DNA molecules in response to temperature changes in a computer-controlled heater.

Plasmid—a small, circular DNA that is used to transfer genes from one organism into another.

Probe—a very short piece of DNA used to find a specific sequence of "letters" in a very long piece of DNA from a chromosome or genome.

Recombinant DNA—DNA formed by joining pieces of DNA from two or more organisms.

RFLP—restriction fragment length polymorphism, which describes the patterns of different (polymorphism) sizes of DNA (fragment length) that result from cutting with restriction enzymes (restriction). See **DNA fingerprinting** above.

Sequence—the order of "letters" in the DNA "recipe." The DNA sequence is the chemical structure that contains information.

Transformation—a procedure to transfer DNA into the cells of an organism. Can be done with Agrobacterium (most dicots), calcium chloride (bacteria), electroporation (any organism), or the particle gun (any organism).

Transgenic—an organism that has been modified by genetic engineering to contain DNA from an external source.

Vector—any DNA structure that is used to transfer DNA into an organism; most commonly used are plasmid DNA vectors or viruses.

For Further Reading

Bio/Technology. A monthly journal devoted specifically to scientific, economic, and public policy issues in biotechnology. For subscription information, phone 1-800-524-0328.

Biotechnology—An Activist's Handbook. Available from the Vermont Biotechnology Group. Phone (802) 223-7222.

"Molecular Advances in Genetic Disease." *Science*. May 8, 1992.

"The Promise and Pitfalls of Molecular Genetics." *Science*. July 10, 1992.

Scientific American. October, 1985. Entire issue devoted to molecular biology.

Understanding DNA and Gene Cloning by Karl Drlica. 2nd Edition. Wiley and Sons. 1990.

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