



A HISTORICAL LOOK AT BIOTECHNOLOGY

The word biotechnology can be traced to 1917, when it was used to refer to large-scale fermentation production techniques. While relatively young in term, the roots of biotechnology can be traced back at least 6,000 years. Here is a brief history of biotechnology [and farming mixed in]:

8000 B.C.

- Humans domesticate crops and livestock.
- Potatoes first cultivated for food.

4000 B.C.

- The Egyptians use yeasts to make bread and wine.

4000-2000 B.C.

- Production of cheese and fermentation of wine (Sumeria, China and Egypt).
- Babylonians control date palm breeding by selectively pollinating female trees with pollen from certain male trees.

1700s B.C.

- Naturalists begin to identify many kinds of hybrid plants — the offspring of breeding between two

varieties of plants.

1750 B.C.

- The Sumerians brew beer.

500 B.C.

- First antibiotic: moldy soybean curds used to treat boils (China).

250 B.C.

- The Greeks use crop rotation to maximize crop fertility.

A.D. 100

- First insecticide: powdered chrysanthemums (China).

1322

- An Arab chieftain first uses artificial insemination to produce superior horses.

1500

- The Aztecs make cakes from Spirulina algae.

1590

- Janssen invents the microscope.

1663

- Cells are first described by Hooke.

1675

- Leeuwenhoek discovers bacteria.

1761

- Koelreuter reports successful crossbreeding of crop plants in different species.

1797

- Jenner inoculates a child with a viral vaccine to protect him from smallpox.

1830

- Proteins discovered.

1833

- First enzyme discovered and isolated.

1835-1855

- Schleiden and Schwann propose that all organisms are composed of cells, and Virchow declares, "Every cell arises from a cell."

1856

- Gregor Mendel begins a meticulous study of specific characteristics he found in various plants which were passed to future plant generations.

1857

- Pasteur proposes microbes cause fermentation.

1859

- Darwin publishes his theory of evolution *On the Origin of Species*.

1861

- Louis Pasteur defines the role of microorganisms and establishes the science of microbiology.

1866

- Mendel proposes basic laws of genetics based on studies with pea plants.

1870-1890

- Using Darwin's theory, plant breeders crossbreed cotton, developing hundreds of varieties with superior qualities.
- Farmers first inoculate fields with nitrogen-fixing bacteria to improve yields.
- William James Beal produces first experimental corn hybrid in the laboratory.

1877

- A technique for staining and identifying bacteria is developed by Koch.

1878

- The first centrifuge is developed by Laval.

1879

- Fleming discovers chromatin, the rod-like structures inside the cell nucleus that later came to be called chromosomes.

1900

- European botanists use Mendel's Law to improve plant species, marking the beginning of classic selection.
- *Drosophila* (fruit flies) used in early studies of genes.

1902

- The term immunology first appears.

1906

- The term genetics is introduced.

1910

- Genes are discovered to be located on chromosomes.

1911

- The first cancer-causing virus is discovered by Rous.

1914

- Bacteria are used to treat sewage for the first time in Manchester, England.

1915

- Phages, or bacterial viruses, are discovered.

1919

- First use of the word biotechnology in print.

1920

- The human growth hormone is discovered by Evans and Long.

1928

- Penicillin discovered as an antibiotic: Alexander Fleming.
- A small-scale test of formulated *Bacillus thuringiensis* (Bt) for corn borer control begins in Europe. Commercial production of this biopesticide begins in France in 1938.
- Karpechenko crosses radishes and cabbages, creating fertile offspring between plants in different genera.
- Laibach first uses embryo rescue to obtain hybrids from wide crosses in crop plants-known today as hybridization.

1930

- U.S. Congress passes the Plant Patent Act, enabling the products of plant breeding to be patented.

1933

- Hybrid corn, developed by Henry Wallace in the 1920s, is commercialized. Growing hybrid corn eliminates the option of saving seeds. The remarkable yields outweigh the increased costs of annual seed purchases, and by 1945, hybrid corn accounts for 78 percent of U.S.-grown corn.

