GENETICS

Sheet no. 2

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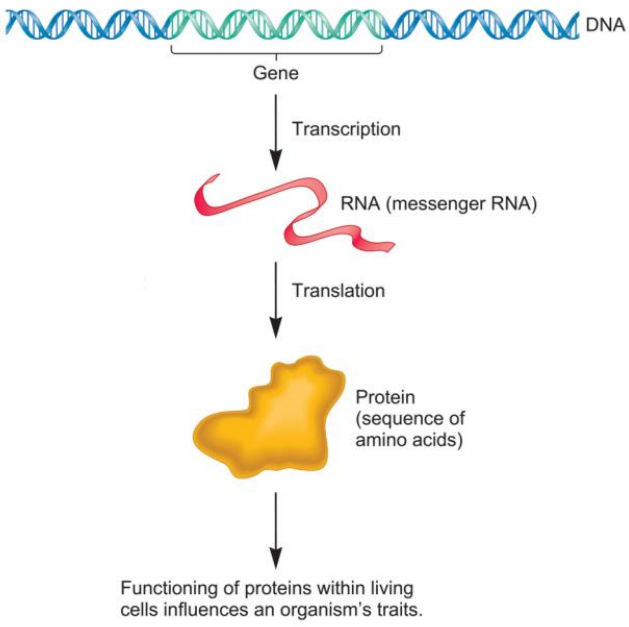
Introduction to Genetics in the Twenty-First Century

The Relationship Between Genes and Traits

-to synthesize the protein, the cell must be able to access the information that is stored within the DNA sequence, so the process of protein synthesis or the protein function inside the cells relies on two steps: transcription and translation (gene expression).

- **Most genes encode polypeptides that are units within functional proteins.**

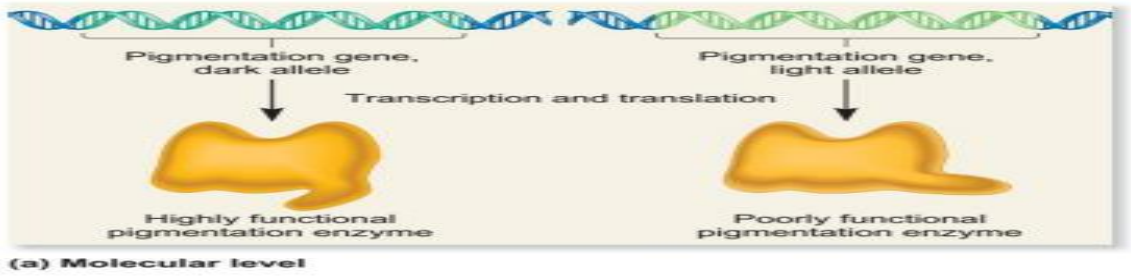
- **Gene expression at the molecular level involves transcription to produce *mRNA* and translation to produce a polypeptide.**



This part of DNA(gene)→ the gene will be transcribed to mRNA(a copy of this DNA instead of the thiamine)→this mRNA will be transported to the cytoplasm for protein synthesis→ and after that, the protein will be modified folded and sent to the final destination.

-to understand the relationship between genes and traits, let's see these examples:

-focus on four levels: molecular, cellular, organism, and population levels.



(a) Molecular level

a)molecular level: we have Gene Alternative forms (alleles): allele A and allele B, and the sequence between these two is slightly different to give different fx, this gene encodes a pigmentary enzyme(which changes the pigmentation of the organism so one allele confers a dark pigmentation while second allele causes a light pigmentation.

(b) Cellular level

b)the cellular level means the function of the proteins within the cell will affect and determine the function and the structure of a particular cell, so the functional differences between the two enzymes from one gene come from the difference in the amount of the pigment produced.

- indicating that enzyme no.1 which has dark pigmentation and is encoded by an allele works properly to give this enzyme that functions very well, meaning when this gene is expressed in the cell of the wings, a large amount of pigment will be made.

