

Timeline of Medical Biotechnology

1950s

1952

- Dr. George Gey establishes a continuous cell line taken from a human cervical carcinoma isolated from Henrietta Lacks, who died of the cancer in 1951. This cell line, containing HeLa cells, is commonly used in medical research.

1953

- Dr. James Watson and Dr. Francis Crick reveal the 3-D structure of DNA.
- Dr. Joseph Murray performs the first kidney transplant between identical twins.

1955

- An enzyme, **DNA polymerase**, involved in the synthesis of a nucleic acid, is isolated for the first time.
- Dr. Jonas Salk develops the first polio vaccine. The development marks the first use of mammalian cells (monkey kidney cells) and the first application of **cell culture technology** to generate a commercial product.

1957

- Scientists prove that sickle-cell anemia occurs due to a change in a single amino acid.

1958

- Dr. Arthur Kornberg of Washington University in St. Louis makes DNA in a test tube for the first time.
- The first automatic protein sequencer, the Moore-Stein amino acid analyzer, is developed.

1960s

1960

- French scientists discover messenger RNA (mRNA).

1961

- Scientists understand genetic code for the first time.

1962

- Dr. Osamu Shimomura of Boston University discovers the green fluorescent protein *Aequorea victoria* in jellyfish. He later develops

it into a tool for observing previously invisible cellular processes.

1963

- Independent groups in the United States, Germany and China synthesize insulin, a pancreatic hormone.

1964

- The existence of **reverse transcriptase** is predicted.
- Dr. Samuel Katz and Dr. John F. Enders develop the first vaccine for measles.

1967

- Dr. Maurice Hilleman develops the first American vaccine for mumps.

1969

- The first vaccine for rubella is developed. It is combined with the measles and mumps vaccines to form the measles/mumps/rubella vaccine in 1972.

1970s

1970

- Restriction enzymes are discovered. These enzymes cut DNA into pieces and are used for various studies and applications. The restriction enzyme technique becomes a fundamental tool in modern genetic research and opens the way for gene **cloning**.
- Dr. Har Gobind Khorana synthesizes the first complete gene at the University of Wisconsin–Madison.

1972

- DNA ligase, which links DNA fragments together, is used for the first time.
- The DNA composition of humans is discovered to be 99 percent similar to that of chimpanzees and gorillas.
- The purified enzyme reverse transcriptase is first used to synthesize complementary DNA from purified messenger RNA in a test tube.

1973

- Dr. Stanley Cohen and Dr. Herbert Boyer use bacterial genes to perform the first successful recombinant DNA experiment, which inserted

a recombinant DNA molecule into a cell for replication.

- Dr. Edwin Southern develops a blotting technique for DNA called the Southern blot. It becomes a seminal technology for studying the structure of DNA.

1974

- The U.S. National Institutes of Health (NIH) forms a Recombinant DNA Advisory Committee to oversee recombinant genetic research.
- The first vaccine for chicken pox is developed in Japan.

1975

- **Colony hybridization** and **Southern blotting** are developed for detecting specific DNA sequences.
- The first monoclonal antibodies are produced. Dr. César Milstein, Dr. Georges Kohler and Dr. Niels Jeme develop monoclonal antibody technology by fusing immortal tumor cells with antibody-producing B-lymphocyte cells to produce **hybridomas** that continuously synthesize identical (or monoclonal) antibodies.

1976

- The NIH releases the first guidelines for recombinant DNA research.
- Molecular **hybridization** is used for the prenatal diagnosis of alpha thalassemia.
- Yeast genes are expressed in *E. coli* bacteria.

1977

- Protocols are developed to rapidly sequence long sections of DNA.
- Genetically engineered bacteria are used to synthesize the human growth protein somatostatin, marking the first time a synthetic recombinant gene is used to clone a protein. Many consider this to be the advent of the Age of Biotechnology.
- Dr. Robert Austrian of the University of Pennsylvania develops the first vaccine for pneumonia.

1978

- Dr. Herbert Boyer of the University of California, San Francisco, constructs a synthetic version of the human insulin gene and inserts it into the bacterium *E. coli*, allowing the bacterium to produce human insulin.
- The first test-tube baby, Louise Brown, is born in the United Kingdom.

- The first vaccine for meningococcal meningitis is developed.

1980s

1980

- The U.S. Supreme Court rules genetically altered life forms can be patented, opening up enormous possibilities for commercially exploiting genetic engineering. The first patent of this nature was awarded to the Exxon oil company to patent an oil-eating microorganism, which would later be used in the 1989 cleanup of the Exxon oil spill at Prince William Sound, Alaska.
- Dr. Stanley Cohen and Dr. Herbert Boyer receive a U.S. patent for gene cloning.
- The first automatic gene machine, or gene-synthesizing machine, is developed in California.
- Founding of Amgen, which will grow to become the world's largest biotechnology medicines company.

