Grade 11 Biology

Genetic Processes

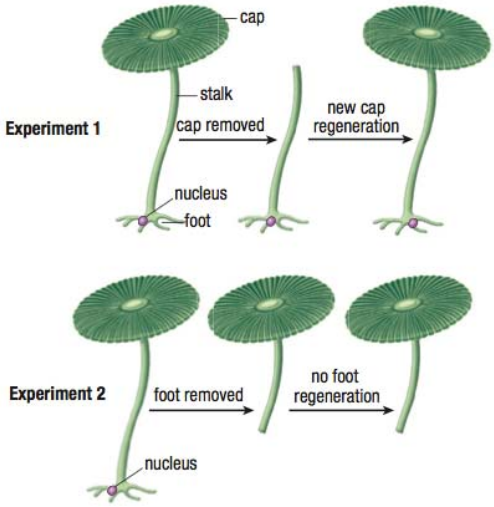
Class 6

DNA and the Code of Life

Figure 1 A human chromosome

- DNA stores and transmits genetic information from parents to offspring
- 1869, Miescher investigated a compound which he called nuclein inside the nucleus

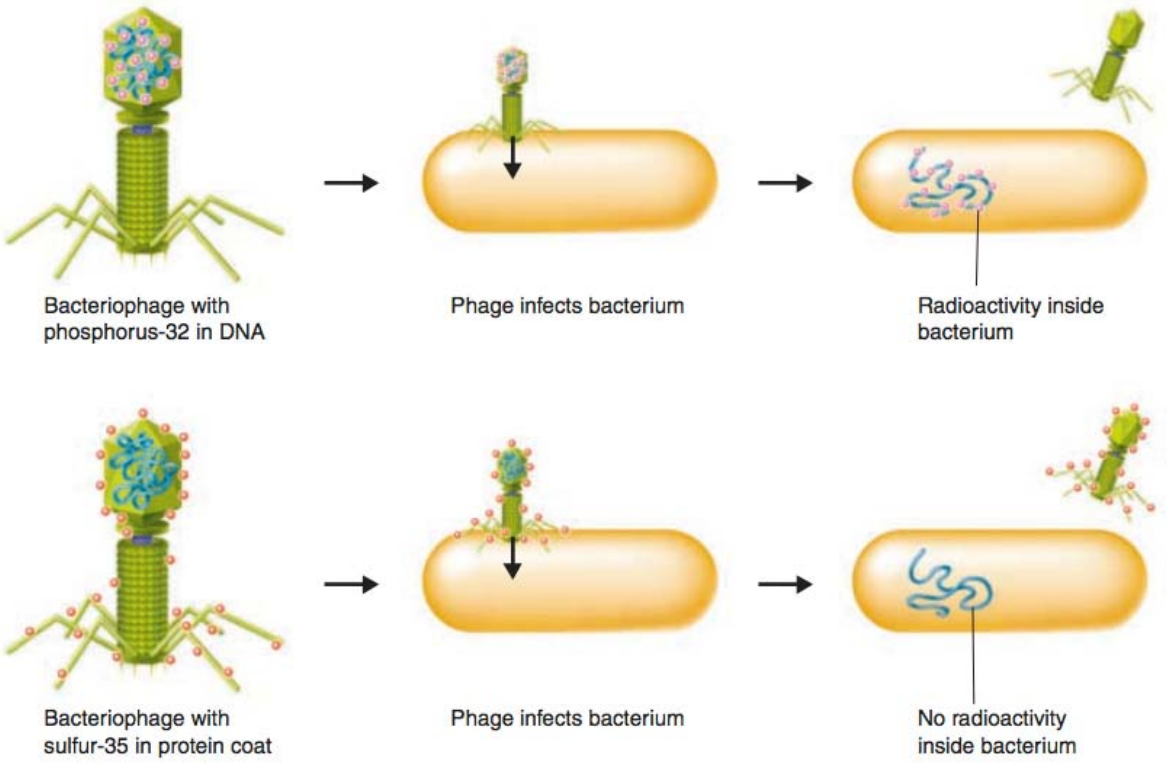
- 1930s, Hammerling verified that genetic material was contained in the nucleus
- Studied *Acetabularia* with three distinct regions: a foot, a stalk and a cap



Experiment 1: Cut off the cap, algae were able to regenerate

Experiment 2: Cut off the foot, but no algae regenerated

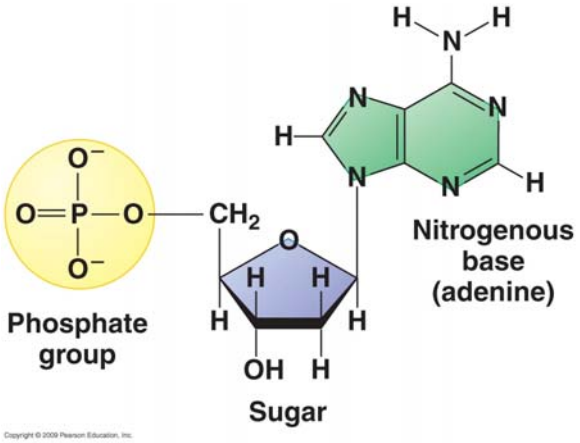
- 1952, Hershey and Chase conducted experiments using a bacterial virus
- Does the protein coat or the DNA inside cause the replication of the bacterial virus?
- Bacterial viruses invade bacterial cells and then use the organelles in bacteria to produce more bacterial viruses
- Concluded that DNA and not the protein coat directed the production of new viruses



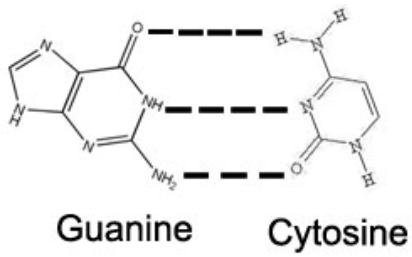
The Hershey-Chase Experiment Alfred Hershey and Martha Chase used different radioactive markers to label the DNA and proteins of bacteriophages. The bacteriophages injected only DNA into the bacteria, not proteins. **From these results, Hershey and Chase concluded that the genetic material of the bacteriophage was DNA.**