- enzymes no.2 are encoded by the allele causing light pigmentation, which means it will encode for these enzymes that function poorly.

-noticing that both dark and light enzymes are encoded by one gene with 2 alternative forms(the light enzymes are encoded by a poorly functioning allele, and the dark enzymes are encoded by a properly functioning allele)

(c) Organism level

c)organisms level: light vs dark wings, tell the amount of pigment in the wing cells will control or govern the color of the wings so that if the pigment is synthesized by enzymes produce a large amount of pigmentation in this wing, the wing will be dark and if the enzyme produces little pigment it will give the light color of the wing.

(d) Population level

d)population level: two types of environments, for the two types of the butterflies` wings: light and dark

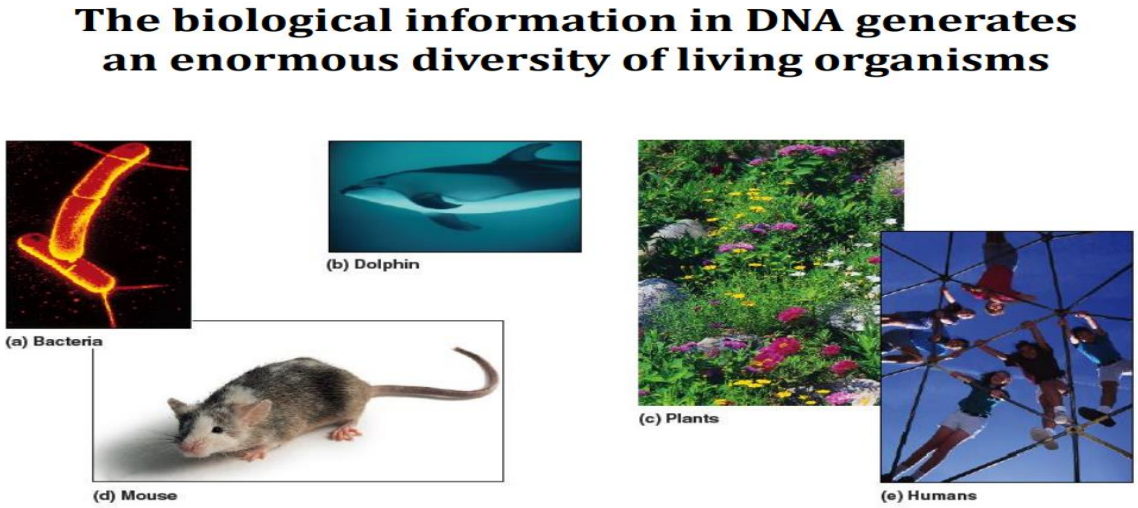
-dark wings butterflies live in dark forests, while light-pigmented butterflies live in light(open) forests, this helps animals adapt to their environments and protects them from predation, so birds or predators will not detect the dark butterflies in their dark forest

*Another example is rabbits in snow have white frau, while in sunny weather, their white pigment changes to adapt to the new environmental circumstances.

-**Genetics, which governs an organism's traits, spans the molecular, cellular, organism, and population levels.**

• Genetic variation underlies variation in traits.

• In addition, the environment also plays a key role in genetic variation



-so the biological information in general in DNA will generate a huge amount of diversities of all living organisms, for example, humans have 46 chromosomes compared with other organisms indicating you know that they have similar functions.

-so organisms' diversity is related to their genetic material

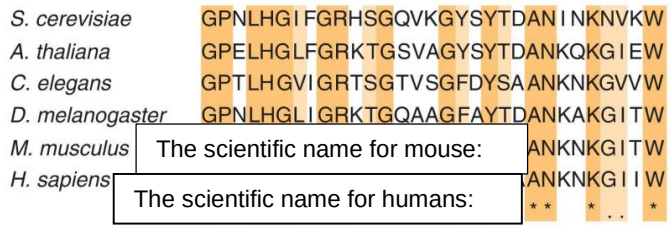
-also, similarities in their genetics indicate similar fx.