1938

- The term molecular biology is coined.

1941

- The term genetic engineering is first used.

1942

- The electron microscope is used to identify and characterize a bacteriophage-a virus that infects bacteria.
- Penicillin mass-produced in microbes.

1944

- DNA is proven to carry genetic information-Avery et al.
- Waksman isolates streptomycin, an effective antibiotic for tuberculosis.

1946

- Discovery that genetic material from different viruses can be combined to form a new type of virus, an example of genetic recombination.
- Recognizing the threat posed by loss of genetic diversity, the U.S. Congress provides funds for systematic and extensive plant collection, preservation and introduction.

1947

- McClintock discovers transposable elements, or "jumping genes," in corn.

1949

- Pauling shows that sickle cell anemia is a "molecular disease" resulting from a mutation in the protein molecule hemoglobin.

1950

- First regeneration of entire plants from an in vitro culture.

1951

- Artificial insemination of livestock using frozen semen is successfully accomplished.

1953

- The double helix structure of DNA is discovered by Watson, Crick and New Zealander, Wilkins. Watson and Crick would later receive the Nobel Prize for their work.

1955

- An enzyme involved in the synthesis of a nucleic acid is isolated for the first time.

1956

- Kornberg discovers the enzyme DNA polymerase I, leading to an understanding of how DNA is replicated.

1958

- Sickle cell anemia is shown to occur due to a change of a single amino acid.
- DNA is made in a test tube for the first time.

1959

- Systemic fungicides are developed. The steps in protein biosynthesis are delineated.

Also in the 1950s

- Discovery of interferons.
- First synthetic antibiotic.

1960

- Exploiting base pairing, hybrid DNA-RNA molecules are created.
- Messenger RNA is discovered.

1961

- USDA registers first biopesticide: *Bacillus thuringiensis*, or Bt.

1963

- New wheat varieties developed by Norman Borlaug increase yields by 70 percent.

1964

- The International Rice Research Institute in the Philippines starts the Green Revolution with new strains of rice that double the yield of previous strains if given sufficient fertilizer.

1965

- Harris and Watkins successfully fuse mouse and human cells.

1966

- The genetic code is cracked, demonstrating that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids.

1967

- The first automatic protein sequencer is perfected.

1969

- An enzyme is synthesized in vitro for the first time.
- The first gene is isolated.

1970

- Norman Borlaug receives the Nobel Peace Prize (see 1963).
- Discovery of restriction enzymes that cut and splice genetic material, opening the way for gene cloning.

1971

- First complete synthesis of a gene.

1972

- The DNA composition of humans is discovered to be 99 percent similar to that of chimpanzees and gorillas.
- Initial work with embryo transfer.

1973

- Researchers develop the ability to isolate genes. Specific genes code for specific proteins.
- The first genetic engineering experiment is conducted by inserting a gene from the African clawed toad into bacterial DNA.

1974

- The National Institutes of Health forms a Recombinant DNA Advisory Committee to oversee recombinant genetic research.

1975

- Government first urged to develop guidelines for regulating experiments in recombinant DNA.
- The first monoclonal antibodies are produced.

1976

- The tools of recombinant DNA are first applied to a human inherited disorder.
- Molecular hybridization is used for the prenatal diagnosis of alpha thalassemia.
- Yeast genes are expressed in *E. coli* bacteria.
- First time the sequence of

base pairs for a specific gene is determined (A, C, T, G).

- First guidelines for recombinant DNA experiments released: National Institutes of Health-Recombinant DNA Advisory Committee.

1977

- First expression of human gene in bacteria.
- Procedures developed for rapidly sequencing long sections of DNA using electrophoresis.

1978

- High-level structure of virus first identified.
- Recombinant human insulin first produced.
- NC scientists show it is possible to introduce specific mutations at specific sites in a DNA molecule.
- Louise Brown, the world's first 'test-tube' baby is born through in vitro fertilization.

1979

- Human growth hormone first synthesized.