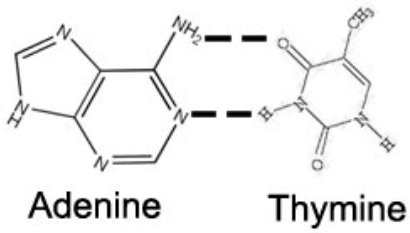
Composition of DNA

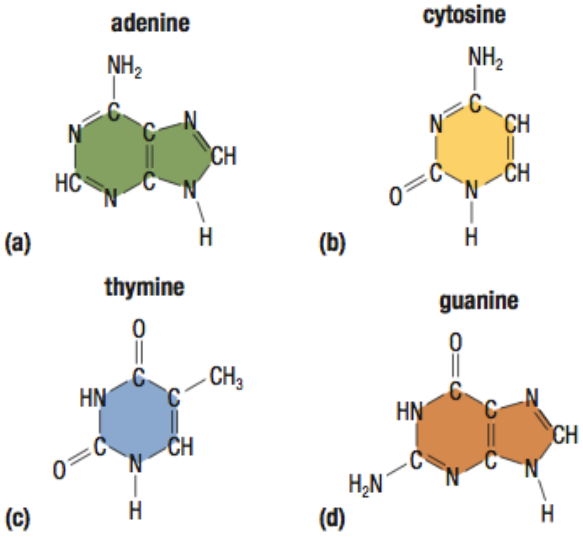
- DNA is made of nucleotides consisting of:
  - A pentose sugar (cyclic, 5-carbon sugar)
  - A phosphate group with a negative charge
  - A nitrogenous base
- Four possible bases:
  - Adenine (A)
  - Guanine (G)
  - Thymine (T)
  - Cytosine (C)



- Amount of Adenine (A) is always equal to amount of Thymine (T)
- Amount of Guanine (G) is always equal to the amount of Cytosine (C)

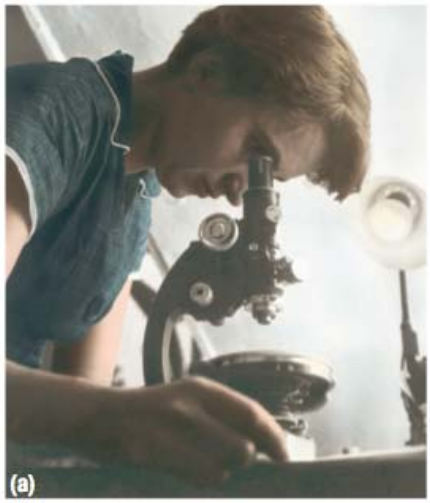


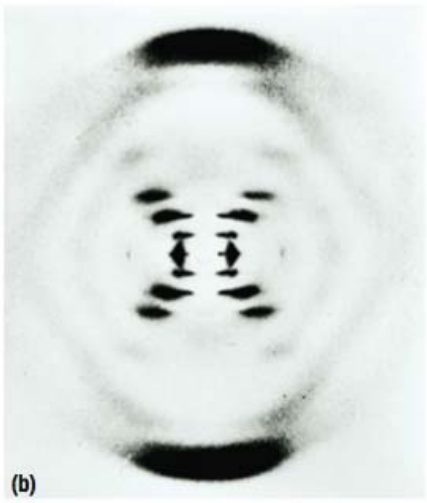




X-Ray Crystallography

- A technique used when a pure substance is subjected to X-rays; pattern in which the X-rays bend and spread helps reveal the structure of the pure substance
- Rosalind Franklin and Maurice Wilkins studied the shape of the DNA molecule and determined that DNA molecules form a helix or corkscrew shape

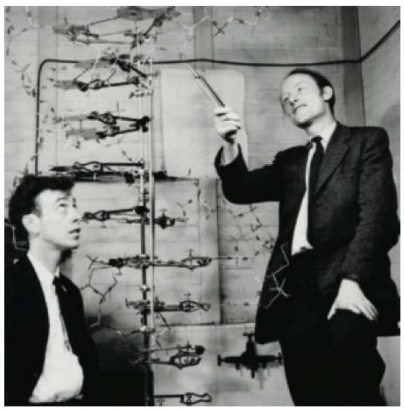




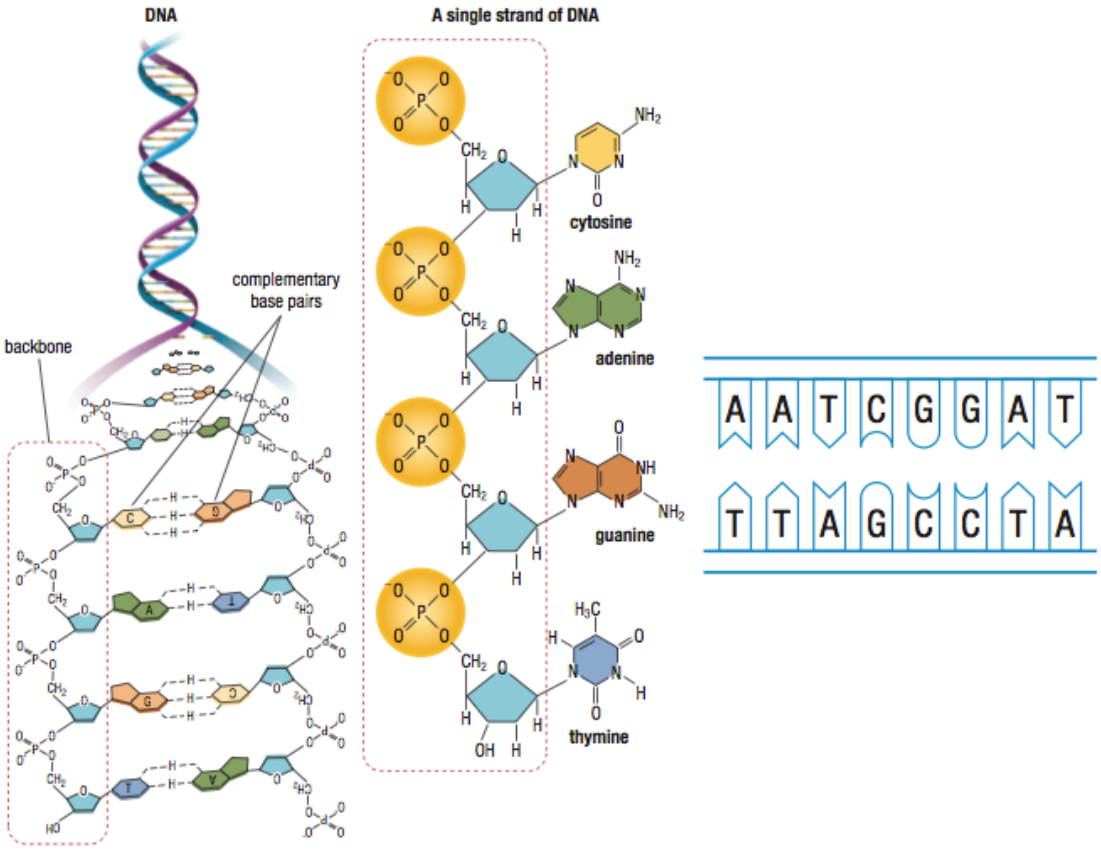
- Wilkins shared the information with Watson and Crick
- Watson and Crick built the model of DNA and showed that it was a double helix

