Introductory Biology II (LS1201)

History of Genetics and Basic concepts in Genetics

Date: 09/05.2022 & 11.05.2022

Syllabus outline

PART-I: (Prof. Jayasri Das Sarma)

Basic concepts in genetics. Mutations and transposons, their nature and source. Mendelian principles: Law of segregation, law of independent assortment. Genetic diseases, Pedigree analysis.

PART-II: (Dr. Sreeramaiah N. Gangappa)

Extensions of Mendelian principles: Incomplete dominance, Co-dominance, penetrance and expressivity. Gene interactions and epistasis. Recombination and crossing over. Gene mapping methods.

PART-III: (Dr. Anuradha Bhat)

Why evolution is true: Evidence; Tree of Life. Theories of evolution: Use and disuse theory, natural selection, new synthesis, sexual selection. Types of selection; mechanisms of evolution

Syllabus outline

Genetics:

- ✓ A brief history of biology and genetics
- ✓ Basic concepts in genetics
- ✓ Pedigree analysis
- ✓ Genetic diseases
- ✓ Mutations and transposons, their nature and source
- ✓ Transposons, their classifications and their importance
- ✓ Mendelian principles: Law of segregation, the law of independent assortment.
- ✓ Extensions of Mendelian principles: Incomplete dominance, Co-dominance, Gene interactions and epistasis.
- ✓ Penetrance and expressivity and multiple alleles
- ✓ Linkage, Recombination and crossing
- ✓ Gene mapping methods

Reference Books

- **Introduction to Genetic Analysis** (9th Edition), A.J.F. Griffihs, RWessler, Richard C Lewontin& Sean B Carroll. W. H. Freeman &Company
- **Principles of genetics**, 8th Edition, Gardner /Simmons/ Snustad. John wiley& sons Inc
- **Fundamentals of Genetics** by B.D. Singh
- **Genetics** (3rd edition) Monroe W Strickberger, Prentice Hall of India Pvt Ltd. New Delhi
- **Essential Cell Biology (**Edition 2), Garland Science Bruce Alberts, Dennis Bray, Karen Hopkin, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts and Peter Walter

Mode of evaluation and marks distribution

Total marks: 32.5

FINAL exam: 25 marks

Class test/Assignment: 7.5 marks

Brief History of Biology

WHICH IS THE MOST IMPORTANT DISCOVERY IN BIOLOGICAL SCIENCES?

Compound Microscope

Invention of First Compound Microscope

First compound microscope (1590)

Hans Lippershey, (1570)

Timeline of Scientific Discoveries

(1632–1723)

Best known for his work on the **improvement of the microscope** & for establishment of microbiology.

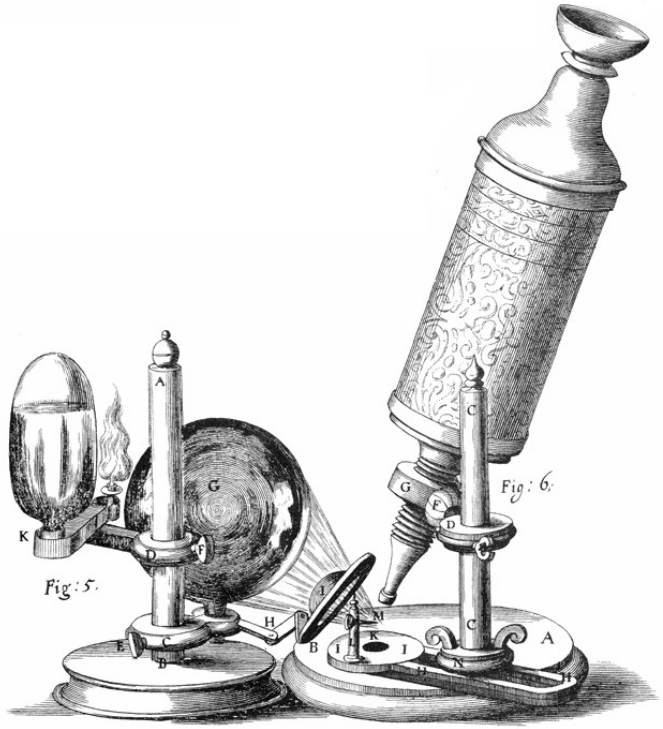
✓ Father of Microbiology

- 1675 – Anton van Leeuwenhoek:

  Observes Microorganisms by Microscope

Ref Google images

Timeline of Scientific Discoveries



- 1665: Robert Hooke discovers cells in cork, then in living plant tissue using an early compound microscope. He coins the term **cell**

Cell Theory -1838

Theodor Schwann (1810 –1882)

Matthias Jakob Schleiden
(1804–1881)

1. All living organisms are composed of one or more cells
2. The cell is the most basic unit of life

Rudolf Virchow -1855 (*Omnis cellula e cellula*)

- "cells can only arise from pre-existing cells"
- Virchow observed abnormal increase in white blood cells in patients named it *leukämie* in 1847
- Virchow was the first to correctly link the origin of cancers from otherwise normal cells

(1821 –1902)
German Biologist

Louis Pasteur

- French chemist and microbiologist
- Germ Theory of Diseases (1861)
- Principles of vaccination
- Microbial fermentation
- Pasteurization

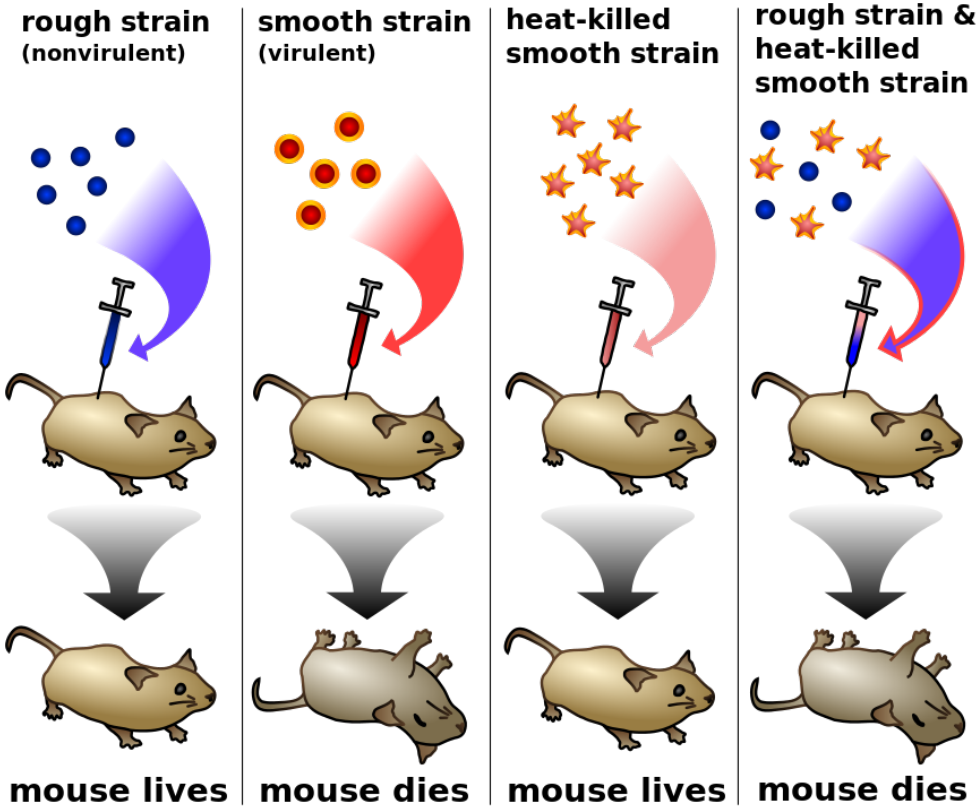
Louis Pasteur (1822-1895)

Ref Google images

Genetic Transformation principle

- **Frederick Griffith** (1928) was the first suggesting that bacteria are capable of transferring genetic information through a process known as **transformation**

- **Pneumococcus** (*Diplococcus pneumoniae*) bacteria which infect mice – a type III-S (smooth) which was virulent, and a type II-R (rough) strain which was nonvirulent.



