

History of Biotech and Biotech Applications

BIT 120

Source for History Information:

www.accessexcellence.org

History of Biotechnology

- The term "biotechnology" was coined in 1919 by Karl Ereky, an Hungarian engineer
- Traditional biotechnology has been used for thousands of years to produce improved food and health care products. Today, modern biotechnology enables us to develop improved products more safely and more rapidly than ever before.
- Biotechnology in one form or another has flourished since prehistoric times.

Examples

- Examples:
 - they could plant their own crops and breed their own animals, they learned to use biotechnology.
 - The discovery that fruit juices fermented into wine, or that milk could be converted into cheese or yogurt, or that beer could be made by fermenting solutions of malt and hops began the study of biotechnology

Examples cont'd

- When the first bakers found that they could make a soft, spongy bread rather than a firm, thin cracker, they were acting as fledgling biotechnologists.
- The first animal breeders, realizing that different physical traits could be either magnified or lost by mating appropriate pairs of animals, engaged in the manipulations of biotechnology.

Definition

- **Definition:** What then is biotechnology? the term "biotechnology" refers to the use of living organisms or their products to modify human health and the human environment.
- **Other definitions: 1.** •Biotechnologists use engineering and science to create new products from biologically based raw materials, such as vaccines or foods. They also develop factory processes to reduce pollution or treat waste products.
- **•2.** Biotechnology uses living cells and materials produced by cells to create pharmaceutical, diagnostic, agricultural, environmental, and other products to benefit society.

Periods of Biotechnology History:

- Pre- 1800: Early applications and speculation
- 1800-1900: Significant advances in basic understanding
- 1900-1953: Genetics
- 1953- 1976: DNA research, science explodes
- 1977- present: modern biotechnology

Biotechnology Time Lines

- **6000 BC**
- Yeast was used to make beer by Sumerians and Babylonians.
- **4000 BC**
- The Egyptians discovered how to bake leavened bread using yeast.
- **420 BC**
- Socrates (470? - 399 BC), the Greek philosopher, speculated on why children don't always resemble their parents.
- **320 BC**
- Aristotle (384 - 322 BC), told his students that all inheritance comes from the father.

Biotechnology Time Lines

- **1000 AD**
- Hindus observed that certain diseases may "run in the family."
Spontaneous Generation is the dominant explanation that organisms arise from non-living matter. Maggots, for example, were supposed to arise from horsehair.
- **1630 AD**
- William Harvey concluded that plants and animals alike reproduce in a sexual manner:—**egg isolated in 1800's**
- **1660-1675 AD**
- Marcello Malpighi (1628-1694) in this period used a microscope to study blood circulation in capillaries, described the nervous system as bundles of fibers connected to the brain by the spinal cord,.

Biotechnology Time Lines

- **1673 AD**
- Anton van Leeuwenhoek (1632 - 1723), He was the first scientist to describe protozoa and bacteria and to recognize that such microorganisms might play a role in fermentation.
- **1701**
- Giacomo Pylarini in Constantiople practiced "inoculation"--intentionally giving children smallpox to prevent a serious case later in life. Inoculation will compete with "vaccination"--an alternative method that uses cowpox rather than smallpox as the protecting treatment--for a century.
- **Gave too much and some children died**

Biotechnology Time Lines

- **1809**
- Nicolas Appert devised a technique using heat to can and sterilize food
- **1827**
- The worldwide search for the elusive mammalian egg ended with the first observation of canine eggs. **Remember 1630 and William Harvey**
- **1850**
- **ONE OF MY FAVORITES** Ignaz Semmelweis used epidemiological observations to propose the hypothesis that **childbed fever can be spread from mother to mother by physicians**. He tested the hypothesis by having physicians wash their hands after examining each patient. He became despised by the medical profession and lost his job.

Biotechnology Time Lines

- **1856**
- Karl Ludwig discovered a technique for keeping animal organs alive outside the body, by pumping blood through them.
- In contrast to the ideas of Justis Liebig, **Louis Pasteur (1822 - 1895)** asserted that microbes are responsible for fermentation.
1859
- **Charles Darwin (1809 - 1882)** hypothesized that animal populations adapt their forms over time to best exploit the environment, a process he referred to as "natural selection." As he traveled in the Galapagos Islands, **he observed how the finch's beaks on each island were adapted** to their food sources.