- Watson and Crick's DNA model built on the following facts:
  - DNA is made of a pentose sugar, a phosphate group and a nitrogenous base (Levene, 1920s)
  - The proportion of adenine to thymine is equal. The proportion of guanine to cytosine is equal (Chargaff, 1940)
  - DNA has the shape of a helix or corkscrew (Franklin and Wilkins, 1951)

A Model for DNA



- Watson and Crick proposed that DNA is made of two strands of repeating DNA nucleotides that run in opposite directions
- Complementary Base Pairing
  - T is always bonded to A
  - C is always bonded to G

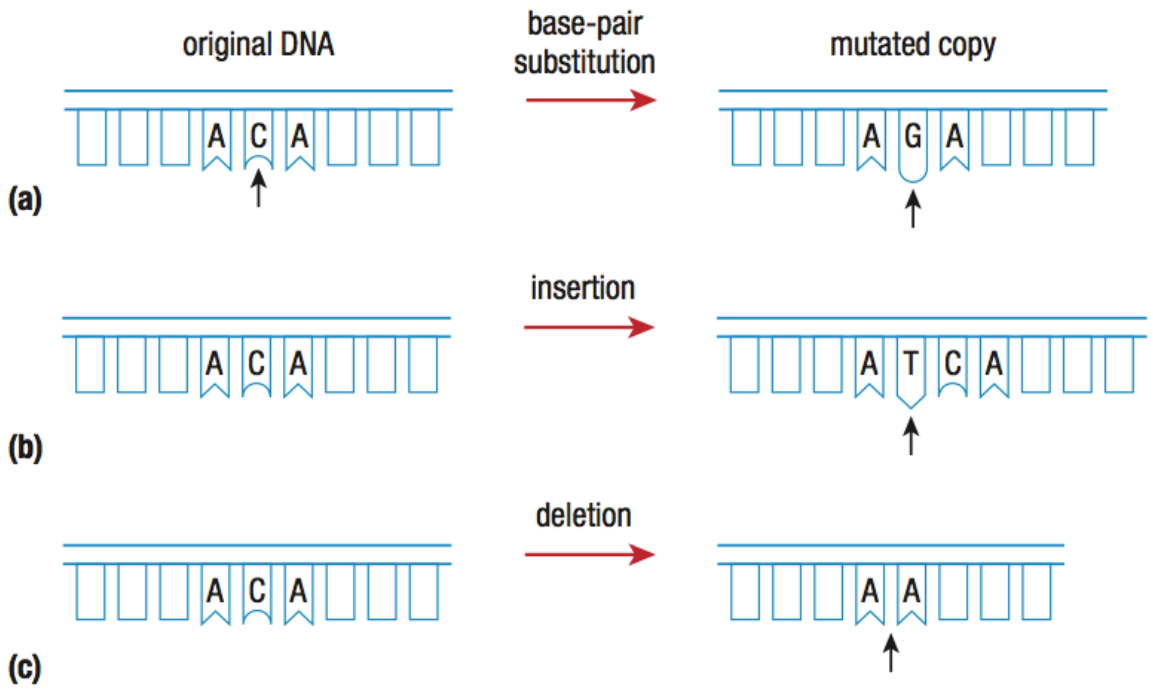


Checkpoint

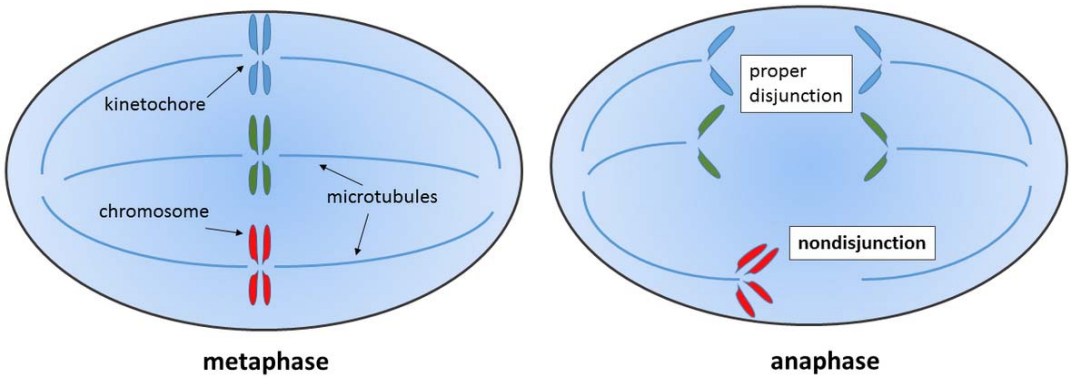
- What are the complementary base sequence of the following?

Mutations

- Mutation – a change in the genetic code of an allele caused by environmental agents (radiation, chemicals, cell division errors)
- **Point Mutations** – Small-scale changes in the base sequence of DNA that may become beneficial, harmful or neutral
  - Ribosomes make proteins based on the base sequence
  - Reads in groups of three nucleotides