Many genes have similar functions in different organisms

-Comparison of gene products in different organisms can reveal identical and similar amino acid sequences

e.g. cytochrome C protein from six species

-similarities between the protein sequences between different species indicate that this particular gene produces a particular protein and has a similar function between the organisms.

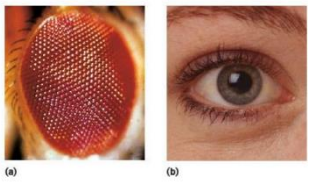


White: for differences

example: Glycine

A gene from one organism can functionally replace a gene in another organism

-Example: Pax6 gene is required for eye development in insects, mice, and humans.



-Expression of human Pax6 gene in Drosophila can induce eye development

-Pax6 gene is responsible for eye development in humans, mice, and drosophila, you can see this gene has the same function between these organisms so this process of this information or this advantage is important to study the gene function.

-if a patient has a mutation, how can we confirm that the mutation which causes the disease? we have to study this mutation in modern models of organisms(fish, frogs, mice, drosophila), it is hard to study it in humans because of the 9 months of pregnancy for the phenotype to appear, however, in modern models like fish animal models for example, zebrafish, and frogs within a week we can expect the effect of these variants on the organisms.

-we will see that there are complete phenocopies and partial phenocopies between the human and the patient by this we can determine the pathogenicity of the variant and this patient and we can help the families after that for prenatal diagnosis or pre-implantation genetic diagnoses to have a normal child or in another way we can also start synthesizing a drug to treat this particular disease for this model organisms are important in our field.

Two critical functions of DNA

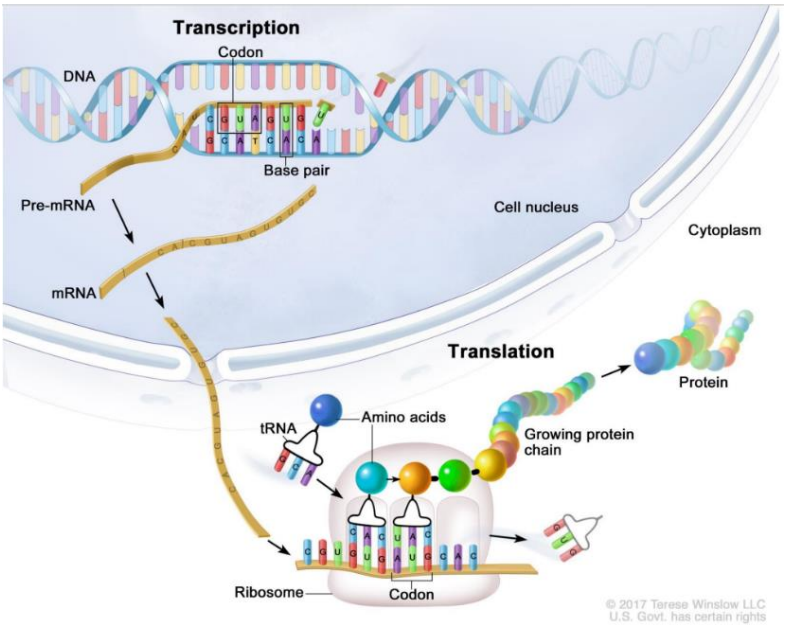
1. Replication – necessary to ensure that genome is replicated each cell division and each generation -heredity

2. Code for proteins (and functional RNAs):

– gene transcription → RNA

– translation – nucleotide sequence of mRNA specifies amino acid sequence of a polypeptide.

• transcription may also generate untranslated RNAs that have functions (eg. rRNA, tRNA, miRNA).

