ECE 370
Introduction to Biomedical Engineering

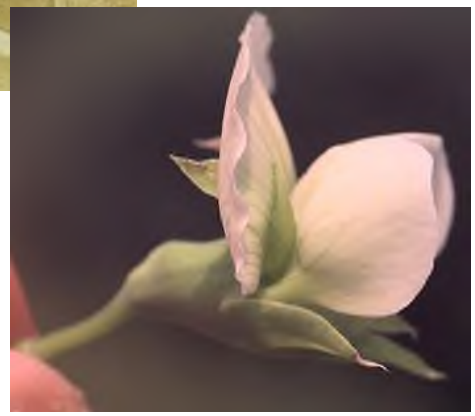
Genetics

Genetics

- **Reproductive process in nature**
  - Consistency in morphological characteristics → offspring resemble their parents to a lesser or greater degree
- **Heredity**
  - Transfer of information from parents to offspring
  - Inheritance units: genes
- **Genetics**
  - Study of the structure and expression of heredity
  - Since the 50s → Molecular Genetics

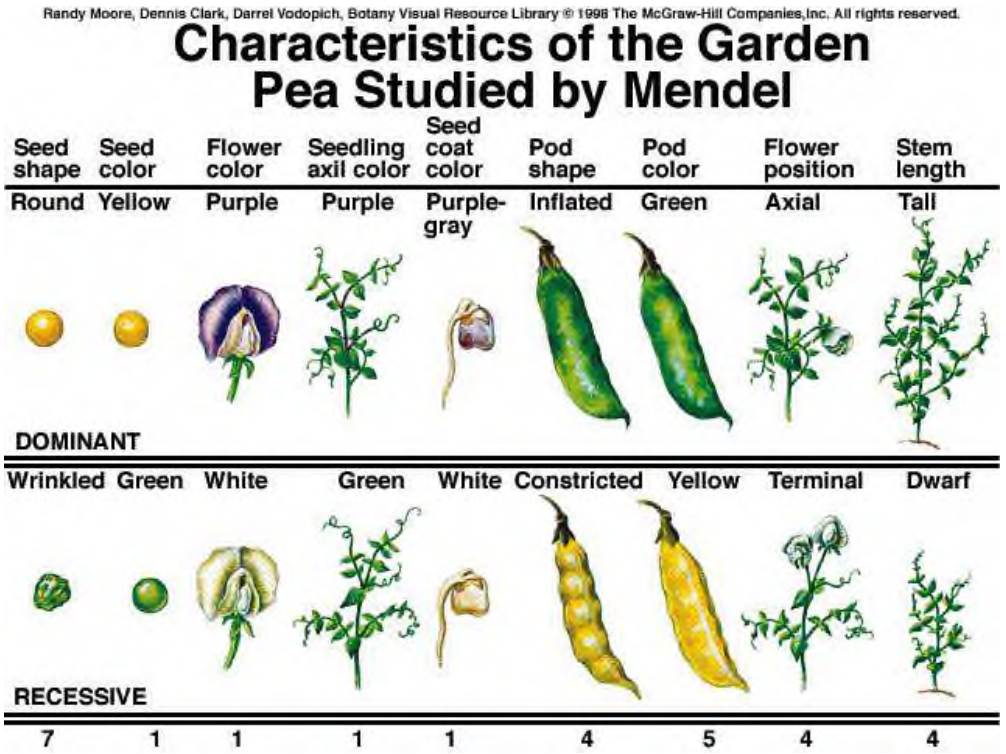
Genetics

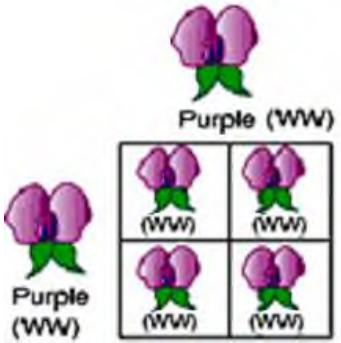
- **Gregory Mendel (1822-1884)**
  - Austrian monk
  - Basic mechanisms of heredity
    - Cultivating peas in a monastery garden in Brno
    - Mechanism by which the characteristics of ancestors reappear in the offspring of hybrids



Genetics

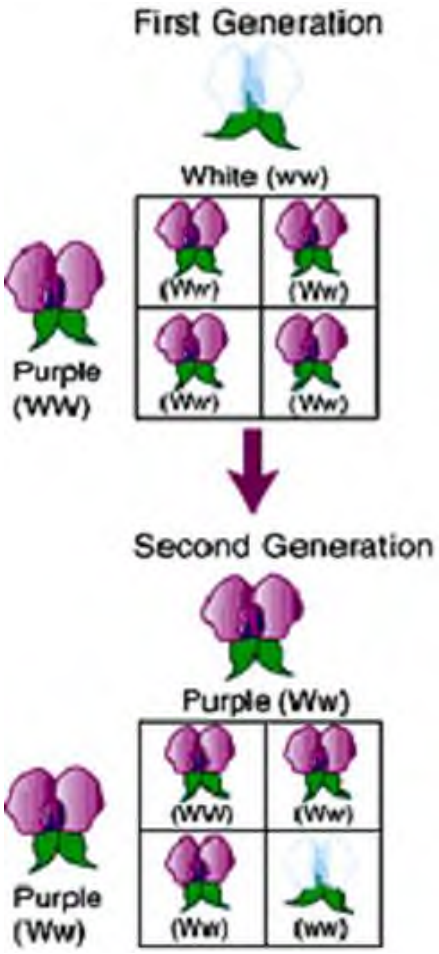
- **Pisum sativum Peas**
  - Number advantages as an experimental subject
    - Grown easily
    - Display many variations in different characteristics (varieties)
    - Easy to undergo artificial insemination
  - Preliminary stage
    - Create pure varieties (inbred strains) → When crossed with each other, result in the same type generation after generation





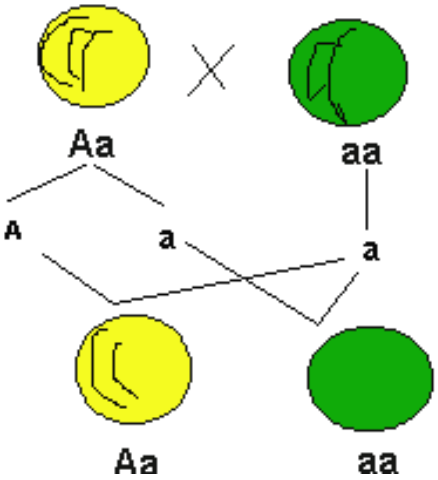
Genetics

- **Cross-bred plants that where different only in one characteristic**
  - E.g. plants which were either white or purple flowers
- **F1: first generation of offspring**
  - All looked the same
  - All looked like the parent plants
- **F2: cross-breeding of two F1**
  - Both characteristics of the original plants were present
  - Approximately in a ration of 3:1
  - One genetic factor was overshadowed by another
- **Principle of dominance**
  - Purple: dominant
  - White: recessive
  - This was completely against the belief, at the time, that heredity was a result of mixing