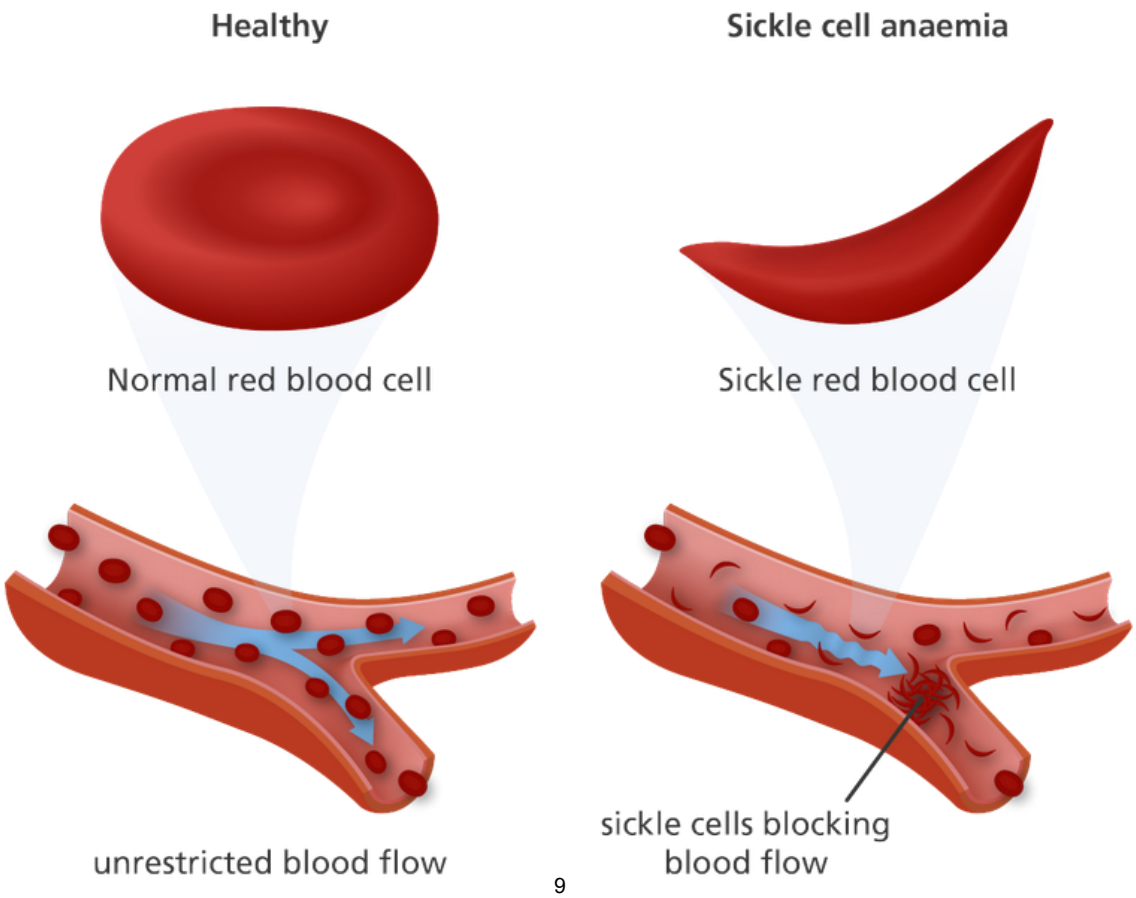


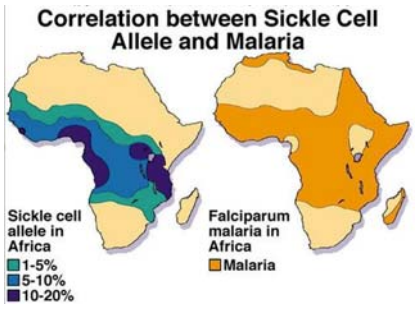
- **Chromosome Mutations** – An error that involves an entire chromosome or a large part of a chromosome
  - Non-disjunction: failure of sister chromatids to separate during meiosis



Inheriting Mutations

- Mutations in the gametes can be passed on to future generations
- Sickle-Cell Anemia – mutated gene in which a single adenine base was substituted by a thymine
  - Red-blood cells become sickle-shaped preventing them from moving through the blood vessels properly
  - Blood flow is impaired and cells are removed or destroyed





- Sickle-cell anemia has a benefit for people in central Africa where there is a high incidence of malaria
- When malaria parasite enters the red blood cell of an individual, the blood cell becomes sickle-shaped which the body recognizes and removes
- Parasite is killed in the process

- Lactose Intolerance – inability to digest lactose, the common sugar in milk due to insufficient or lack of lactase, the enzyme to digest lactose
- Undigested lactose is digested by intestinal bacteria leading to bloating, cramping and diarrhea
- 75% of adults in the world are lactose intolerant
- Remaining 25% inherited a genetic mutation that allow them to continue to produce lactase throughout their lives

- Scientists hypothesized that the mutation for lactose tolerance happened after the domestication of dairy animals
- Many Asians are lactose intolerant; most European are lactose tolerant
- Researchers have identified the gene on human chromosome 2

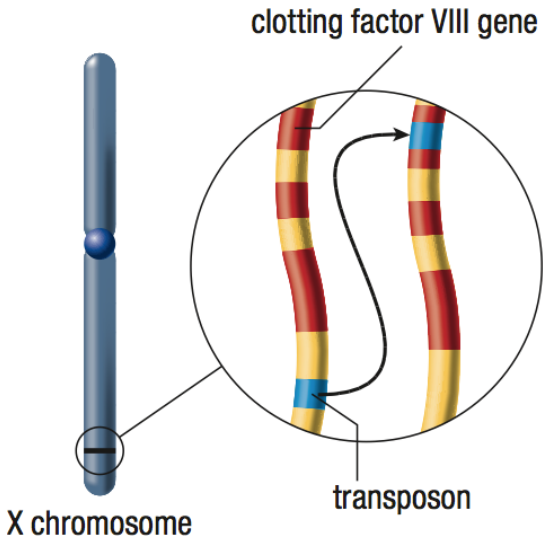
- Spontaneous mutations – mutation that is not caused by outside factors due to incorrect copying of DNA during the replication of chromosomes in mitosis and meiosis
- Induced mutations – result of exposure to a physical or chemical agent such as radiation or cigarette smoke

Antibiotic Resistance

- Resistant bacteria are able to survive exposure to antibiotics and pass the genes that make them resistant to the next generation
- High doses and more toxic antibiotics are needed to fight the “superbug”