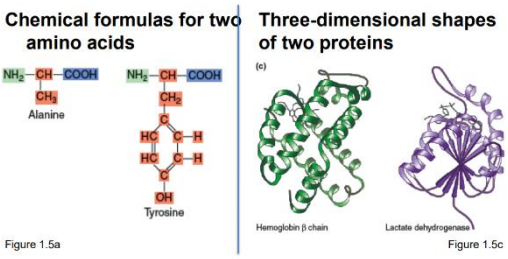


you can see the process of genetic expression: transcription to pre-mRNA or immature RNA: it needs splicing, capping, tailing-this Messenger will transport it through the nuclear envelope pores to the cytoplasm to the ribosome other ribosomes will produce the protein which will be modified and folded and then sent to the final destinations to the muscle as a hormone or whatever

The amino acid sequence determines the three-dimensional shape of the protein

-protein is a large molecule composed of building blocks which are amino acids(20 essential AA)

-note: the building blocks for proteins are AAs, for DNA are nucleotides, and for chromosomes are nucleosomes.



Amino acid bonds are between the Amino group(NH2) and the carboxyl group(COOH) forming peptide bonds.

Also, the ends are N terminal and C terminals

Proteins could be antibodies, enzymes, messenger proteins, growth hormones, structural components, dystrophin, actins, transport, and storage function for proteins, ferritin, and hemoglobin,….

-there are primary, secondary, tertiary, and quaternary structures of proteins

-Hb is a quaternary protein

Proteins

- **make up most of the mass of a cell**
- **regulate all cellular processes directly or indirectly**
- **enzymes involved in energy utilization, energy storage.**
- **enzymes for biosynthesis or breakdown of other macromolecules (including DNA).**
- **proteins form scaffolds to hold other proteins and macromolecules in place – to organize the cell.**
- **proteins regulate transport into and out of cells and signaling between cells.**
- **motor proteins and other proteins regulate intracellular transport.**

Molecular Diagnosis

Molecular diagnosis of human disorders is the detection of the various disease-causing variants in DNA and /or RNA samples

Molecular Diagnos**tics**

- **Is the use of molecular biology techniques to increase the scientific knowledge of the natural history of certain diseases, identify individuals who are at risk for developing specific diseases, and make diagnosis of human disorders**

• Advance in the understanding of the structure and chemistry of nucleic acids has facilitated the development of technologies that can be employed effectively in molecular diagnostics

-medical genetics or molecular diagnostics is an important field now in the Practical Medical Practice to diagnose diseases to invent a drug to help patients control the prognosis of the disease in the patients and also to prevent the occurrence of new phenotypes or to decrease the effect of the current phenotypes in molecular diagnostics is important now for patients, for scientists and, for our life.

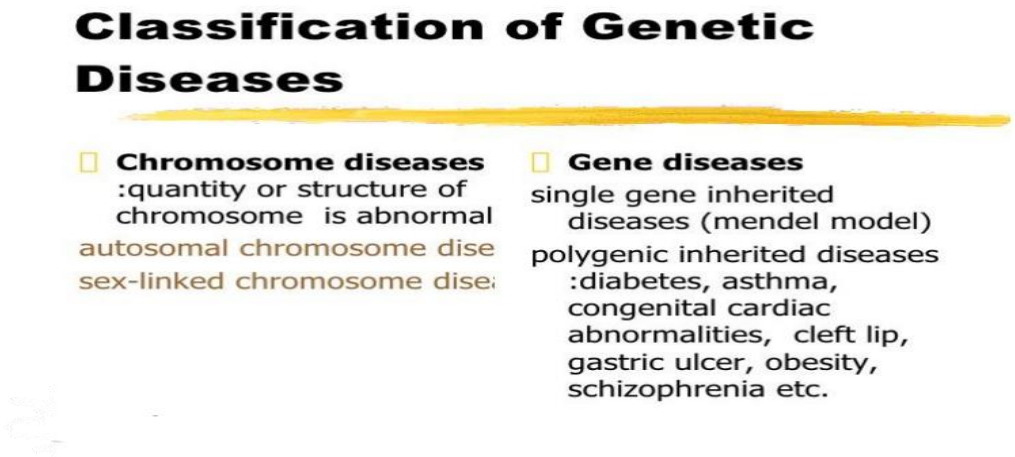
Cytogenetics

- **Cytogenetics: is the study of the structure and function of chromosomes (material of inheritance in the cell nucleus), chromosomal behavior during somatic cell division in growth and development (mitosis) and germ cell division in reproduction (meiosis), chromosomal influence on the phenotype and the factors that cause chromosomal changes (Hare & Singh, 1979)**