Biotechnology Time Lines

- **1863**
- Louis Pasteur invented the process of pasteurization, heating wine sufficiently to inactivate microbes (that would otherwise turn the "vin" to "vin aigre" or "sour wine") while at the same time not ruining the flavor of the wine.
- Anton de Bary proved that a fungus causes potato blight. A challenge for scientists during this period was to discern whether a microbe was the cause of, or the result of, a disease.

Biotechnology Time Lines

- **1865**
- Gregor Mendel (1822 - 1884), an Augustinian monk, presented his laws of heredity to the Natural Science Society in Brunn, Austria. Mendel proposed that invisible internal units of information account for observable traits, and that these "factors" - which later became known as genes - are passed from one generation to the next. Mendel's work remained unnoticed, languishing in the shadow of Darwin's more sensational publication from five years earlier, until 1900, when Hugo de Vries, Erich Von Tschermak, and Carl Correns published research corroborating Mendel's mechanism of heredity.

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Biotechnology Time Lines

- Pasteur investigated silkworm disease and established that diseases can be transmitted from one animal to another.
- Joseph Lister began using disinfectants such as phenol (=carbolic acid) in wound care and surgery as Pasteur developed the germ theory of disease

Biotechnology Time Lines

■ 1868

- Davaine used heat treatment to cure a plant of bacterial infection.
- Fredrich Miescher, a Swiss biologist, successfully isolated nuclein, a compound that includes nucleic acid, from pus cells obtained from discarded bandages.

■ 1870

- W. Flemming discovered mitosis.

Biotechnology Time Lines

- **1871**
- **DNA was isolated from the sperm of trout found in the Rhine River.**
- **1873-6**
- Robert Koch investigated anthrax and developed techniques to view, grow, and stain organisms. He then photographed them, aided by Gram, Cohn, and Weigart.
- **1880**
- Studying fowl cholera, Pasteur published his work on "attenuated" or weakened strains of organisms that could not cause disease but protected against severe forms of the same disease.

Biotechnology Time Lines

- **1881 ANTRAX**
- Robert Koch described bacterial colonies growing on potato slices, on gelatin medium, and on agar medium. Nutrient agar became a standard tool for obtaining pure cultures and for identifying genetic mutants. This is considered by T.D. Brock to be the single most important discovery in the rise of microbiology.
- Pasteur used attenuation to develop vaccines against the bacterial pathogens of fowl cholera and anthrax; this was a founding moment in immunology and opened new areas in the field of preventive medicine.

Biotechnology Time Lines

- 1884
- **ROBERT KOCH STATED HIS "POSTULATES" FOR TESTING WHETHER A MICROBE IS THE CAUSAL AGENT OF A DISEASE.**
- Pasteur developed a **rabies vaccine**.
- Christian Gram described the differential staining technique for bacteria known as the Gram stain.
- Gregor Mendel died after 41 years of meticulously studying the heredity "factors" of pea plants. Having received no scientific acclaim during his lifetime, he said not long before his death, "My time will come."

Biotechnology Time Lines

- **1900 - 1953 - Converging on DNA**
- **1900 MENDEL'S WORK FINALLY TOOK ON IMPORTANCE**
- The science of genetics was finally born when Mendel's work was rediscovered by three scientists - Hugo DeVries, Erich Von Tschermak, and Carl Correns - each one independently researching scientific literature for precedents to their own "original" work.
- **1902 HUMAN GENETICS BORN**
- Walter Stanborough Sutton stated that chromosomes are paired and may be the carriers of heredity. He suggested that Mendel's "factors" are located on chromosomes.

Biotechnology Time Lines

- **1905 X AND Y CHROMOSOMES RELATED TO GENDER**
- Edmund Wilson and Nellie Stevens proposed the idea that separate X and Y chromosomes determine sex. They showed that a single Y chromosome determines maleness, and two copies of the X chromosome determine femaleness.
- **1905-1908**
- William Bateson and Reginald Crudell Punnett, along with others, demonstrated that some genes modify the action of other genes.
- **1906**
- Paul Erlich investigated atoxyl compounds and discovered the beneficial properties of Salvarsan - the first chemotherapeutic agent.

Biotechnology Time Lines

- **1907**
- Thomas Hunt Morgan began his work with fruit flies that will prove that chromosomes have a definite function in heredity, establish mutation theory, and lead to a fundamental understanding of the mechanisms of heredity.
- **1909 MENDEL'S LAWS TO ANIMALS**
- Wilhelm Johannsen coined the terms 'gene' to describe the carrier of heredity; 'genotype' to describe the genetic constitution of an organism; and 'phenotype' to describe the actual organism, which results from a combination of the genotype and the various environmental factors.

