

# Historical Events in Biotechnology

## BC

**1750** The Sumerians use microorganisms to brew ale.

**500** The Chinese use moldy soybean curds as an antibiotic to treat boils.

**250** The Greeks practice crop rotation to maximize soil fertility.

**100** Powdered chrysanthemum is used in China as an insecticide.

## AD: Before the 20th Century

**1590** The microscope is invented by Janssen.

**1663** Cells are first described by Hooke.

**1675** Leeuwenhoek discovers protozoa and bacteria.

**1797** Jenner inoculates a child with a viral vaccine to protect him from smallpox.

**1802** The word "biology" first appears.

**1824** Dutrochet discovers that tissue is composed of living cells.

**1830** Proteins are discovered.

**1833** The cell nucleus is discovered. The first enzymes are isolated.

**1855**

- The Escherichia coli bacterium is discovered. It later becomes a major research, development, and production tool for biotechnology.
- Pasteur begins working with yeast, eventually proving they are living organisms.

**1863** Mendel, in his study of peas, discovers that traits were transmitted from parents to progeny by discrete, independent units, later called genes. His observations lay the groundwork for the field of genetics.

**1869** Miescher discovers DNA in the sperm of trout.

**1877** A technique for staining and identifying bacteria is developed by Koch.

**1878**

- The first centrifuge is developed by Laval.
- The term "microbe" is first used.

**1879** Flemming discovers chromatin, the rod-like structures inside the cell nucleus that later come to be called "chromosomes."

**1883** The first rabies vaccine is developed.

**1888** The chromosome is discovered by Waldyer.

## AD: First Half of the 20th Century

**1902** The term "immunology" first appears.

**1906** The term "genetics" is introduced.

**1907** The first in vivo culture of animal cells is reported.

**1909** Genes are linked with hereditary disorders.

**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** The word "biotechnology" is first used by a Hungarian agricultural engineer.

**1920** The human growth hormone is discovered by Evans and Long.

**1927** Muller discovers that X-rays cause mutation.

**1928** Fleming discovers penicillin, the first antibiotic.

**1938** The term "molecular biology" is coined.

**1941** The term "genetic engineering" is first used by a Danish microbiologist.

**1942** The electron microscope is used to identify and characterize a bacteriophage- a virus that infects bacteria.

**1943** Avery demonstrates that DNA is the "transforming factor" and is the material of genes.

**1944** DNA is shown to be the material substance of the gene.

**1949** Pauling shows that sickle cell anemia is a "molecular disease" resulting from a mutation.

## 1950 to 1960

**1951** McClintock discovers transposable elements, or "jumping genes," in corn.

**1953** Watson and Crick reveal the three-dimensional structure of DNA.

**1954** Cell-culturing techniques are developed.

**1955** An enzyme involved in the synthesis of a nucleic acid is isolated for the first time.

**1956** The fermentation process is perfected in Japan.

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

**1957** Sickle cell anemia is shown to occur due to a change of a single amino acid.

**1960** Exploiting base pairing, hybrid DNA-RNA molecules are created.

Messenger RNA is discovered.

**1961** The genetic code is understood for the first time.

**1967** The first automatic protein sequencer is perfected.

**1969** An enzyme is synthesized in vitro for the first time.

## 1970s

**1970** Specific restriction nucleases are identified, opening the way for gene cloning.

**1972** The DNA composition of humans is discovered to be 99% similar to that of chimpanzees and gorillas.

**1973** Cohen and Boyer perform the first successful recombinant DNA experiment, using bacterial genes.

**1974** The National Institute of Health forms a Recombinant DNA Advisory Committee to oversee recombinant genetic research.

**1975** Colony hybridization and Southern blotting are developed for detecting specific DNA sequences.

**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.

**1977** Genetically engineered bacteria are used to synthesize human growth protein.

**1978** North Carolina scientists Hutchinson and Edgell show it is possible to introduce specific mutations at specific sites in a DNA molecule.

## 1980s

**1980**

- The U.S. Supreme Court, in the landmark case *Diamond v. Chakrabarty*, approves the principle of patenting genetically engineered life forms.
- The U.S. patent for gene cloning is awarded to Cohen and Boyer.

**1981**

- The North Carolina Biotechnology Center is created by the state's General Assembly as the nation's first state-sponsored initiative to develop biotechnology. Thirty-five other states follow with biotechnology centers of various kinds.
- The first gene-synthesizing machines are developed.
- The first genetically engineered plant is reported.
- Mice are successfully cloned.

**1982** Humulin, Genentech's human insulin drug produced by genetically engineered bacteria for the treatment of diabetes, is the first biotech drug to be approved by the Food and Drug Administration.

**1983**

- 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.
- The first genetic markers for specific inherited diseases are found.

- Efficient methods are developed to synthesize double-stranded DNA from first-strand cDNA involving minimal loss of sequence information.