Genetics

- **Every inherited characteristic**
  - Controlled by two “factors” (= genes)
  - When the gametes (reproductive cells) are formed they divide so that they contain only one
  - After fertilization they form pairs again
  - **Phenotype:** what the characteristic looks like
  - **Genotype**: the genes that form the phenotype
- **Pioneering conclusions**
  - He raised this idea at a time before the mechanisms of cell division (mitosis and miosis) were even discovered
  - Published his conclusions but nobody was interested until the beginning of the century (1900)

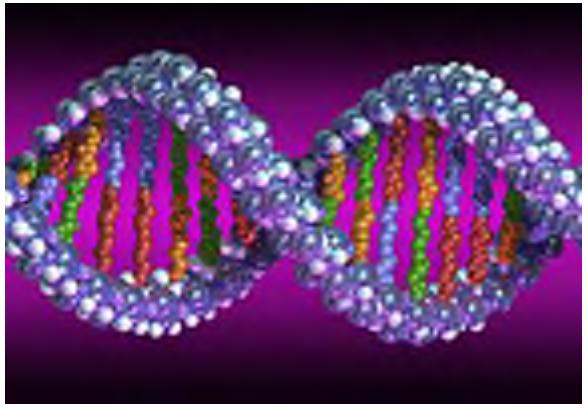


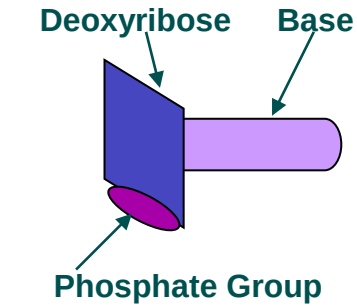
Genetic Material

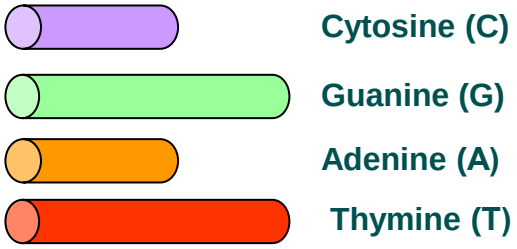
- **A material capable of transferring information from one generation to another**
  - Stores information
    - Control of metabolism and growth
  - Can be copied without mistakes during cell division
    - Transferred from generation to generation
  - Stable
    - Can be transferred to many subsequent generations
  - Undergoes changes (known as mutations)
    - Generate variants
    - Organisms adapt better to changing conditions

DNA

- **Macromolecule: Deoxyribonucleic acid (DNA)**
- **Consists of nucleotides**
  - Sugar (deoxyribose)
  - Phosphate group
  - Nitrogenous base
    - Adenine (A), guanine (G), cytosine (C) and thymine (T)
- **Rule of complementarity**
  - Adenine binds only to thymine
  - Cytosine only to guanine
  - or conversely
    - A = T and G = C in all kinds
    - (A + T / G + C) differs from species to species

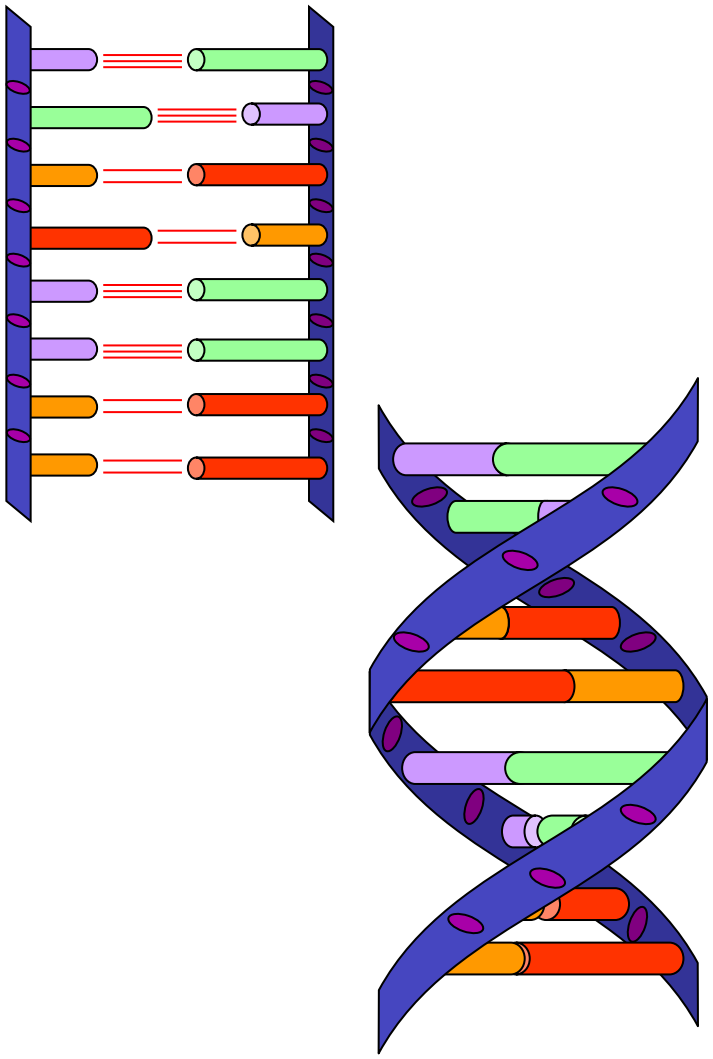






DNA

- **DNA double helix**
  - 1953 Watson and Crick → model of DNA double helix
    - X-ray diffraction images
    - Most important discovery of the 20th century in biology
- **Two polynucleotide chains**
  - Clockwise double helix
  - Nitrogenous bases linked by hydrogen bonds to the opposite
- **The two chains of a DNA molecule are complementary**
  - Specify one another
  - Each chain is a template for the synthesis of the complementary

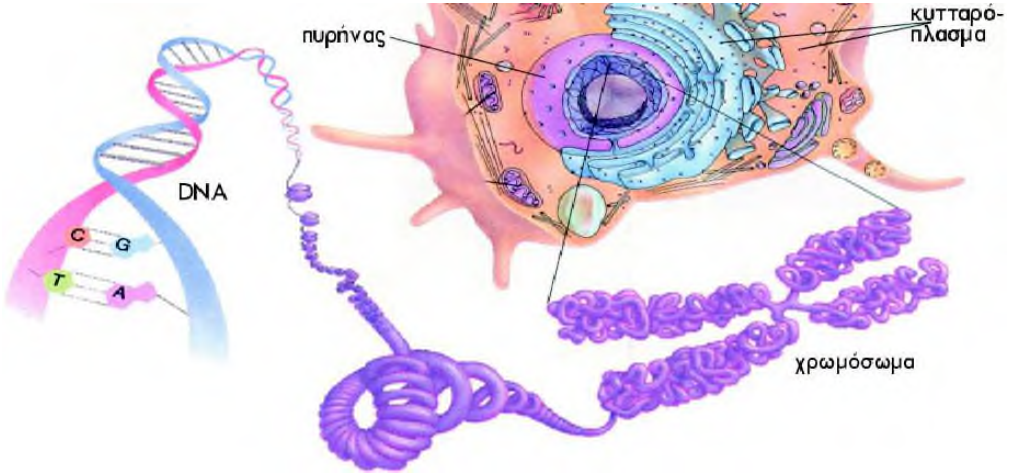


DNA

- **Self-replication**
  - "Unzip" like a zipper
  - Each chain can serve as a template
    - formation of a complementary strand
  - Production of two identical double-stranded DNA molecules
    - Specific enzymes "repair" problems
    - “Errors" can happen (ie mutations)