Also in the 1970s

- The Green Revolution introduces hybrid seeds into food-short Third World countries.
- First commercial company founded to develop genetically engineered products.
- Discovery of polymerases.
- Techniques for rapid sequencing of nucleotides perfected.
- Gene targeting.
- RNA splicing.

1980

- The U.S. Supreme Court, in the landmark case *Diamond v. Chakrabarty*, approves the principle of patenting recombinant life forms, which allows the Exxon Oil Company to patent an oil-eating microorganism.
- The U.S. patent for gene cloning is awarded to Cohen and Boyer.
- The first gene-synthesizing machines are developed.
- Researchers successfully introduce a human gene-one that

codes for the protein interferon-into a bacterium.

- Nobel Prize in Chemistry awarded for creation of the first recombinant molecule: Berg, Gilbert, Sanger.

1981

- Scientists at OH University produce the first transgenic animals by transferring genes from other animals into mice.
- Chinese scientist becomes the first to clone a fish—a golden carp.
- The first gene-synthesizing machines are developed.

1982

- The U.S. Food and Drug Administration approves the first genetically engineered drug, a human insulin produced by bacteria.
- Applied Biosystems, Inc., introduces the first commercial gas phase protein sequencer, dramatically reducing the amount of protein sample needed for sequencing.
- First recombinant DNA vaccine for livestock developed.

1983

- The first transgenic plant is created – petunia plants genetically engineered to be resistant to kanamycin, an antibiotic.
- The chromosomal location of the inherited disease, Huntington's disease, is discovered leading to the development of a screening test.
- The polymerase chain reaction (PCR) technique is conceived. PCR, which uses heat and enzymes to make unlimited copies of genes and gene fragments, later becomes a major tool in biotech research and product development worldwide.
- The first genetic transformation of plant cells by TI plasmids is performed.
- The first artificial chromosome is synthesized.

1984

- The DNA fingerprinting

technique is developed.

- The entire genome of the human immunodeficiency virus is cloned and sequenced.

1985

- Genetically engineered plants resistant to insects, viruses and bacteria are field tested for the first time.
- New Zealand develops a hormone extract product from sheep, used to induce reproduction in genetically superior animals throughout the world.
- DNA fingerprinting is first used in a criminal investigation.
- Genetic markers found for kidney disease and cystic fibrosis.
- The NIH approves guidelines for performing gene-therapy experiments in humans.

1986

- New Zealand passes the Hazardous Substances and New Organisms (HSNO) Act which controls the development and importation of genetically modified organisms.
- First recombinant vaccine for humans: Hepatitis B.
- First anti-cancer drug produced through biotech: interferon.
- The U.S. government publishes the Coordinated Framework for Regulation of Biotechnology, establishing more stringent regulations for rDNA organisms than for those produced with traditional genetic modification techniques.
- A University of CA-Berkeley chemist describes how to combine antibodies and enzymes (abzymes) to create pharmaceuticals.
- The first field tests of transgenic plants (tobacco) are conducted.
- The Environmental Protection Agency approves the release of the first transgenic crop-generated tobacco plants.
- The OECD Group of National Experts on Safety in Biotechnology states: "Genetic

changes from rDNA techniques will often have inherently greater predictability compared to traditional techniques" and "risks associated with rDNA organisms may be assessed in generally the same way as those associated with non-rDNA organisms."

1987

- First approval for field test of modified food plants: virus-resistant tomatoes.
- Frostban, a genetically altered bacterium that inhibits frost formation on crop plants, is field-tested on strawberry and potato plants in CA, the first authorized outdoor tests of a recombinant bacterium.

1988

- Harvard molecular geneticists are awarded the first U.S. patent for a genetically altered animal—a transgenic mouse.
- A patent for a process to make bleach-resistant protease enzymes to use in detergents is awarded.
- Congress funds the Human Genome Project, a massive effort to map and sequence the human genetic code as well as the genomes of other species.

1989

- First approval for field test of modified cotton: insect-protected (Bt) cotton.
- Plant Genome Project begins.