#### 1984

- The DNA fingerprinting technique is developed.
- The first genetically engineered vaccine is developed.
- Chiron clones and sequences the entire genome of the HIV virus.

**1985** Fully active murine RT is cloned and overexpressed in *E. coli*.

#### 1986

- The first field tests of genetically engineered plants (tobacco) are conducted.
- Ortho Biotech's Orthoclone OKT3, used to fight kidney transplant rejection, is approved as the first monoclonal antibody treatment.
- The first biotech-derived interferon drugs for the treatment of cancer, Biogen's Intron A and Genentech's Roferon A, are approved by the FDA. In 1988, the drugs are used to treat Kaposi's sarcoma, a complication of AIDS.
- The first genetically engineered human vaccine, Chiron's Recombivax HB, is approved for the prevention of hepatitis B.

#### 1987

- Humatrope is developed for treating human growth hormone deficiency.
- Advanced Genetic Sciences' Frostban, a genetically altered bacterium that inhibits frost formation on crop plants, is field tested on strawberry and potato plants in California, the first authorized outdoor tests of an engineered bacterium.
- Genentech's tissue plasminogen activator (tPA), sold as Activase, is approved as a treatment for heart attacks.
- Reverse transcription and PCR are combined to amplify mRNA sequences.
- Cloned murine RT is engineered to maintain polymerase and eliminate RNase H activity.

**1988** 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

- Amgen's Epogen is approved for the treatment of renal disease anemia. Microorganisms are used to clean up the Exxon Valdez oil spill.
- The gene responsible for cystic fibrosis is discovered.

## 1990s

**1990** The first federally approved gene therapy treatment is performed successfully on a 4-year-old girl suffering from an immune disorder.

#### 1991

- Amgen develops Neupogen, the first of a new class of drugs called colony stimulating factors, for the treatment of low white blood cells in chemotherapy patients.
- Immunex's Leukine, used to replenish white blood counts after bone marrow transplants, is approved.
- Genzyme's Ceredase is approved for the treatment of Gaucher's disease.

#### 1992

- Recombinate, developed by Genetics Institute and used in the treatment of hemophilia A, becomes the first genetically engineered blood clotting factor approved in the U.S.
- Chiron's Proleukin is approved for the treatment of renal cell cancer.

#### 1993

- Chiron's Betaseron is approved as the first treatment for multiple sclerosis in 20 years.
- The FDA declares that genetically engineered foods are "not inherently dangerous" and do not require special regulation.
- The Biotechnology Industry Organization (BIO) is created by merging two smaller trade associations.

#### 1994

- Genentech's Nutropin is approved for the treatment of growth hormone deficiency.
- The first breast cancer gene is discovered.
- Calgene's Flavr Savr tomato, engineered to resist rotting, is approved for sale.

## 1995

- 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*.

## 1996

- Biogen's Avonex is approved for the treatment of multiple sclerosis. The company builds a \$50 million plant in Research Triangle Park, N.C., to manufacture the recombinant interferon drug.
- Scottish scientists clone identical lambs from early embryonic sheep.

## 1997

- Scottish scientists report cloning a sheep, using DNA from adult sheep cells.
- A group of Oregon researchers claims to have cloned two Rhesus monkeys.
- A new DNA technique combines PCR, DNA chips, and a computer program, providing a new tool in the search for disease-causing genes.

## 1998

- University of Hawaii scientists clone three generations of mice from nuclei of adult ovarian cumulus cells.
- Human skin is produced in vitro.
- Embryonic stem cells are used to regenerate tissue and create disorders mimicking diseases.
- The first complete animal genome for the *elegans* worm is sequenced.  
A rough draft of the human genome map is produced, showing the locations of more than 30,000 genes.
- The Biotechnology Institute is founded by BIO as an independent national, 501(c)(3) education organization with an independent Board of Trustees.

## 1999

- The complete genetic code of the human chromosome is first deciphered.  
The rising tide of public opinion in Europe brings biotech food into the spotlight.

# 2000 and Beyond

## 2000

- A rough draft of the human genome is completed by Celera Genomics and the Human Genome Project.
- Pigs are the next animal cloned by researchers, hopefully to help produce organs for human transplant.
- "Golden Rice," modified to make vitamin A, promises to help third-world countries alleviate blindness.
- The 2.18 million base pairs of the commonest cause of bacterial meningitis, *Neisseria meningitidis*, are identified.

**2001** The sequence of the human genome is published in *Science* and *Nature*, making it possible for researchers all over the world to begin developing treatments.

**2002** Scientists complete the draft sequence of the most important pathogen of rice, a fungus that destroys enough rice to feed 60 million people annually. By combining an understanding of the genomes of the fungus and rice, scientists will describe the molecular basis of the interactions between the plant and pathogen.

**2003** Dolly, the cloned sheep that made headlines in 1997, is euthanized after developing progressive lung disease. Dolly was the first successful clone of a mammal.

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