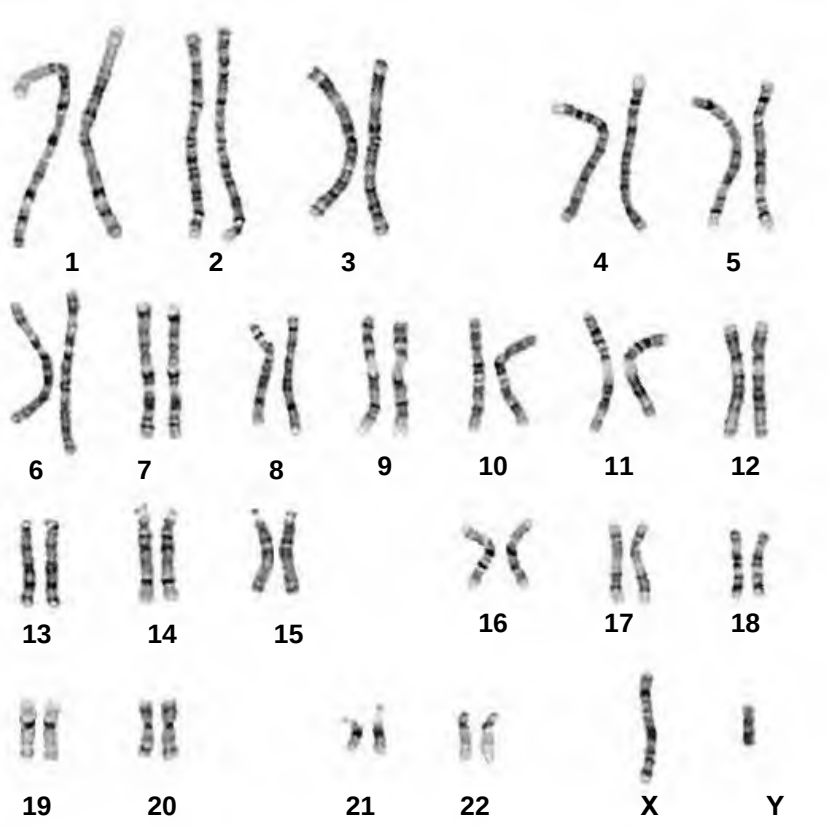
Chromosomes

- **Chromosomes**
  - Strongly stained with special dyes
  - Located in the cell nucleus
  - Carry the genetic information in eukaryotic cells (= cells with a nucleus)
  - Independent hereditary units
  - DNA is the basic ingredient



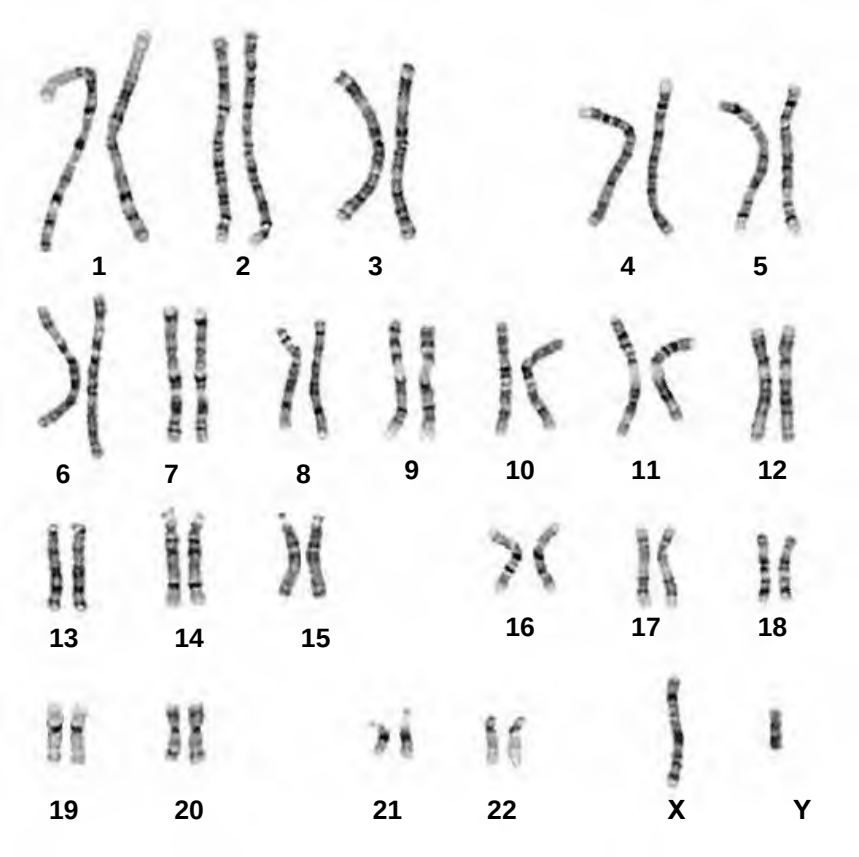
Chromosomes

- **Number of chromosomes**
  - Specific for each species
    - Human → 46
    - Olive Tree → 46
    - Worms → 1
    - Crabs → 200 και πλέον
    - In general, from 10 to 50
  - Differentiate one spicies from another
    - Not so much the number
    - More the genetic information in the chromosomes