Also in the 1980s

- Scientists discover how to transfer pieces of genetic information from one organism to another, allowing the expression of desirable traits in the recipient organism. This is called genetic engineering, one process used in biotechnology. Using the technique of "gene splicing" or "recombinant DNA technology" (rDNA), scientists can add new genetic information to form a new protein that creates traits that protect plants from diseases and pests.

- Studies of DNA used to determine evolutionary history.
- Recombinant DNA animal vaccine approved for use in Europe.
- Use of microbes in oil spill cleanup: bioremediation technology.
- Ribozymes and retinoblastomas identified.

1990

- The first successful field trial of genetically engineered cotton plants (Bt cotton) is conducted.
- DEKALB® receives the first patent for transformed corn.
- Chy-Max™, an artificially produced form of the chymosin enzyme for cheese-making, is introduced. It is the first product of recombinant DNA technology in the U.S. food supply.
- The Human Genome Project—an international effort to map all the genes in the human body—is launched.
- The first experimental gene therapy treatment is performed successfully on a 4-year-old girl suffering from an immune disorder.
- The first transgenic dairy cow—used to produce human milk proteins for infant formula—is created.
- First food product of biotechnology approved in U.K.: modified yeast.
- First field test of a genetically modified vertebrate: trout.

1992

- American and British scientists unveil a technique for testing embryos in vitro for genetic abnormalities such as cystic fibrosis and hemophilia.
- The FDA declares that transgenic foods are “not inherently dangerous” and do not require special regulation.

1993

- Merging two smaller trade associations creates the Biotechnology Industry Organization (BIO).
- FDA approves bovine

somatotropin (BST) for increased milk production in dairy cows.

1994

- The Flavr-Savr tomato, designed to resist rotting, is approved by the FDA for sale in the United States.
- The first breast cancer gene is discovered.
- Approval of recombinant version of human DNase, which breaks down protein accumulation in the lungs of CF patients.
- BST commercialized as POSILAC bovine somatotropin.

1995

- The first Bt corn product, Event 176, receives commercial approval in the U.S.
- The first baboon-to-human bone marrow transplant is performed on an AIDS patient.
- The first full gene sequence of a living organism other than a virus is completed, for the bacterium *Hemophilus influenzae*.
- Gene therapy, immune system modulation and recombinantly produced antibodies enter the clinic in the war against cancer.

1995-1996

- Monsanto's Roundup Ready® soybeans, which are resistant to herbicides, and YieldGard® Corn, which is protected from the corn borer, are approved for sale in the United States. Bollgard® cotton first commercialized in the U.S.

1996

- Novartis Bt 11, insect protected corn, receives approval for commercial sale in the U.S.
- Event 176 (corn borer resistance) receives approval for import into European Union.
- Posilac bovine somatotropin, designed to increase milk efficiency in dairy cattle, is approved for use in the United States.
- First commercial introduction of a ‘gene chip’ designed to rapidly detect variances in the HIV virus

and select the best drug treatment for patients.

- The discovery of a gene associated with Parkinson's disease provides an important new avenue of research into the cause and potential treatment of the debilitating neurological ailment.

1997

- Roundup Ready® cotton first commercialized in the US.
- First animal cloned from an adult cell: a sheep named Dolly in Scotland.
- First weed- and insect-resistant biotech crops commercialized: Roundup Ready soybeans and Bollgard insect-protected cotton.
- Biotech crops grown commercially on nearly 5 mil. acres worldwide: Argentina, Australia, Canada, China, Mexico and the United States.
- A group of Oregon researchers claims to have cloned two Rhesus monkeys.
- A new DNA technique combines PCR, DNA chips and a computer program to create a new tool in the search for disease-causing genes.

1998

- DEKALB markets the first Roundup Ready corn.
- YieldGard Corn is approved for import into European Union.
- New Zealand researchers produce Elsie, a clone of Lady, the last of the rare Enderby cattle line, thereby securing the future of the species.
- Embryonic stem cells are grown successfully, opening new doors to cell- or tissue-based therapies.
- New Zealand researchers develop the first genetically engineered radiata pine in the laboratory.
- University of Hawaii scientists clone three generations of mice from nuclei of adult ovarian cumulus cells.
- Human embryonic stem cell lines are established.
- Scientists at Japan's Kinki

University clone eight identical calves using cells taken from a single adult cow.