- Human cytogenetics is concerned with how these processes may go wrong, because changes in number or in structures of certain chromosomes(s) can cause diseases

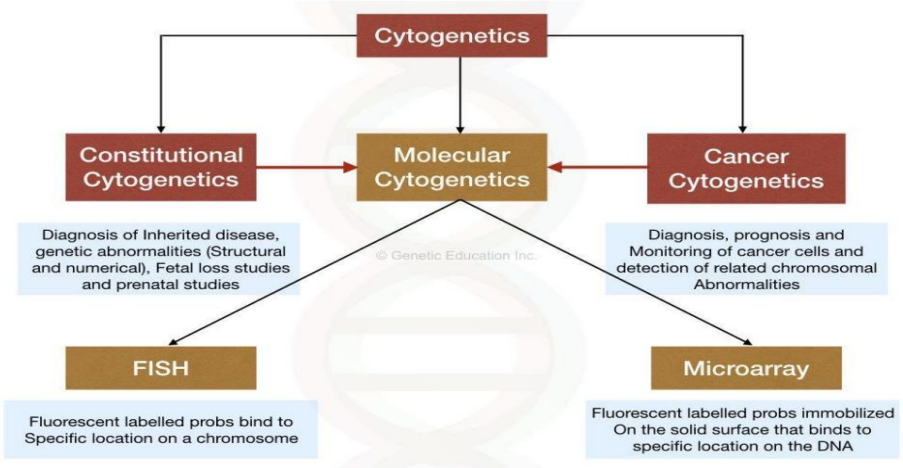
-it studies chromosome structure, number, shape, their link to the disease, and if they have extra or missing genes.

-we take chromosomes from ***metaphase*** stage in the cell cycle and study their characteristics.



-so the GENETIC diseases can be divided into either **chromosomal diseases**(abnormalities in chromosomal structure, and missing or extra-genetic material chromosomes that can be detected under the microscope) or **genetic diseases** (at the genetic level so we can detect the mutations inside the gene)

- number of genetic diseases that we have in our communities and in the world is still increasing, reaching up to more than 9,000 diseases in 20000 genes.



in this chart, you can see the cogenetic branches:

- we have constitutional, looking at the chromosomes under the microscope for the structure, shape, and number of these chromosomes and also the length of chromosomal abnormalities with cancer to diagnose, prognose, and monitor the cancer cells so we have to look for the chromosomal analysis for Cancers and we have also molecular cytogenetics.

-we can either go through the two techniques**: the fish technique** (Fluorescence in situ hybridization) using DNA sequence that is complementary to the specific part of the genome sequence: for example, if we have missing parts of DNA in a particular chromosome these missing parts couldn't be seen under the microscope, go to more deep chromosome missing segments florescence will not bind because it will not detect the complementary sequence on the target DNA, there will be no fluorescence to be detected under the florescent microscope while If there are extra duplications, the intensity of the signal under the microscope will be duplicated compared to the normal signal.

-the second technique is **microarray**: which is more advanced than FISH, because FISH detects particular segments while microarray detects hundreds to thousands of parts of DNA at the same time.

-Sanger sequencing can sequence a particular part of the genome one gene or one exon for example in reaction while Next Generation sequencing is advanced.

-advanced techniques reaction advances with Technologies to study genetic diseases or chromosomal abnormalities.

EXTRA:

Sanger sequencing relies on DNA polymerase to synthesize new DNA strands in the presence of modified nucleotides that terminate DNA strand elongation when incorporated. By using a mixture of normal and modified nucleotides, DNA synthesis reactions can produce fragments of different lengths, each ending with a specific labeled nucleotide. These fragments are then separated by size via gel electrophoresis, and the sequence is determined based on the order of the labeled nucleotides.