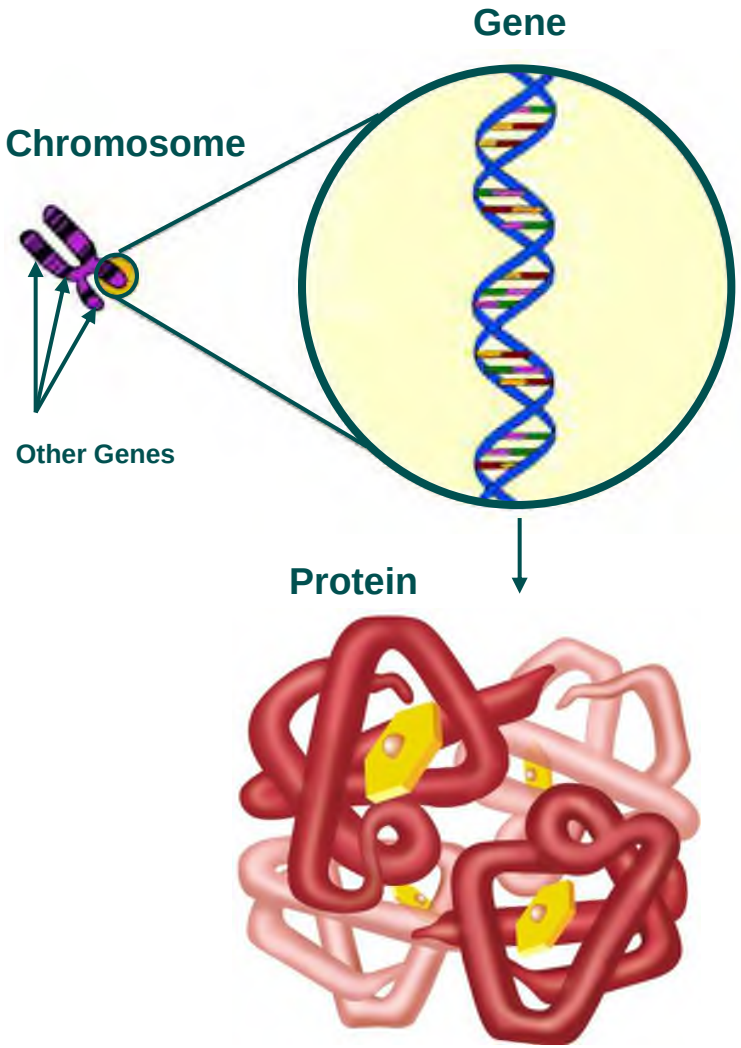
Chromosomes

- **Chromosomes**
  - In pairs in somatic cells
    - One pair of each kind → diploid cell (or 2n)
    - 46 chromosomes → 23 different pairs
  - Each pair
    - Homologous chromosomes
    - Similar in size and shape
    - Exception: the sex chromosomes
  - Only one each in the gametes (egg and sperm)
    - Haploid cells (or 1n)



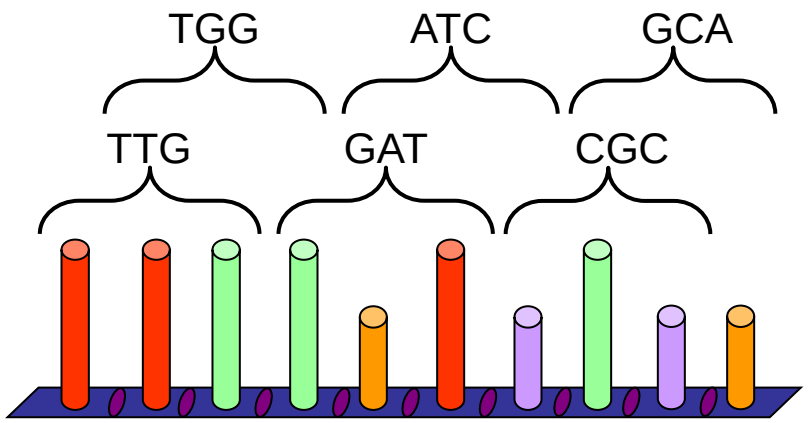
Genes

- **Chromosomes**
  - Contain hundreds or even thousands of different genes
  - In a linear arrangement
- **Genes**
  - Information units
    - A characteristic of the organism
      - Color of the eyes in humans
      - Length of wings in flies
      - Color of the seed in peas, etc.
    - A specific series of nucleotides
  - Control the structure of all the proteins of an organism
    - The function of a protein is related directly (if it is a structural protein) or indirectly (if it is an enzyme) to the structure
- **Number of different genes**
  - Viruses ~ 5-15
  - Mammals ~ 50.000
  - Humans > 100.000 (;)



DNA Code

- **Proteins**
  - Combination of 20 aminoacids
- **How are they encoded using 4 bases (letters);**
  - One base
    - A, T, G, C
    - 4 codes
  - Two bases
    - AA, AT, AG, AC, TA, TT, etc
    - 16 (4^2) codes
  - Three bases
    - AAA, AAT, …, GCT, GTT, etc
    - 64 (4^3) codes
    - Triplets → codons
- **DNA Code**
  - Based on triplets
  - Start and end codons
  - Degenarate
  - Overlapping