Biotechnology Time Lines

- **1910 BASIS OF MODERN GENETICS**
- **Thomas Hunt Morgan proved that genes are carried on chromosomes, establishing the basis of modern genetics.** With his co-workers, he pinpointed the location of various fruit fly genes on chromosomes, establishing the use of *Drosophila* fruit flies to study heredity..
- **1911**
- Thomas Hunt Morgan explained the separation of certain inherited characteristics that are usually linked as caused by the breaking of chromosomes sometimes during the process of cell division. Morgan began to map the positions of genes on chromosomes of the fruit fly.

Biotechnology Time Lines

- **1912**
- **Lawrence Bragg discovered that X-rays can be used to study the molecular structure of simple crystalline substances.**
- **1918**
- **Herbert M. Evans found (incorrectly) that human cells contain 48 chromosomes.**
- **1924 EUGENICS IN THE UNITED STATES**
- **Politicians encouraged by the eugenics movement passed the U.S. Immigration Act of 1924, limiting the influx of poorly educated immigrants from Southern and Eastern Europe on the grounds of suspected genetic inferiority.**

Biotechnology Time Lines

- **1926**
- Thomas Hunt Morgan published 'The theory of the gene', the culmination of work on the physical basis for Mendelian genetics based on breeding studies and optical microscopy.
- **Hermann Muller discovered that X-rays induce genetic mutations in fruit flies 1,500 times more quickly than under normal circumstances.** This discovery provided researchers with a way to induce mutations, an important tool for discovering what genes do on their own.

Biotechnology Time Lines

- **1928**
- Fredrick Griffiths noticed that a rough type of bacterium changed to a smooth type when an unknown "transforming principle" from the smooth type was present. Sixteen years later, Oswald Avery identified that "transforming principle" as DNA.
- Alexander Fleming noticed that all the bacteria in a radius surrounding a bit of mold in a petrie dish had died. **The age of penicillin thus began, although it would be almost 15 years before it was made available to the community for medicinal use.**

Biotechnology Time Lines

- **1938**
- Proteins and DNA were studied in various labs with X-ray crystallography.
- **The term "molecular biology" was coined.**
- **1941 ONE GENE ONE ENZYME**
- George Beadle and Edward Tatum experimented with *Neurospora*, a mold that grows on bread in the tropics, developing the "one-gene-one-enzyme" hypothesis: each gene is translated into an enzyme to perform tasks within an organism.

Biotechnology Time Lines

- **1943**
- The Rockefeller Foundation, collaborating with the Mexican government, initiated the Mexican Agricultural Program. This was the first use of plant breeding as foreign aid.
- **1943-1953**
- **Cortisone was first manufactured in large amounts. KIND OF A FIRST BIOTECH PRODUCT**
- **1944**
- Waksman isolated **streptomycin**, an effective antibiotic for TB.

Biotechnology Time Lines

- **1945**
- The U.N. Food and Agriculture Organization (**FAO**) was formed in Quebec, Canada.
- **1945 - 1950**
- **CELLS GROWN IN LAB** Isolated animal cell cultures were grown in laboratories.
- **1947**
- Barbara McClintock first reported on "transposable elements" - known today as "jumping genes." The scientific community failed to appreciate the significance of her discovery at the time.

Biotechnology Time Lines

- **1950**
- Erwin Chargaff found that in DNA the amounts of adenine and thymine are about the same, as are the amounts of guanine and cytosine. These relationships are later known as "**Chargaff's Rules**" and serve as a key principle for Watson and Crick in assessing various models for the structure of DNA. **AT ABOUT THE SAME; GC ABOUT THE SAME**

Biotechnology Time Lines

- **1953 - 1976: Expanding the Boundaries of DNA Research**
- The discovery of the structure of DNA resulted in an explosion of research in molecular biology and genetics, paving the way for the biotechnology revolution.
- **1953**
- Nature magazine published James Watson's and Francis Crick's manuscript describing the double helix structure of DNA.

Biotechnology Time Lines

- 1953

- Gey developed the HeLa human cell line.