- The first complete animal genome, for the *C. elegans* worm, is sequenced.
- A rough draft of the human genome map is produced, showing the locations of over 30,000 genes.
- Five Southeast Asian countries form a consortium to develop disease-resistant papayas.

1999

- President Clinton awards four Monsanto scientists National Medal Of Technology.
- A U.S. company announces the successful cloning of human embryonic cells from an adult skin cell.
- New Zealand researchers develop a new vaccine for bovine and human tuberculosis.
- Chinese scientists clone a giant panda embryo.

Also in the 1990s

- First conviction using genetic fingerprinting in the U.K.
- Isolation of gene that clearly participates in the normal process of regulating weight.
- Discovery that hereditary colon cancer is caused by defective DNA repair gene.
- Recombinant rabies vaccine tested in raccoons.
- Biotechnology based biopesticide approved for sale in the U.S.
- Patents issued for mice with specific transplanted genes.
- First European patent on a transgenic animal issued for transgenic mouse sensitive to carcinogens.
- Breast cancer susceptibility genes cloned.

2000

- First complete map of a plant genome developed: *Arabidopsis thaliana*.
- 108.9 mil. acres of biotech crops grown in 13 countries.

- “Golden Rice” announcement allows the technology to be available to developing countries in hopes of improving the health of undernourished people and preventing some forms of blindness.
- First biotech crop field-tested in Kenya: virus-resistant sweet potato.
- Rough draft of the human genome sequence is announced.

2001

- First complete map of the genome of a food plant completed: rice.
- Scientific journals publish complete human genome sequence.
- Researchers in Australia report developing a technique using “hairpin RNA” that vaccinates crop plants against viruses like Barley Yellow Dwarf Virus.
- Chinese National Hybrid researchers report developing a “super rice” that could produce double the yield of normal rice.
- The European Commission issues rules requiring the labeling of all foods and animal feed derived from GMOs.
- Complete DNA sequencing of the agriculturally important bacterium *Sinorhizobium meliloti*.
- A single gene from *Arabidopsis* inserted into tomato plants to create the first crop able to grow in salty water and soil.
- Genome sequence for *Agrobacterium tumefaciens*, important in agriculture, released.
- Researchers grow thale cress that lights up when it is damaged or stressed—a step toward developing hardier, stress-resistant crops.
- First comprehensive molecular map completed of the peanut.

2002

- The draft version of the complete map of the human genome is published, and the first part of the Human Genome Project comes to an end ahead of schedule and under budget.

- Biotech crops grown on 145 mil. acres in 16 countries, a 12 percent increase in acreage grown in 2001. Over one-quarter (27 percent) of the global acreage was grown in nine developing countries.
- Researchers announce successful results for a vaccine against cervical cancer, the first demonstration of a preventative vaccine for a type of cancer.
- Scientists complete the draft sequence of the most important pathogen of rice, a fungus that destroys enough rice to feed 60 mil. people annually. By combining an understanding of the genomes of the fungus and rice, scientists will elucidate the molecular basis of the interactions between the plant and pathogen.
- Researchers sequence the DNA of rice, the main food source for two-thirds of the world’s population. It is the first crop to have its genome decoded.

2003

- Monsanto Mon 863 approved for commercial sale in the United States
- Liberty Link LL Cotton 25 approved for commercial sale in U.S.

2004

- Global plantings of biotech crops reach 200 million acres.
- European Union authorizes use of NK603, Roundup Ready corn for human consumption
- Univ. of Nebraska researcher develops soybean with healthier oil that could improve consumer health.

Information sources: Access Excellence, Genentech, Inc. Biotech 90: Into the Next Decade, G. Steven Burrill with the Ernst & Young High Technology Group, Biotechnology Industry Organization, International Food Information Council, ISB News Report, NC Biotechnology Center, TX Society for Biomedical Research.