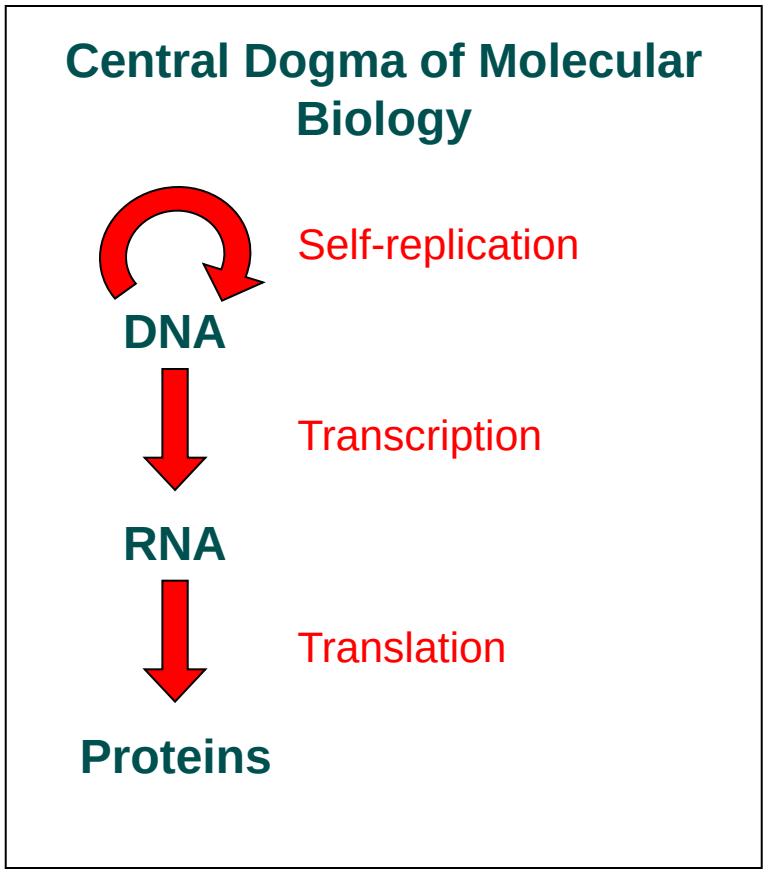


ACT
ACC
ACA
ACG } **Θρεονίνη**

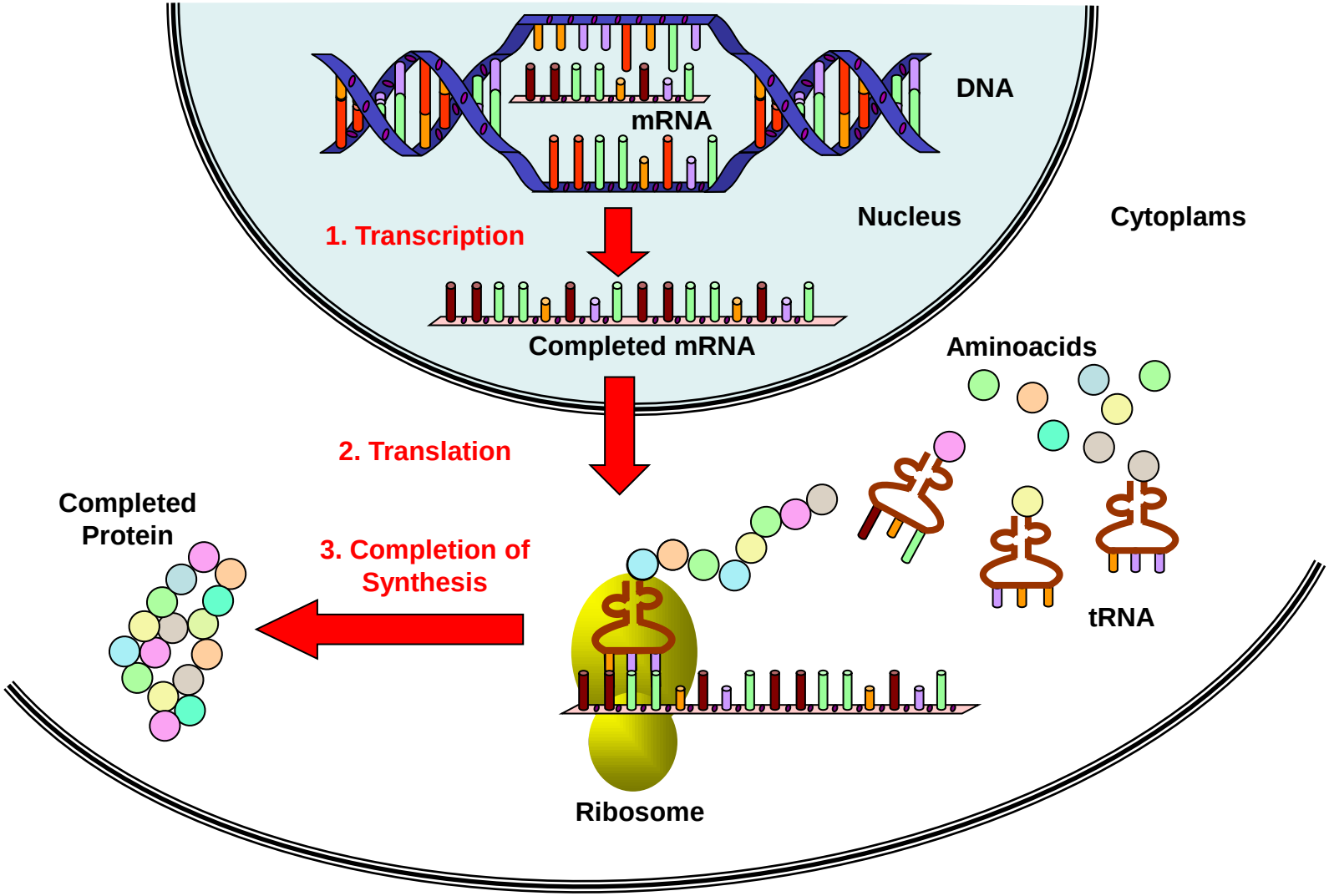
TGG } **Τρυπτοφάνη**

Protein Synthesis

- **Transcription**
  - Transfer information from DNA to RNA
  - RNA synthesis (mRNA)
- **RNA**
  - A copy of a gene
  - Same code
    - Uracil (U) instead of thymine (T)
- **RNA synthesis**
  - Performed accurately
  - Errors can appear
  - Errors are not inherited by next generation

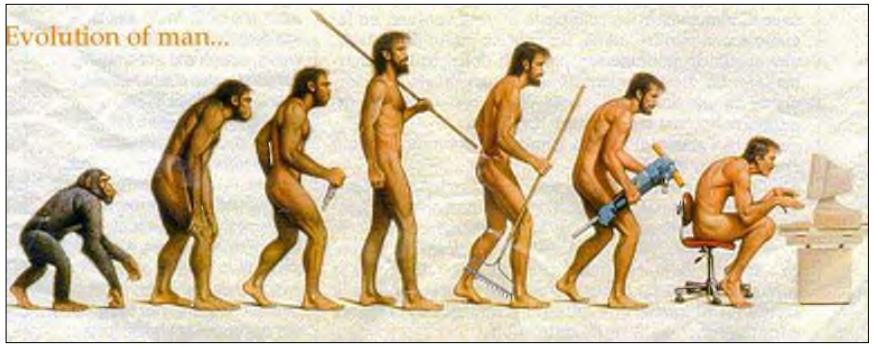


Protein Synthesis



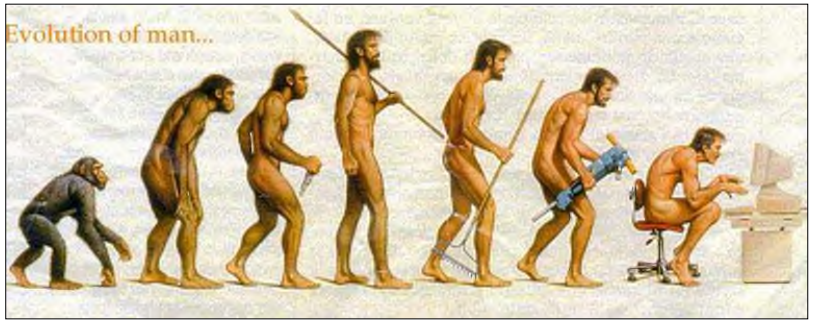
Mutations

- **Genetic Stability**
  - Necessary for the transfer of information
    - Unchanged from generation to generation
  - Precision of the molecular mechanisms
    - DNA replication
    - Cell division
- **Genetic diversity is also important**
  - The origin of evolutionary process
    - New mutated genes → new genetic feature
- **Mutations and gene combinations during reproduction**
  - New organisms
  - Better adapted to the current environment
  - Able to better adapt to upcoming changes



Mutations

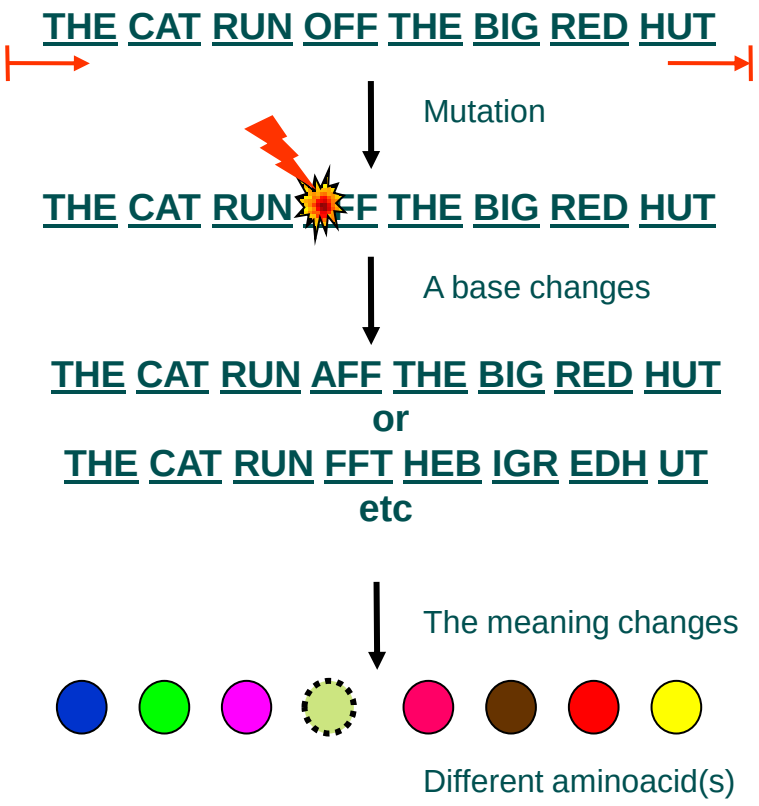
- **Mutations**
  - During the formation of the gametes
    - Inherited by subsequent generations
  - In somatic cells
    - Not inherited by progeny
    - Only appear in the daughter cells coming from cell division
    - Cell death or some form of cancer
  - Causes
    - Random
    - Effect of mutagenic agents
      - Various radiations (e.g., radioactivity, ultraviolet rays, X-rays, etc.)
      - Chemical substances (eg various pesticides, cigarette smoke, etc.)
  - Gene mutations and chromosomal abnormalities



The next great step in carrot evolution.