HENRIETTA LACKS- DIED IN 1951 OF CERVICAL CANCER- MOTHER OF 5- HER CELLS FIRST SHOWN TO GROW OUTSIDE THE BODY FOR EXTENDED PERIODS- USED TO DEVELOP THE POLIO VACCINE

Biotechnology Time Lines

- **1957 CENTRAL DOGMA OF DNA- HOW DNA MAKES A PROTEIN**
- Francis Crick and George Gamov worked out the "central dogma," explaining how DNA functions to make protein.
- **1959**
- Francois Jacob and Jacques Monod established the existence of genetic regulation - mappable control functions located on the chromosome in the DNA sequence - which they named the repressor and operon.

Biotechnology Time Lines

- **1962**
- Watson and Crick shared the 1962 **Nobel Prize for Physiology and Medicine with Maurice Wilkins. Unfortunately, Rosalind Franklin, whose work greatly contributed to the discovery of the double helical structure of DNA, died before this date, and the Nobel Prize rules do not allow a prize to be awarded posthumously**

Biotechnology Time Lines

- **1966 GENETIC CODE CRACKED**
- The genetic code was "cracked". Marshall Nirenberg, Heinrich Mathaei, and Severo Ochoa demonstrated that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids.

Biotechnology Time Lines

- **1967**
- **Arthur Kornberg** conducted a study using one strand of natural viral DNA to assemble 5,300 nucleotide building blocks. Kornberg's Stanford group then synthesized infectious viral DNA.
- **1970**
- **ONCOGENES** Peter Duesberg and Peter Vogt, virologists at UCSF, discovered the first oncogene in a virus. This SRC gene has since been implicated in many human cancers

Biotechnology Time Lines

- **1972 FIRST RECOMBINANT DNA MOLECULE**
- Paul Berg isolated and employed a restriction enzyme to cut DNA. Berg used ligase to paste two DNA strands together to form a hybrid circular molecule. This was the first recombinant DNA molecule.
- **1972 NIH GUIDELINES FOR RECOMBINANT DNA**
- In a letter to Science, Stanford biochemist Paul Berg and others called for the National Institutes of Health to enact guidelines for DNA splicing.. Their concerns eventually led to the 1975 Asilomar Conference.

Biotechnology Time Lines

- **1973 AMES TEST**
- Bruce Ames, a biochemist at UC Berkeley, developed a test to identify chemicals that damage DNA. The Ames Test becomes a widely used method to identify carcinogenic substances.
- **1975 RECOMBINANT DNA MORATORIUM**
- A moratorium on recombinant DNA experiments was called for at an international meeting at Asilomar, California, where scientists urged the government to adopt guidelines regulating recombinant DNA experimentation. The scientists insisted on the development of "safe" bacteria and plasmids that could not escape from the laboratory

Biotechnology Time Lines

■ 1976 MORE ABOUT ONCOGENES

- J. Michael Bishop and Harold Varmus, virologists at UCSF, showed that oncogenes appear on animal chromosomes, and alterations in their structure or expression can result in cancerous growth.

■ 1976 RELEASE OF NIH GUIDELINES

- The NIH released the first guidelines for recombinant DNA experimentation. The guidelines restricted many categories of experiments.

Biotechnology Time Lines

- **1977 - Present: The Dawn of Biotech**
- Genetic engineering became a reality when a man-made gene was used to manufacture a human protein in a bacteria for the first time. Biotech companies and universities were off to the races, and the world would never be the same again. In 1978, in the laboratory of Herbert Boyer at the University of California at San Francisco, a synthetic version of the human insulin gene was constructed and inserted into the bacterium *Escheria coli*. Since that key moment, the trickle of biotechnological developments has become a torrent of diagnostic and therapeutic tools, accompanied by ever faster and more powerful DNA sequencing and cloning techniques.

Biotechnology Time Lines

- **1977**
- Genentech, Inc., reports the production of the first human protein manufactured in a bacteria: **somatostatin**, a human growth hormone-releasing inhibitory factor. For the first time, a synthetic, recombinant gene was used to clone a protein. Many consider this to be **the advent of the *Age of Biotechnology***.
- **1978**
- **RECOMBINANT INSULIN** Genentech, Inc. and The City of Hope National Medical Center announced the successful laboratory production of human insulin using recombinant DNA technology.