Jumping Genes

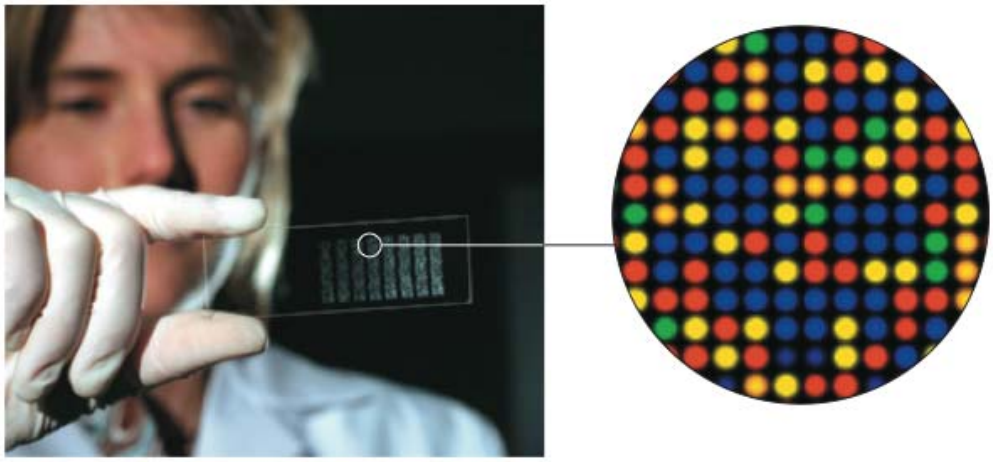
- Transposons – specific segment of DNA that can move along or between the chromosomes
- Transposition – the process of moving a gene sequence from one part of the chromosome to another



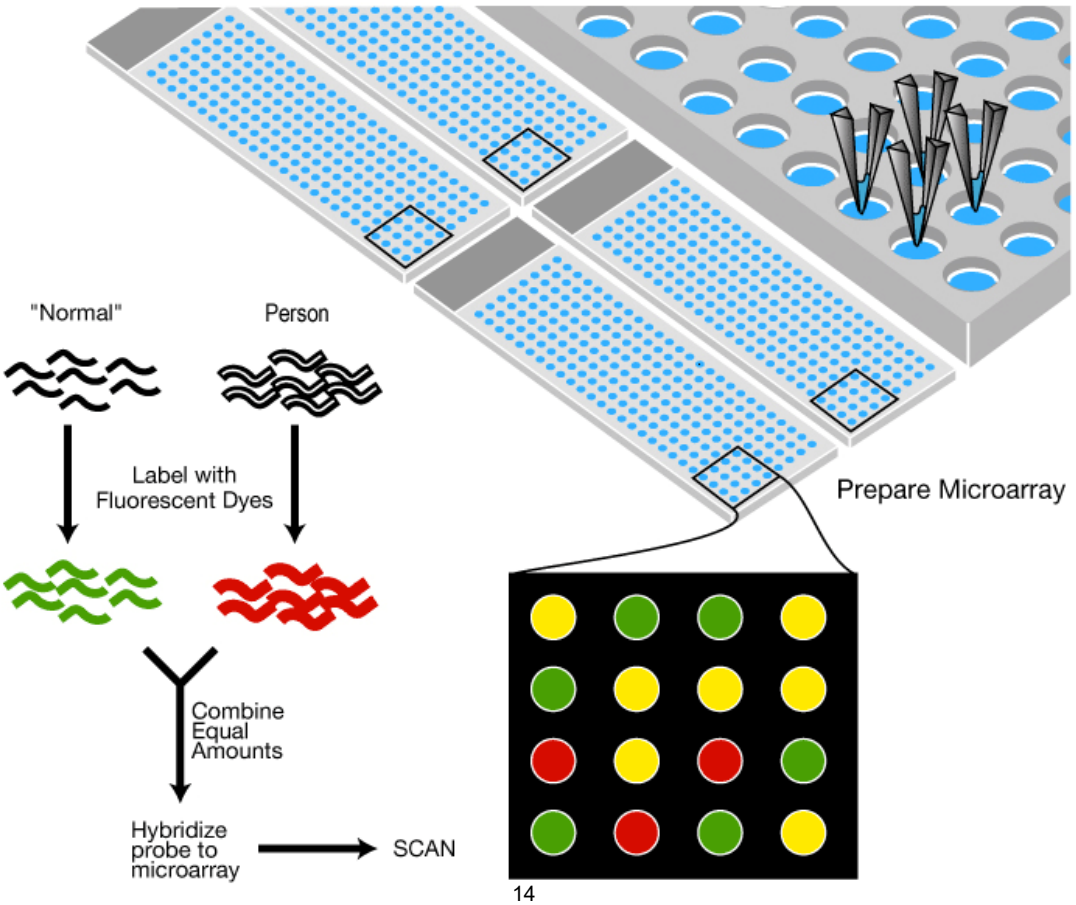
- Transposon (blue) has jumped and become inserted into the blood-clotting factor gene and individual is affected by hemophilia

Microarray Technology

- Microarray consists of a small membrane or glass slide that contains samples of thousands of DNA fragments arranged in a regular pattern
- Each DNA fragment corresponds to a particular gene
- Samples are spread over the microarray tube and analyzed to see the interaction with the gene fragments

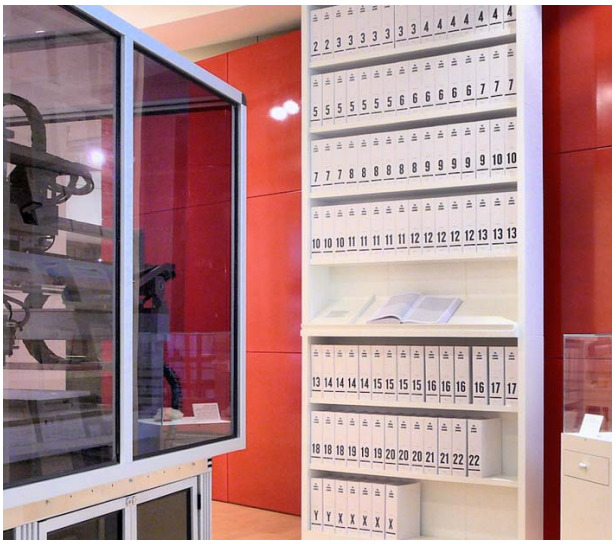


- Depending on the colour and intensity of colour, the array can reveal if a particular gene is active or mutated



Genomes

- Human Genome Project – to determine the 3 billion nitrogenous base sequence of human DNA
- Completed in 2003
- Areas that coded for genes were called coding DNA (2% of the human genome)
- Areas that did not code for genes were called non-coding DNA (98% of the human genome)