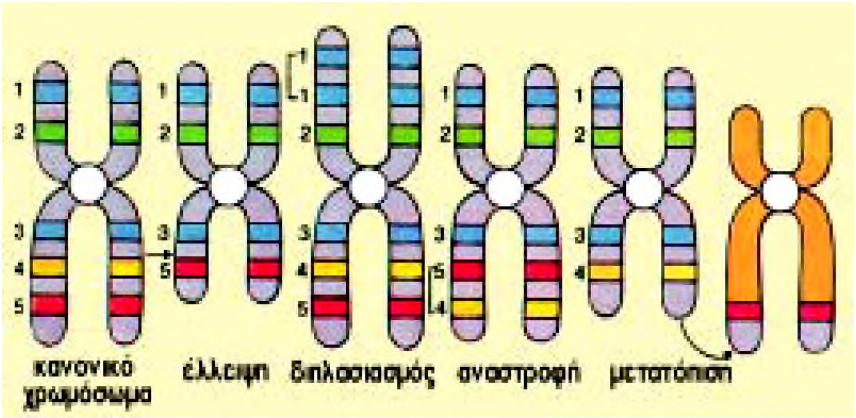
Mutations

- **Gene Mutations**
  - Changes in the sequence or number of nucleotides of a gene
    - Replacement, addition or removal of one nucleotide
  - New alleles
    - metabolic disorders
    - enzyme malfunctions
      - Phenylketonuria, albinism, Mediterranean and sickle cell anemia



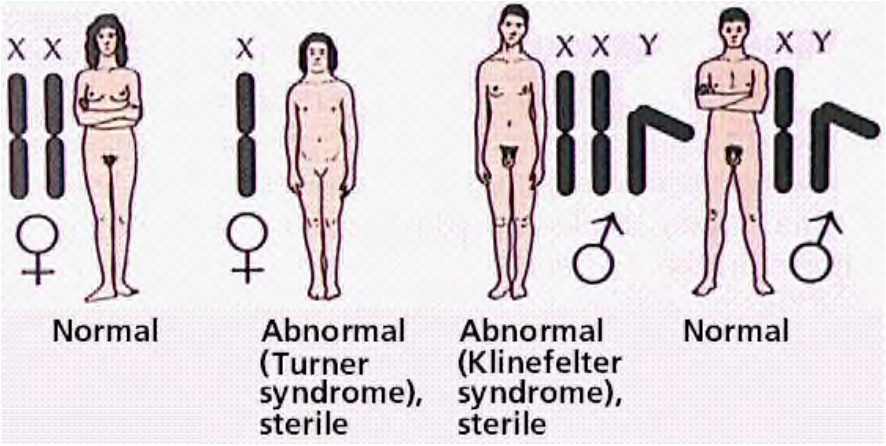
Mutations

- **Chromosomal abnormalities**
  - Changes
    - In the structure of the chromosomes
    - The number of chromosomes
  - Improper separation of chromosomes during cell division
- **Structural abnormalities**
  - A chromosome breaks and the fragment adheres to
  1. A homologous chromosome
     - Abnormally long chromosome
       - Doubling of certain genes
     - Another much shorter chromosome
       - Lack of certain genes
  2. Another non-homologous chromosome
     - Relocation
  3. The original chromosome in reverse order
     - Inversion



Mutations

- **Numerical Abnormalities**
  - Mainly because of problems during cell division
  - Smaller or larger number of chromosomes instead of normal
- **Diagnosed chromosomal numerical abnormalities**
  - 1% of the total live births
  - Indications that the percentage is higher at conception
    - 17-20% of all pregnancies end in termination
    - Almost half of those fetuses exhibit chromosomal abnormalities
    - Autosomal trisomies, triploid and tetraploid, and Turner syndrome



- **A missing autosomal chromosome**
  - Very rare
  - Very incompatible with life
  - Abortion of the fetus very early
  - Before the woman even realizes she is pregnant
  - 50% of the total abortions

Mutations

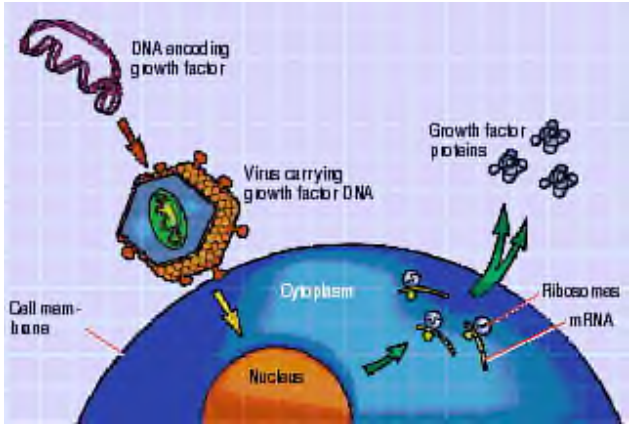
- **Down Syndrome**
  - One of the most frequent chromosomal abnormalities in humans
    - Face, eyelids, tongue, hands and elsewhere
    - Mental and physical retardation
  - Most have 47 chromosomes
    - Trisomy 21
  - Older average age at which a woman has a child → increased incidence
    - > 45 years 100X higher probability compared to <19 years
    - correlation with paternal age is insignificant

Artificial Mutations

- **Biological processes**
  - In order to improve products
    - diet
    - medicine
    - other activities
- **As old as civilization**
  - Animals crossed artificially
    - Improvement of the varieties
  - Metabolic processes of microorganisms
    - Yeasts
    - Baking and wine making