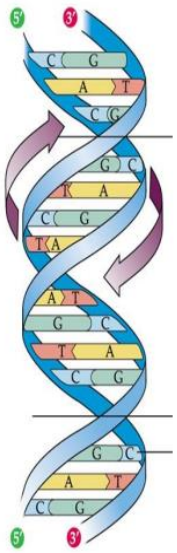
FISH (Fluorescence In Situ Hybridization): FISH is a cytogenetic technique used to visualize and localize specific DNA sequences within chromosomes or cell nuclei. In FISH, fluorescently labeled DNA probes that are complementary to the target DNA sequence are hybridized to the chromosomes or nuclei. The probes bind to their complementary sequences, allowing researchers to visualize the location and abundance of specific DNA sequences under a fluorescence microscope.

Microarray: Microarrays are a high-throughput technology used to analyze the expression levels of thousands of genes simultaneously. In a microarray experiment, DNA or RNA molecules from a sample are labeled and hybridized to a microarray chip containing thousands of known DNA or RNA probes. The degree of hybridization between the labeled sample molecules and the probes on the chip is detected and quantified, providing information about the expression levels of various genes in the sample.

Next-generation sequencing (NGS) is a term used to describe modern high-throughput sequencing technologies that allow rapid sequencing of DNA and RNA samples. These technologies have revolutionized genomics research and have

numerous applications in various fields, including medical diagnostics, evolutionary biology, and agriculture.NGS platforms differ from traditional Sanger sequencing (often referred to as "first-generation sequencing")

Genetic variation (at DNA or RNA level) ➔ the clinical phenotype



- There are lots of different mutations/ variations that can occur in our DNA.
- Large-scale mutations/ variations at the level of chromosome
- Small- scale mutations/ variations at the level of gene

These questions are just for practicing:

1. In cells the DNA replication takes place in _____ phase.
a) G0
b) G1
c) S
d) G2

View Answer

Answer: c
Explanation: In cells the DNA is replicated in the S phase. In G1 and G2 phase mainly the proteins required for mitosis is increased in quantity.

2. Which of the following doesn't agree with the chromosomal theory of inheritance?
a) The genes are located on the chromosome
b) The genes on the same chromosome are always passed together
c) The genes are located linearly on the chromosomes
d) The distance between two genes can be mapped

View Answer

Answer: b
Explanation: Genes from the same chromosome can show independent assortment as well by recombination. However, very close gene tend to be linked and are passed on together.

5. Which of Mendel's laws will be violated by linkage?
a) Panspermia
b) Diminance
c) Segregation
d) Independent assortment

View Answer

Answer: d
Explanation: Due to linkage parental chromosomes will have a tendency to be inherited together, thus the genes will not reasonably assort independent of each other. Panspermia aw is by Darwin.

7. Considering the concept of Multiple alleles, one organism can have ____ alleles.
a) One
b) Two
c) Three
d) Four

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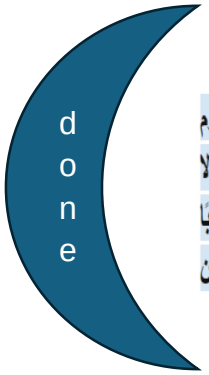
Answer: b
Explanation: Multiple allele states that there can be more than one or even more than 2 alleles for one gene, but one organism can have only 2 such alleles as there are 2 loci only.



ربي إن إخوتنا في غزة ذاقوا وبال القصف والحصار، اللهم ثبت أقدامهم وأنصرهم على القوم الكافرين. اللهم انصر أهلنا في غزة وأرنا في أعدائهم عجائب قدرتك ولا تترك منهم أحدًا إلا وأخذته أخذ عزيز مقتدر يا الله. أسألك يا الله أن تحمي غزة وأهلها وأن تنزل على أعدائهم عذابًا لا تعذبه لأحد من العالمين.