Biotechnology Time Lines

- **1980 PATENTS ALLOWED**

- The U.S. Supreme Court ruled in that genetically altered life forms can be patented a Supreme Court decision in 1980 allowed **the Exxon oil company to patent an oil-eating microorganism.**

- Kary Mullis and others at Cetus Corporation in Berkeley, California, invented a technique for multiplying DNA sequences in vitro by, the polymerase chain reaction (PCR). **PCR POLYMERASE CHAIN REACTION**

Biotechnology Time Lines

- **1982**
- Genentech, Inc. received approval from the Food and Drug Administration to market genetically engineered human insulin. **1982 The U.S. Food and Drug Administration** approves the first genetically engineered drug, a form of human insulin produced by bacteria.
- Michael Smith at the University of British Columbia, Vancouver, developed a procedure for making precise amino acid changes anywhere in a protein. **SITE DIRECTED MUTAGENESIS**

Biotechnology Time Lines

■ 1983

- Eli Lilly received a license to make insulin.

■ 1985

- Genetic fingerprinting enters the **court room**.
- Cal Bio cloned the gene that encodes human **lung surfactant protein**, a major step toward reducing a premature birth complication.
- **Genetically engineered plants resistant** to insects, viruses, and bacteria were field tested for the first time.
- The NIH approved guidelines for performing experiments in **gene therapy on humans**.

Biotechnology Time Lines

■ 1986

- The FDA granted a license for the **first recombinant vaccine** (for hepatitis) to Chiron Corp.
- The EPA approved the release of the first genetically engineered crop, **gene-altered tobacco plants.**

■ 1987

- Calgene, Inc. received a patent for the tomato polygalacturonase DNA sequence, used to produce an antisense RNA sequence that can extend the **shelf-life of fruit.**

Biotechnology Time Lines

■ 1988

- Harvard molecular geneticists Philip Leder and Timothy Stewart awarded the first patent for a **genetically altered animal, a mouse** that is highly susceptible to breast cancer.

■ 1990

- UCSF and Stanford University were issued their 100th recombinant DNA patent license. By the end of fiscal 1991, both campuses had earned \$40 million from the patent. **PATENTS AND MONEY**

Biotechnology Time Lines

- 1990
- The first gene therapy takes place, on a four-year-old girl with an immune-system disorder called ADA deficiency. The therapy appeared to work, but set off a fury of discussion of ethics both in academia and in the media.
- The Human Genome Project, the international effort to map all of the genes in the human body, was launched. Estimated cost: \$13 billion. 1990 Formal launch of the international Human Genome Project.
- Publication of Michael Crichton's novel Jurassic Park, in which bioengineered dinosaurs roam a paleontological theme park; the experiment goes awry, with deadly results.

Biotechnology Time Lines

- **1992**
- **The U.S. Army begins collecting 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.
- **1993**
- **Kary Mullis won the Nobel Prize in Chemistry for inventing the technology of polymerase chain reaction (**PCR**).**

Biotechnology Time Lines

- **1994**
- The first genetically engineered food product, the Flavr Savr tomato, gained FDA approval.
- The first crude but thorough linkage map of the human genome appears. (See Science, v.265, Sep.30, '94, for the full color pull-out).
- **1995**
- A new coalition of mainstream religions launched a campaign seeking to overturn current laws allowing the patenting of genes used for medical and research applications. The group also includes Jeremy Rifkin, the controversial and outspoken critic of the biotechnology industry. **SHOULD PATENTS BE ALLOWED?**

Biotechnology Time Lines

■ 1996

- A new inexpensive diagnostic biosensor test for the first time allow instantaneous detection of the toxic strain of E. coli E. coli strain 0157:H7, the bacteria responsible for several recent food-poisoning outbreaks. **CAN IT BE DONE FOR ANTRAX OR OTHER BIOTERRORISM AGENTS?**
- 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.
- Surveys indicate the public regards research into the workings of the human genome and gene therapy with a combination of fear and mistrust

Biotechnology Time Lines

■ 1997

- Researchers at Scotland's Roslin Institute report that they **have cloned a sheep--named Dolly--**from the cell of an adult ewe. Polly the first sheep cloned by nuclear transfer technology bearing a human gene appears later. **Nuclear transfer involves transferring the complete genetic material (the DNA contained in a nucleus) from one cell into an unfertilized egg cell whose own nucleus has been removed.**



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Biotechnology Time Lines

- 1998
- Two research teams succeed in growing embryonic stem cells, the long sought grail of molecular biology.
- Scientists at Japan's Kinki University clone eight identical calves using cells taken from a single adult cow.
- A rough draft of the human genome map is produced, showing the locations of more than 30,000 genes.

Biotechnology Time Lines

- **1999**
- **MAD COW DISEASE** A new medical diagnostic test will for the first time allow quick identification of BSE/CJD a rare but devastating form of neurologic disease transmitted from cattle to humans.