Biotechnology

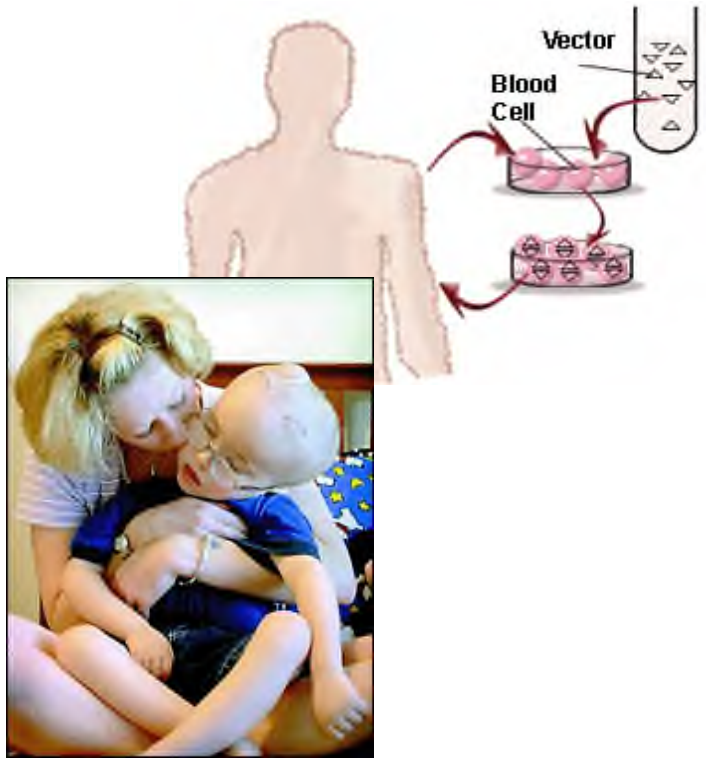
- **Genetic Engineering and Biotechnology**
  - Produce differentiated cells
    - bacterial, plant or animal cell
    - containing a foreign gene
    - Not necessarily based on pre-existing organisms
- **Modification of the genetic code**
  - Gene Transfer
  - In plant and animal organisms
  - Creation of transgenic organisms
- **Transgenic Organisms**
  - Genes can be introduced into eukaryotic cells
    - Incorporated into their DNA
    - Expressed
  - They can be used for
    - Gene Therapy
    - Modified plants and animals



Biotechnology

Gene Therapy

- **Correction of genetic defects in humans**
  - Severe hereditary diseases, eg
    - Leukemias → cells of the bone marrow and lymphocytes with "corrected" genes
    - Diabetes → pancreatic cells with insulin gene
- **Unfortunately there are no clinical applications**
  - Experimental stage
- **Need to improve the technology**
  - Improvement of techniques
    - Survival of cells
    - Control of the position where the DNA is placed
    - Degree of control we have over the expression of each newly introduced gene



Biotechnology

Transgenic Organisms

- **Products**
  - A whole organism
  - Protein that can be used as a vaccine
  - A drug
  - Various other organic compounds
  - Procedures that are not able to perform to date
    - Decontamination of areas
    - Increasing soil fertility
    - Selective destruction of insects
- **New frontiers in agriculture, medicine, and many other areas**

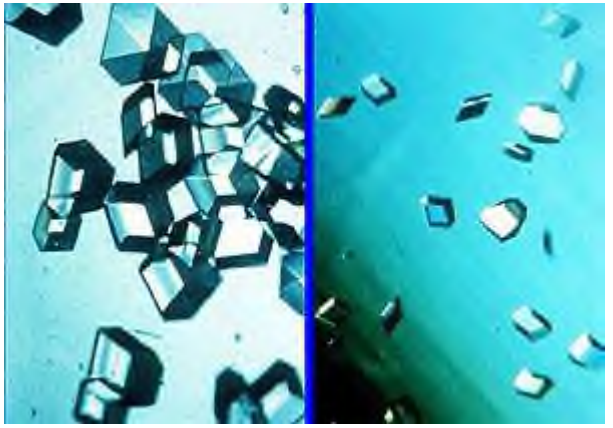
Biotechnology

- **Today commercially available**
  - Hormones and related proteins
    - From modified bacteria
  - Vaccines
    - From synthetic DNA
  - Genetically Modified Organisms
  - And much more!

Biotechnology

Applications: Proteins

- **Difficult to produce in a different way**
  - A single dose of growth hormone in humans
    - Pituitary of at least fifty calves
  - Insulin
    - From the pancreas of cattle and pigs
    - Very expensive process
    - Often created allergic reactions
- **Produced in large quantities and at low cost by bacteria**
  - Hormones for animals
    - Produce more meat



Biotechnology

Applications: Vaccines

- **Older vaccines**
  - By-products of metabolism or attenuated pathogens
    - Bacteria, viruses or fungi
  - Adverse effects on people
- **Recombinant DNA technology**
  - Production of clean vaccines
  - A vaccine for hepatitis-B
  - Expected vaccines for malaria and AIDS in the future

Genetic Modification

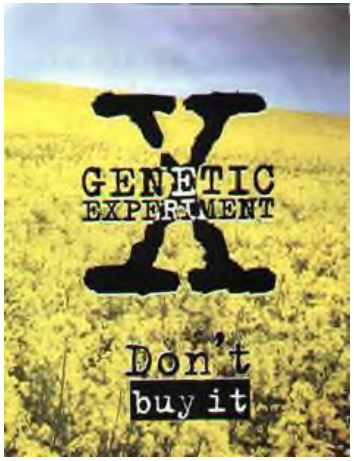
- **GM products**
  - Vaccines, medicines, foods, food ingredients and animal feed
- **Selection of the genes**
  - Special and highly desirable characteristics
  - Genes of organisms belonging to different species
  - eg
    - resistance to harmful insects from one species to another plant
    - plant to produce fruit with selected nutrients

Genetic Modification

- **GM Food**

- **Advantages and Benefits?**
  - Products of plant origin
  - Products of animal origin
  - Benefits to the environment
  - Benefits for society

- **Disadvantages and Risks?**
  - Safety
  - Intellectual property
  - Ethical issues
  - Social issues
  - Labeling



Genetic Modification

- Modified Food
- To date there are no data to suggest that the GMF have caused illness or harm to humans
- Each GMF should be evaluated independently and thoroughly

The Human Genome

- **Long-term international program**
  - Decrypting the sequence of the human genetic code
  - Took several years (1991-2003) for just one genome
  - Total cost of several billion dollars
- **Objectives**
  - To slice the human DNA into small pieces
  - To separate the pairs in a strong electric field
  - To determine the biochemical map of the entire DNA,
  - To compare the sequences with genes
  - To determine the distance between the genes, the physical map of the DNA

The Human Genome

- **Techical issues**
- **Work monotonous, hard, and non-creative**
  - Much of the human DNA contains genes which lack function
- **Possible applications**
  - Prophylaxis or treatment of diseases
  - Gene therapy
    - gene replacement
    - eg cancer → lymphocytes undergoing genetic manipulation in the laboratory
  - Identify individuals by their genetic fingerprints
    - identify criminals
    - determine the father of a child.

Ethical Dilemmas

- **Carriers genes responsible for certain diseases**
  - Identify these persons by introducing mandatory genetic testing of all citizens of a country ?
- **Predisposition to a severe chronic or fatal illness**
  - Should a person be informed of the genetic predisposition?
  - What if the risk is inevitable and the disease incurable?
  - Under what conditions should be allowed such a person to have access to this information?
- **Lately many employers are reluctant to hire smokers and obese people**
  - Should an employer have access to the genetic data of job seekers?
- **Prenatal diagnosis of genetic disorders can become routine**
  - Should a pregnancy be discontinued if a genetic disease gene is discovered?
- **Knowledge of the genetic structure of people will have a significant impact on the culture .**
  - Foster a purely biochemical view of man?
- **Upon completion of the genetic map**
  - Should it be permitted to purposely design people?