1981

- Dr. Baruch Blumberg and Dr. Irving Millman develop the first vaccine for hepatitis B (not recombinant) four years after the virus is discovered.
- Scientists in Switzerland clone mice.
- The first transgenic animals are produced by transferring genes from other animals into mice.

1982

- The U.S. Food and Drug Administration (FDA) approves the first biologic—or recombinant protein: Humulin®, Genentech's human insulin drug produced by genetically engineered bacteria for the treatment of diabetes.

1983

- Dr. Luc Montagnier of the Pasteur Institute in Paris isolates the AIDS virus.
- Dr. Kary Banks Mullis invents the polymerase chain reaction (PCR), a technique for multiplying DNA sequences. PCR is recognized as the most revolutionary molecular biology technique of the 1980s.
- The FDA approves a monoclonal antibody-based diagnostic test to detect *Chlamydia trachomatis*.
- The first artificial chromosome is synthesized.
- The first genetic markers for specific inherited diseases are found.

1984

- The **DNA fingerprinting** technique is developed. When a restrictive enzyme is applied to DNA from different individuals, the resulting sets of fragments sometimes differ markedly from one person to the next. Such variations in DNA are called restriction fragment length polymorphisms and are extremely useful in genetic studies.
- The first genetically engineered vaccine is developed for hepatitis B.
- The entire genome of the HIV virus is cloned and sequenced.

1985

- Genetic fingerprinting enters the courtroom.
- Genentech becomes the first biotechnology company to launch its own **biopharmaceutical** product.
- Genetically engineered plants resistant to insects, viruses and bacteria are field-tested for the first time.
- Cloning of the gene that encodes human lung surfactant protein is accomplished. This is a major step toward reducing premature birth complications.
- The NIH approves guidelines for performing experiments in gene therapy on humans.

1986

- University of California, Berkeley, chemist Dr. Peter Schultz describes how to combine antibodies and enzymes (abzymes) to create therapeutics.
- The automated DNA sequencer is invented in California.
- The FDA approves the first monoclonal antibody treatment to fight kidney transplant rejection.
- The FDA approves first biotech-derived **interferon** drugs to treat cancer. In 1988, the drugs are used to treat Kaposi's sarcoma, a complication of AIDS.
- The FDA approves the first genetically engineered human vaccine to prevent hepatitis B.

1987

- The FDA approves a genetically engineered tissue plasminogen activator to treat heart attacks.
- Dr. Maynard Olson and colleagues at Washington University invent yeast artificial

chromosomes, which are expression vectors for large proteins.

- Reverse transcription and the polymerase chain reaction are combined to amplify messenger RNA sequences.
- DNA microarray technology, the use of a collection of distinct DNAs in arrays for expression profiling, is first described. The arrayed DNAs are used to identify genes whose expression is modulated by interferon.
- The FDA approves a diagnostic serum tumor marker test for ovarian cancer.

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.
- The first agreement between two companies with parallel patents for cross-licensing of biotech products occurs and becomes the prototype.

1989

- The FDA approves Amgen's first biologically derived human therapeutic.
- Oil-eating bacteria are used to clean up the *Exxon Valdez* oil spill.
- A 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 called adenosine deaminase deficiency.
- The Human Genome Project, the international effort to map all of the genes in the human body, is launched. Estimated cost: \$13 billion.
- The FDA licenses the first hepatitis C antibody test, which helps to ensure the purity of blood bank products.
- The FDA approves a bioengineered form of the protein interferon gamma to treat chronic granulomatous disease.
- The FDA approves a modified enzyme for enzyme replacement therapy to treat severe combined immunodeficiency disease. It is the first successful application of enzyme replacement therapy for an inherited disease.

1992

- The U.S. Army collects blood and tissue samples from all new recruits as part of a genetic dog tag program aimed at better identification of soldiers killed in combat.
- The FDA approve the first genetically engineered blood-clotting factor—a recombinant protein used to treat hemophilia A.
- The FDA approves a recombinant protein to treat renal cell cancer.
- American and British scientists unveil a technique for testing embryos **in vitro** for genetic abnormalities such as cystic fibrosis and hemophilia.

1993

- The FDA approves a recombinant protein to treat multiple sclerosis—marking the first new multiple sclerosis treatment in 20 years.
- An international research team, led by Dr. Daniel Cohen of the Center for the Study of Human Polymorphisms in Paris, produces a rough map of all 23 pairs of human chromosomes.
- Two smaller trade associations merge to form the Biotechnology Industry Organization, an international biotechnology advocacy group.