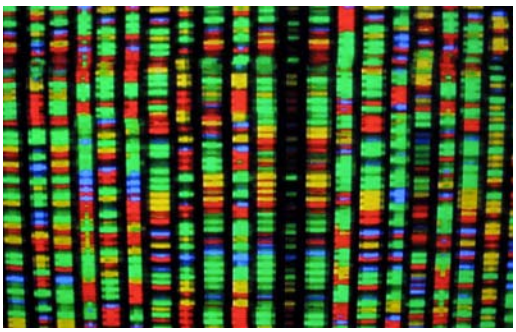


Table 1 Number of Genes Believed Present in Different Genomes

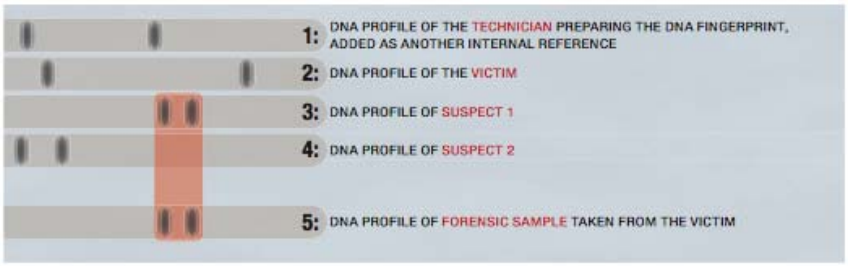
Organism	Size of genome	Approximate number of genes
amoeba	670 billion	unknown
newt (salamander)	84 billion	unknown
wheat	17 billion	unknown
human	3 billion	20 000
mouse	2.6 billion	25 000
Asian rice	446 million	50 000
fruit fly	137 million	13 602
yeast	12.1 million	6 034
E. coli	4.6 million	3 200
influenza virus	1.8 million	1 700

- Larger genome does not mean higher complexity or a greater number of coding genes

Functional Genomics

- Functional Genomics – the study of the relationship between genes and their function
- Scientists use model organisms to study biological functions of humans due to its genetic similarity
  - Ex: Mice and humans share many genetic similarities

DNA Identification



- DNA Bank – a database of DNA sequences, the sequences can be from animals, plants or humans
- DNA Fingerprinting – a pattern of bands on a gel that is unique to each individual
  - Used in forensic science, paternity tests, unmarked graves

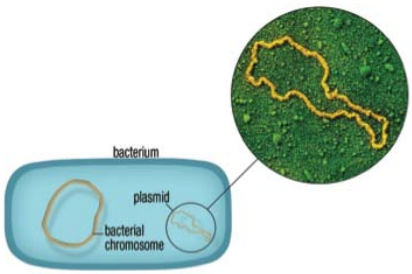
- David Milgaard spent over 20 years in prison for the rape and murder of nursing assistant Gail Miller
- DNA fingerprinting showed that he was wrongfully convicted
- Compensated $10 million by the Canadian government

National DNA Data Bank

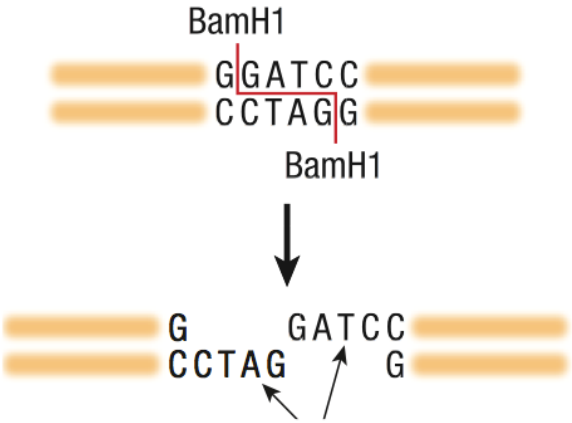
- In Canada, it is legal for a judge to request blood or hair samples from suspects and convicted criminals to be added to Canada's DNA Data Bank
- Allows police to:
  - Link crimes together
  - Identify suspects and eliminate suspects
  - Determine the involvement of a serial offender

Manipulating the Genome

- Plasmids – small circular pieces of DNA that can exit and enter bacterial cells
- Restriction enzymes – molecules with the ability to cut DNA at a specific site, different restriction enzymes recognize and cut different sites

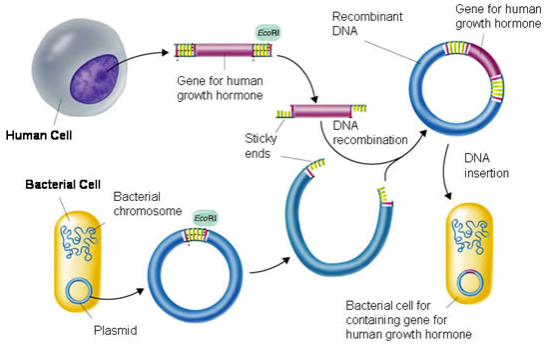


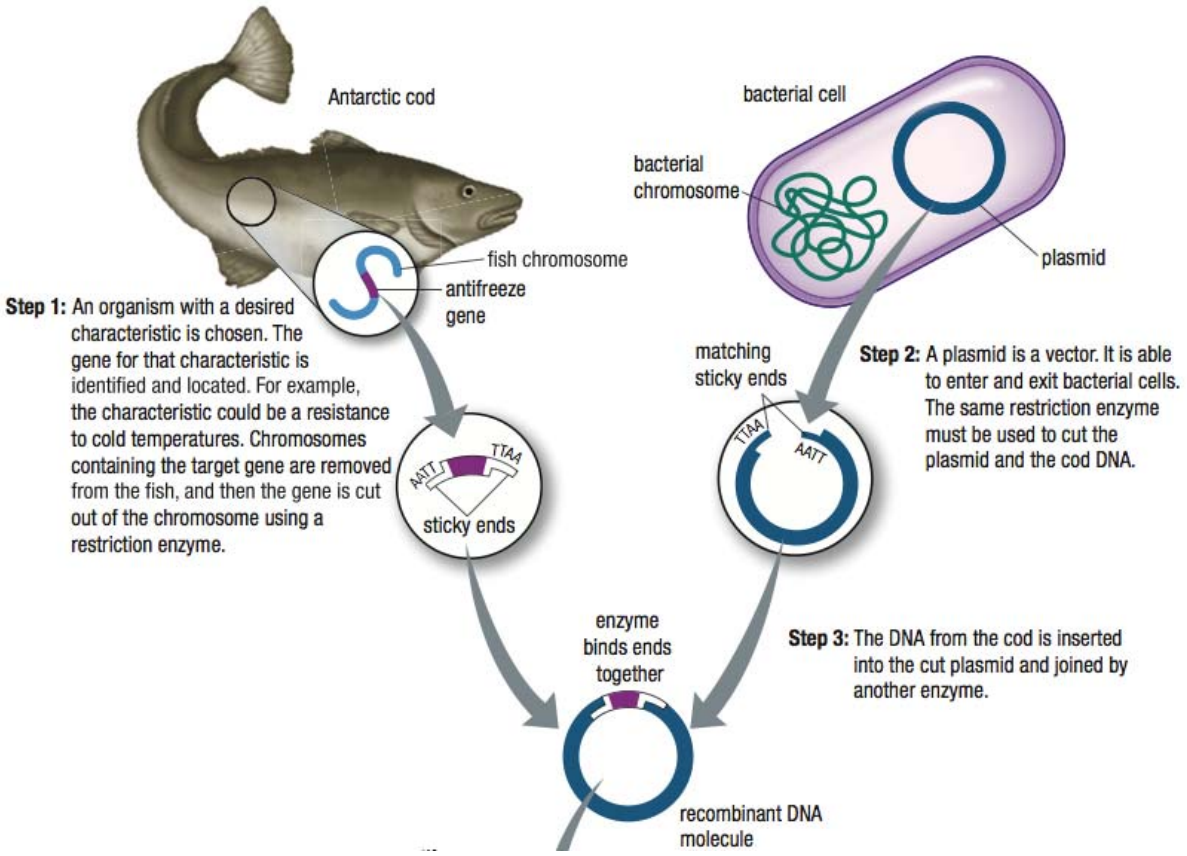
- Restriction enzymes cut DNA molecules wherever they encounter a particular sequence of bases
- Ex: BamH1 restriction enzyme cuts DNA at all GGATCC locations