Cloning

- **Unexpected arrival of cloning technology**
  - Dolly: the first clone adult mammalian
  - Revised the perception of the mechanisms of reproduction of the human species
  - Storm of protest
    - possible to clone Jesus from DNA that was supposedly left on the Shroud???!!!
- **Applied with increasing frequency to farm animals and laboratory animals**
- **Homo Sapiens → Homo Xerox;**

10/3/1997

Cloning

- **Clones**
  - A population of genetically identical organisms or cells
  - Have been derived from a single original organism or cell
- **It is not a new phenomenon**
  - monozygotic twins
    - random natural phenomenon of cloning of embryos
    - 4,000 times a day throughout the world
  - rosewood branch
    - when transplanted grows into a clone of the original plant
  - unicellular and multicellular organisms
    - reproduce asexually

8/11/1993

Cloning

Cloning methods

- **Various methods**
  - Similarities with techniques in assisted reproduction
    - DNA of the “original” organism → “empty” egg → “copy” embryo or
    - more than one embryo from the same-already-fertilized egg
  - is not a particularly difficult technique but has poor efficiency
    - requires many attempts

19/2/2001

Cloning

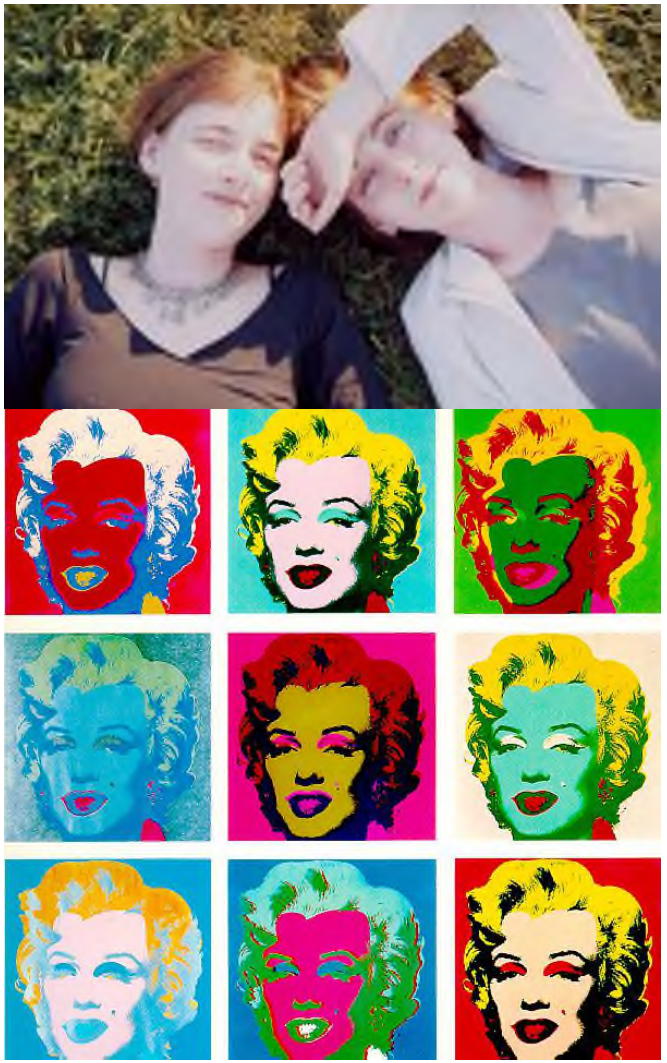
- **The End of Dolly**
  - Dolly gave birth to four lambs
  - She died on 14/2/2003
    - at the age of 7 years
    - severe pulmonary issues
    - most sheep live 11 to 12 years
  - Was the premature death related to the fact that Dolly was a clone?

Ethical Dilemmas

- **Is cloning a solution to infertility problems? When should it be applied?**
- **Is cloning a new form of slavery since it predetermines the future? How much genes predetermine the future?**
- **Will cloning cause the marginalization of genetically inferior people and introduce “custom-build” people (Gattaca)? Can society prevent this situation?**
- **Will cloning endanger biodiversity and species survival? Has negative selection already been diminished because of the technological development of man?**
- **Should experimentation on stem cells be allowed? Are the cloned stem cells really a fetus?**

Myths and Exaggerations

- **A few weeks after the introduction of Dolly**
- **Der Spiegel → numerous copies of Hitler**
- **Questions**
  - Clone of Hitler
    - Would he try to occupy Europe again?
  - Clones of Mozart
    - Would they became great composers, or at least excellent DJs;
- **Effect of environment on behavioral characteristics**
  - Proven beyond doubt
  - Equally important in determining character
  - Identical twins are different in character
    - Although they grow simultaneously in similar environment

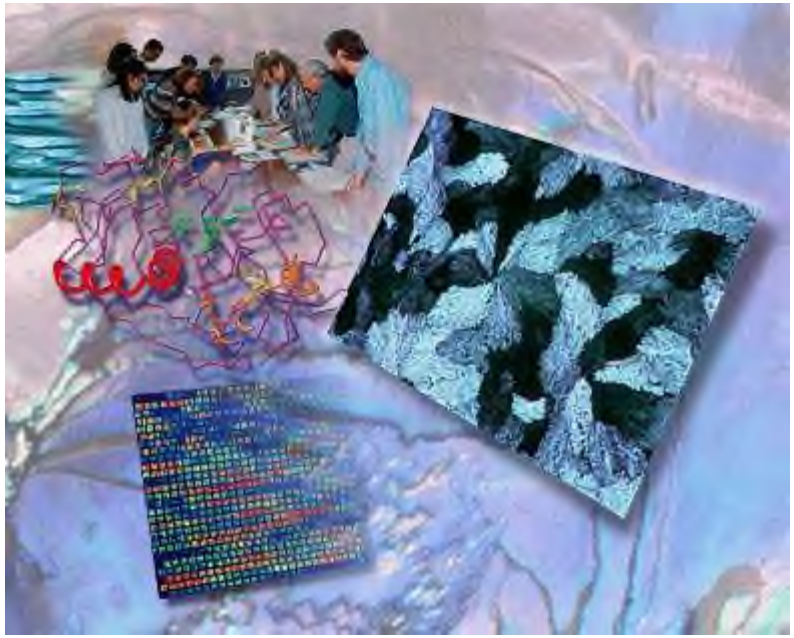


Myths and Exaggerations

- **The vision of Steven Spielberg for a "Jurassic Park"**
  - Cells of a dead organism
  - Must be maintained under appropriate conditions
    - Immersed in liquid nitrogen or in paraffin blocks
    - Over time, the DNA becomes fragmented and eventually decomposes
  - Successful isolation of DNA from entrapped insect
    - Strongly contested because of the high probability of sample contamination by exogenous DNA.

The Legal Framework

- **Protocol for the Prohibition of Cloning Human Beings of the Council of Europe**
  - Greece was one of the first five countries that have ratified it
  - 29 of 43 countries have signed
- **Laws or control authorities**
  - Do indirectly prevent cloning in humans
  - Prohibited to conduct research on human embryos for any purpose
  - Prohibited to sell sperm and ova and “hire” women for gestation of fetuses
- **Bioethics committees**
  - Approval required before scientists start research programs in embryos or reproductive techniques




Oh My God!
I have been
cloned!!!