Biotechnology Stats

- **Some biotech statistics:**
- **2001: 200,000 employees, \$30 billion in revenues; 1450 total companies and 350 public companies**
- **1992: 80,000 employees, \$8.1 billion in revenues; about same # companies**
- Compensation in biotechnology companies is competitive and includes incentives, such as stock option plans, 401K plans, company-wide stock purchase plans, and cash bonus plans.

Approved Biotech Products

- 1938: Howard Florey/Ernst Chain, Oxford U., England isolated penicillin
- 1940-1945: Large scale production of penicillin
- 1943-1953: Cortisone first manufactured in large amounts
- 1977: Genentech produced somatostatin (human growth hormone-releasing inhibitory factor), manufactured in bacteria. First time a recombinant gene was used to clone a protein.
- 1978: Harvard researchers produced rat insulin by recombinant DNA.

Approved Biotech Products

- 1982: FDA approves genetically engineered human insulin
- 1986: Orthoclone OKT3 (Muromonab-CD3) approved for reversal of kidney transplant rejection.
- 1986: first recombinant vaccine approved- hepatitis
- 1987: Genentech gets approval for rt-PA (tissue plasminogen activator) for heart attacks

Approved Biotech Products

- 1990: Actimmune (interferon 1b) approved for chronic granulomatous disease
- Adagen (adenosine deaminase) approved for severe combined immunodeficiency disease
- 1994: first genetically engineered food the Flavr Savr tomato is approved.
- 1994: Genentech's Nutropin is approved (growth hormone deficiency)

Approved Biotech Products

- 1994: Centocor's ReoPro approved (for patients undergoing balloon angioplasty)
- Genzymes Ceredase/Cerezyme approved for Gaucher's Disease (inherited metabolic disease)
- Recombinant GM-CSF approved (chemotherapy induced neutropenia)
- 1998: Centocor's Remicade™ approved (monoclonal antibody for Crohn's disease)

Focus on “Famous” Biotech Product: Insulin

- Insulin:
- **Insulin is a hormone, and therefore, a protein.**
- **Insulin was the first hormone identified** (late 1920's) which won the doctor and medical student who discovered it the Nobel Prize (Banting and Best).
- They discovered insulin by tying a string around the pancreatic duct of several dogs.
- Note that there are other hormones produced by different types of cells within pancreatic islets (glucagon, somatostatin, etc) but insulin is produced in far greater amounts under normal conditions making the simple approach used by Banting and Best quite successful.

Properties of Insulin

- Insulin is secreted by groups of cells within the pancreas called islet cells.
- The pancreas is an organ that sits behind the stomach and has many functions in addition to insulin production.
- The pancreas also produces digestive enzymes and other.
- Without insulin, you can eat lots of food and actually be in a state of starvation since many of our cells cannot access the calories contained in the glucose very well without the action of insulin.

Insulin (cont'd)

- **The first successful insulin preparations came from cows (and later pigs).** The pancreatic islets and the insulin protein contained within them were isolated from animals slaughtered for food in a similar but more complex fashion than was used by our doctor and med-student duo.

Biotech Applications

■ **Diagnostics**

- **Antibodies**
- **Biosensors**
- **PCR**

■ **Therapeutics**

- **Natural Products**
- **Foxglove:**
- **digitalis: heart conditions**
 - **Yew tree- cancer agent (taxol) breast and ovarian cancers**
 - **Endogenous Therapeutic agents – proteins produced by the body that can be replicated by genetically engineered: tPA – tissue plasminogen factor (dissolves blood clots)**

Biotech Applications

- **Biopolymers and Medical Devices- natural substances useful as medical devices**
 - hyaluronate- an elastic, plastic like substance used to treat arthritis, prevent postsurgical scarring in cataract surgery, used for drug delivery
 - adhesive substances to replace stitches
- **Designer Drugs – using computer modeling to design drugs without the lab-protein structure**

Biotech Applications

- **Replacement Therapies- lack of production of normal substances**
 - Factor VIII- missing in hemophilia
 - Insulin
- **Use of Transgenic Animals and Plants**

Biotech Applications

- **Gene Therapy – replace defective genes with functional ones**
 - ADA (adenosine deaminase) deficiency
 - cystic fibrosis
- **Immunosuppressive Therapies – used to inhibit rejection (organ transplants)**
- **Cancer Therapies -one method is antisense technology**
- **Vaccines – biggest break through in biotechnology- prevention of disease**