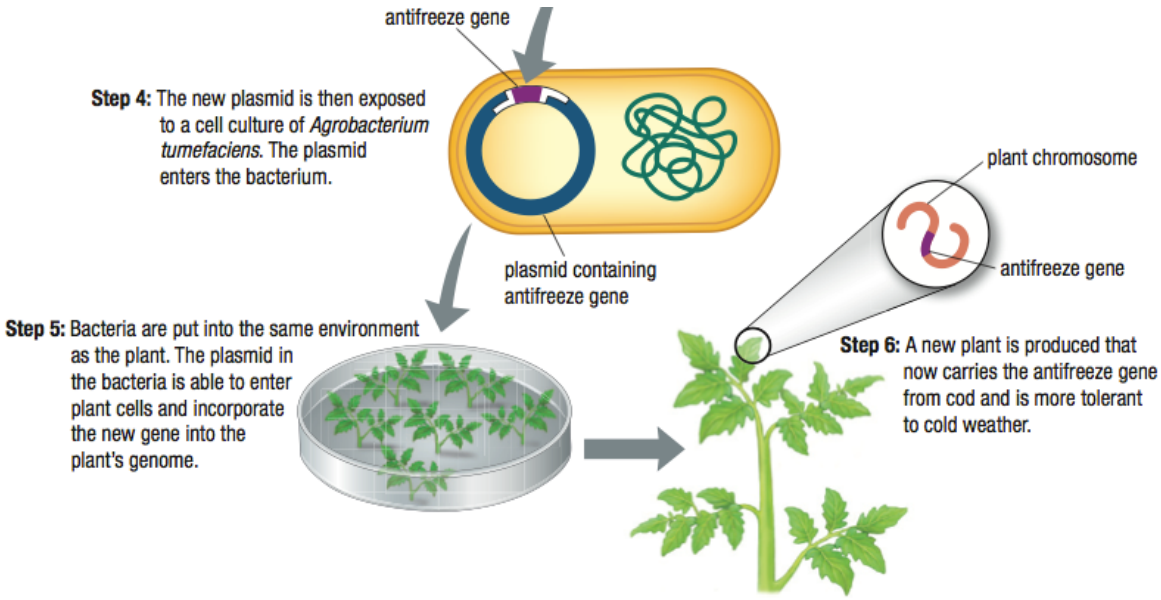


The exposed complementary bases are called "sticky ends"

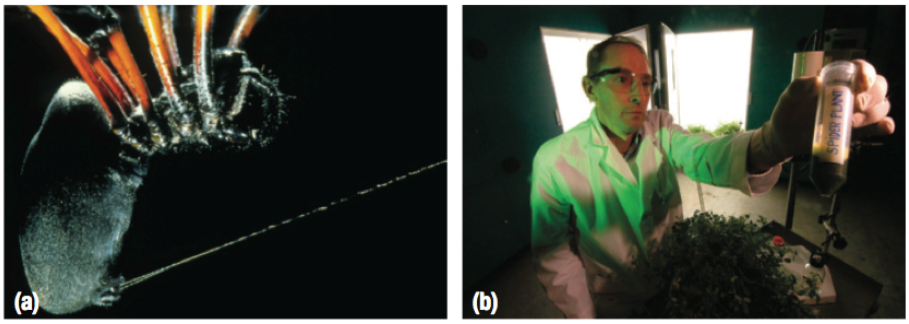
- Recombinant DNA is a fragment of DNA made by combining nucleotide sequences from at least two different sources via plasmids and restriction enzymes
- Common applications:
  - Produce insulin in bacteria
  - Provide herbicide resistance to crops
  - Increase crop yield




Antarctic cod
fish chromosome
antifreeze gene
Step 1: An organism with a desired characteristic is chosen. The gene for that characteristic is identified and located. For example, the characteristic could be a resistance to cold temperatures. Chromosomes containing the target gene are removed from the fish, and then the gene is cut out of the chromosome using a restriction enzyme.
AATT
TTAA
sticky ends
bacterial cell
bacterial chromosome
plasmid
matching sticky ends
Step 2: A plasmid is a vector. It is able to enter and exit bacterial cells. The same restriction enzyme must be used to cut the plasmid and the cod DNA.
enzyme binds ends together
Step 3: The DNA from the cod is inserted into the cut plasmid and joined by another enzyme.
recombinant DNA molecule


antifreeze gene
Step 4: The new plasmid is then exposed to a cell culture of *Agrobacterium tumefaciens*. The plasmid enters the bacterium.
plasmid containing antifreeze gene
plant chromosome
antifreeze gene
Step 5: Bacteria are put into the same environment as the plant. The plasmid in the bacteria is able to enter plant cells and incorporate the new gene into the plant's genome.
Step 6: A new plant is produced that now carries the antifreeze gene from cod and is more tolerant to cold weather.