✓ **Griffith concluded that the type II-R had been "transformed" into the lethal III-S strain by a "transforming principle" that was somehow part of the dead III-S strain bacteria.**

Oswald Avery, McCarty & Macleod : proves that DNA is the genetic material of the chromosome (**1944)**

Oswald Avery | Maclyn McCarty | Colin MacLeod

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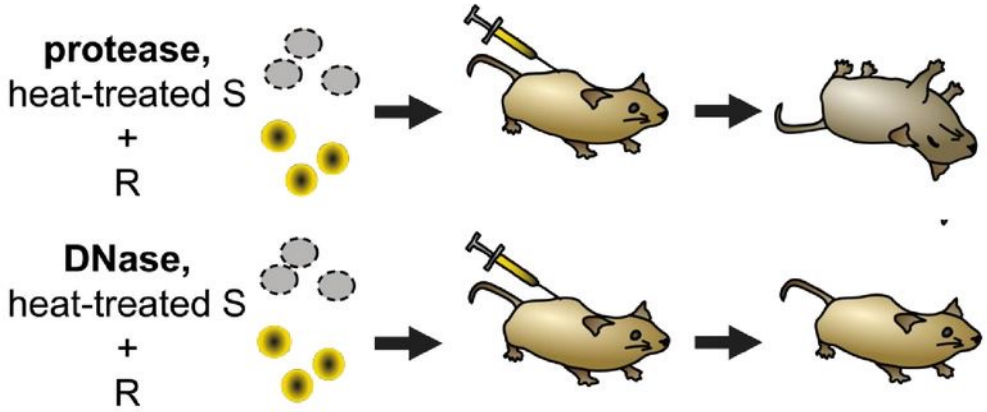
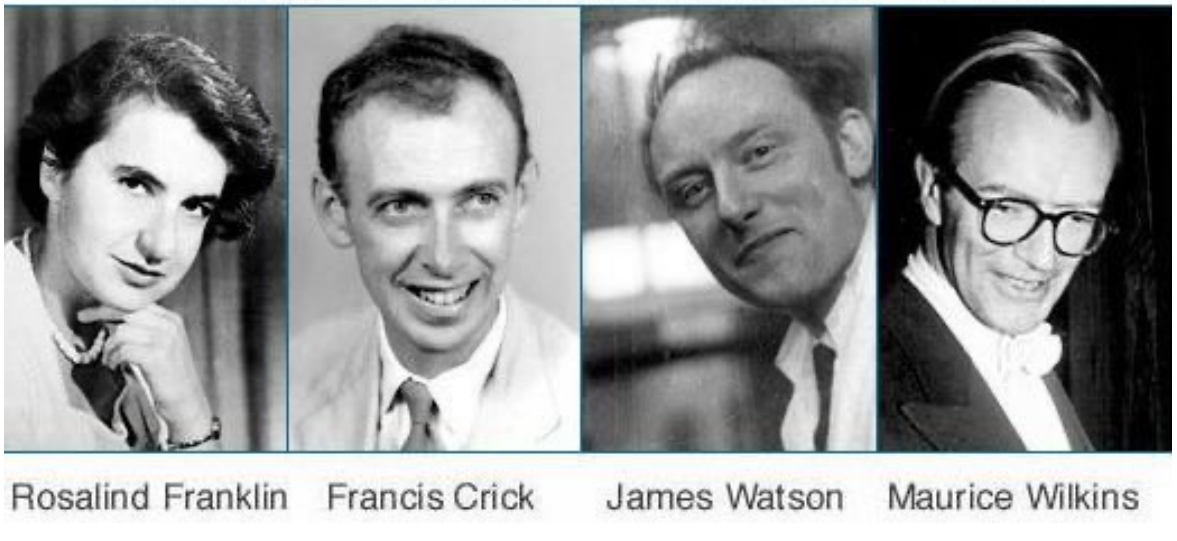
- Adding S-strain DNA to R-strain bacteria killed the mice.
- Adding S-strain protein to R-strain bacteria did not.



Crick and Watson (1953)



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- ✓ Discovery of DNA double helix, basis for molecular biology (1953)
- ✓"Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid" published in the scientific journal *Nature*
- ✓This article is often termed a "pearl" of science because it contains the answer to a fundamental mystery about living organisms