1994

- The FDA approves a recombinant protein to treat growth hormone deficiency.
- Dr. Mary-Claire King at the University of California, Berkeley, discovers the first breast cancer gene, BRCA1.
- The FDA approves a modified enzyme to treat Gaucher's disease.
- A multitude of genes, human and otherwise, are identified and their functions described. These include:
 - Ob, a gene predisposing to obesity
 - BCR, a breast cancer susceptibility gene
 - BCL-2, a gene associated with apoptosis (programmed cell death)
 - Hedgehog genes (named because of their shape) produce proteins that guide cell differentiation in advanced organisms
 - Vpr, a gene governing reproduction of the HIV virus
- Linkage studies identify genes for a variety of ailments, including bipolar disorder, cerulean cataracts, melanoma, hearing loss, dyslexia, thyroid cancer, sudden infant death syndrome, prostate cancer and dwarfism.
- The FDA approves a genetically engineered

version of human DNase, which breaks down protein accumulation in the lungs of cystic fibrosis patients. It represents the first new therapeutic drug for managing cystic fibrosis in more than 30 years.

1995

- The first baboon-to-human bone marrow transplant is performed on an AIDS patient.
- The first vaccine for hepatitis A is developed. The NIH, the U.S. Army and the Centers for Disease Control and Prevention are significantly involved in the development and clinical testing of the vaccine.
- Scientists at the Institute for Genomic Research complete the first full gene sequence of a living organism (other than a virus) for the bacterium *Haemophilus influenzae*.
- A European research team identifies a genetic defect that appears to be the most common cause of deafness.

1996

- The Department of Biochemistry at Stanford University and Affymetrix develop the GeneChip, a small glass or silica microchip that contains thousands of individual genes that can be analyzed simultaneously. This marks a technological breakthrough in gene expression and DNA-sequencing technology.
- A group of scientists sequence the complete genome of a complex organism, *Saccharomyces cerevisiae*, otherwise known as baker's yeast. The achievement marks the complete sequencing of the largest genome to date—more than 12 million base pairs of DNA.
- A new, inexpensive diagnostic biosensor test is developed to allow instantaneous detection of a toxic strain of *E. coli*, the bacteria responsible for many food-poisoning outbreaks.

1997

- The first human artificial chromosome is created. A combination of natural and synthetic DNA is used to create a genetic cassette that can potentially be customized and used in gene therapy.
- The FDA approves a recombinant follicle-stimulating hormone to treat infertility.
- The FDA approves the first bloodless HIV-antibody test that uses cells from patients' gums.
- Scientists at the Institute for Genomic Research sequence the complete genome of the Lyme

disease pathogen, *Borrelia burgdorferi*, along with the genome for the organism linked to stomach ulcers, *Helicobacter pylori*.

- Scientists at the University of Wisconsin–Madison sequence the *E. coli* genome.
- The FDA approves the first therapeutic antibody to treat cancer in the United States. It is used for patients with non-Hodgkin's lymphoma.

1998

- Human skin is produced for the first time in the lab.
- Two research teams culture embryonic stem cells. Embryonic stem cells are used to regenerate tissue and create disorders mimicking diseases.
- Scientists at the Sanger Institute of the Washington University School of Medicine in St. Louis sequence the first complete animal genome for the *Caenorhabditis elegans* worm.
- A rough draft of the human genome map is produced, showing the locations of more than 30,000 genes.
- The first vaccine for Lyme disease is developed.
- The FDA approves a novel monoclonal antibody to treat Crohn's disease.
- A monoclonal antibody therapy used against breast cancer has favorable results, heralding a new era of treatment based on molecular targeting of tumor cells.
- Approval of the Her-2 inhibitor for the treatment of breast cancer patients who have tested positive for the Her-2 mutation brings personalized medicine to oncology.

1999

- The complete genetic code of the human chromosome is deciphered.

2000s

2000

- Scientists at Celera Genomics and the Human Genome Project complete a rough draft of the human genome.

2001

- *Science* and *Nature* magazines publish the human genome sequence, making it possible for scientists all over the world to begin researching new treatments for diseases that have genetic origins, such as cancer, heart disease, Parkinson's and Alzheimer's.

2002

- An era of very rapid shotgun sequencing of major genomes is completed. Included are the mouse, chimpanzee, dog and hundreds of other species.

2003

- Celera and NIH complete sequencing of the human genome.

2004

- The FDA approves the first monoclonal antibody that is an antiangiogenic, inhibiting the growth of blood vessels—or **angiogenesis**—for cancer therapy.
- The FDA clears a DNA microarray test system, which aids in selecting medications for a variety of conditions. This is an important step toward personalized medicine.

2006

- The FDA approves a recombinant vaccine against human papillomavirus, which causes genital warts and can cause cervical cancer.
- Scientists determine the 3-D structure of the human immunodeficiency virus, which causes AIDS.

2007

- Scientists discover how to use human skin cells to create embryonic stem cells.

2008

- Chemists in Japan create the first DNA molecule made almost entirely of artificial parts. The discovery can be used in the fields of gene therapy.
- Dr. Craig Venter and his team replicate a bacterium's genetic structure entirely from laboratory chemicals, moving a step closer toward creating the world's first living artificial organism.