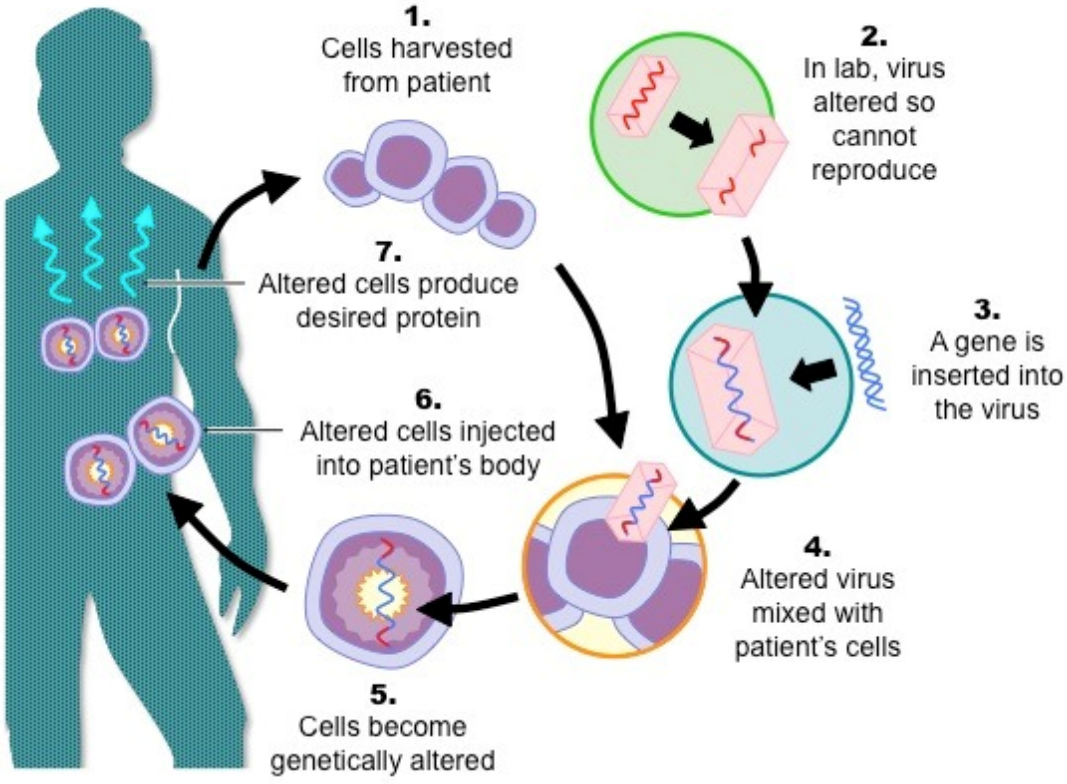
- Products of Genetic Engineering
  - Spider silk – five times stronger than steel, waterproof and ductile
  - Recombinant DNA technology allows the spider silk to be made in the milk of goats
  - Silk is purified from the milk and used in manufacturing, outerwear, parachutes, etc.



- Bt Corn – *Bactillus thuringiensis* (Bt) produces a natural pesticide that is lethal of certain insects and larvae but are harmless to humans
- Genes for the Bt toxin have been inserted into corn allowing it to produce its own pesticides
- These are called genetically modified (GM) food
- Advantages – use less pesticides, less contamination, less cost of production
- Disadvantages – possible allergic reaction, genetic diversity of corn reduced, escape to wild plant population

Gene Therapy

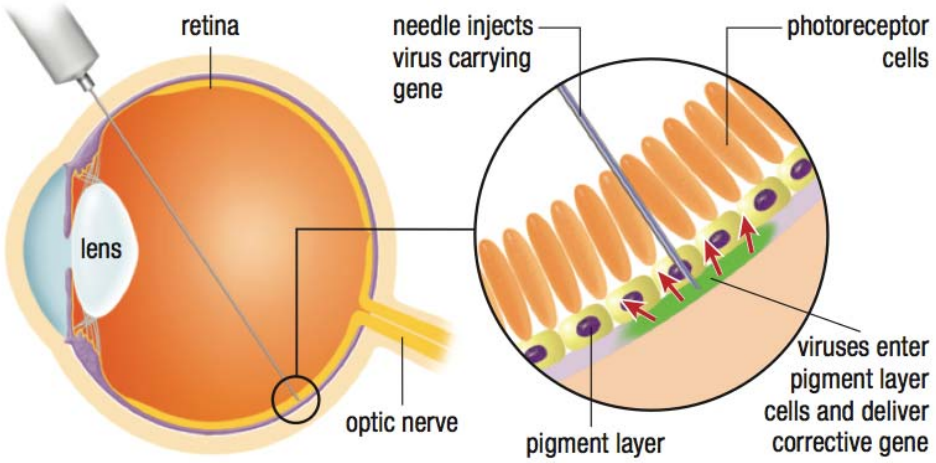
- Gene therapy – the process by which defective genes in a genome are corrected with a normal copy of the gene
- Scientists remove or alter viral DNA so that the viruses cannot harm the cells they enter
- Copies of the DNA that include the normal human gene are placed inside the virus
- Large numbers of the viruses are used to infect the target cells



- Limitations of Gene Therapy:
  - No way to control where the normal gene is inserted
  - If the gene is insert into a coding region, it may disrupt the normal functioning of other important genes
- In 1999, Jesse Gelsinger died after being treated for ornithine transcarboxylase deficiency (OTCD) using gene therapy
- Jesse had an unexpected immune response to the virus

- 2003, two children who were being treated using gene therapy for the severe combined immunodeficiency (SCID) syndrome developed leukemia
- Other obstacles:
  - Normal gene inserted into the target cell must work for the duration of the target cell's life
  - Body's immune response must be constantly monitored
  - Many disorders are caused by more than one gene
  - Genes in the target cell need to be regulated

- Successes:
  - Gene therapy performed on 12 patients with Leber's congenital amaurosis (LCA) resulted is almost complete restoration of their vision



- Duchenne Muscular Dystrophy (DMD) – a severe recessive form of muscular dystrophy
  - Sex-linked and mostly affects males
  - Meganuclease molecules are able to repair the incorrect base-pair sequence in the faulty dystrophin gene
- Deafness – sounds move tiny hairs in the cochlea in the inner ear which translate sound into nerve signals that are delivered to the brain
  - Gene that stimulated hair group in the cochlea restored hearing to guinea pigs