Brief History of Genetics

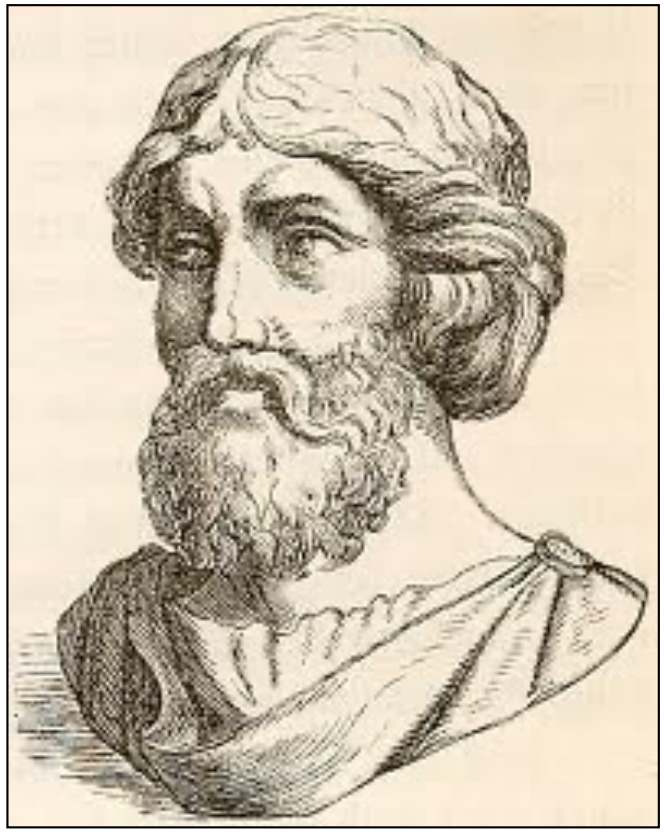
Theories about Heredity: Pre Mendelian Era

1. Vapour and Fluid Theory
2. Preformation Theory
3. Epigenesis theory
4. Particulate Theories

VAPOUR AND FLUID THEORIES

- **PYTHAGORAS(500BC)**

  Proposed that every organ of animal body gives out some type of vapours . These vapours unite and form a new individual.



Preformation Theory (Preformationism)

- ✓ The preformists assumed that the **entire organism was preformed in the sperm** (animalkulism) or in the eggs (ovism or ovulism) and only had to unfold and grow

Preformed human in sperm (1672)

Marcello Malphigi, 1672)

Marcello Malpighi
(1628-1694)

Ref- wikipedia

Epigenesis theory

- ✓This theory was advocated by Wolff (1738—1794), a German biologist
- ✓He states that egg or sperm cells do not contain miniature human. In other words, egg or sperm cells are undifferentiated
- ✓The differentiation into various organs or parts takes place only after fertilization from the zygote resulting into development of adult tissues and organs. This concept is known as **epigenesis** which is universally accepted

PARTICULATE THEORIES

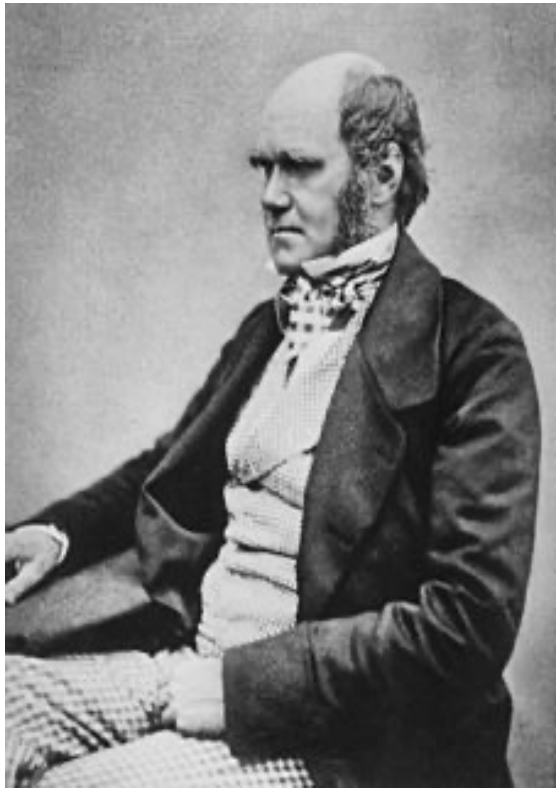
1. Inheritance of acquired characters (Lamarkism)
2. Theory of Pangenesis
3. Germ Plasm Theory
4. Blending inheritance

INHERITANCE OF ACQUIRED CHARACTERS

- **LAMARCK (1744-1829)** in 1809 proposed the phenomenon of **"inheritance of acquired characters"** among living organisms.
- But he failed to provide convincing evidences in support of his concepts.

Theory of Pangenesis

- **Proposed by Charles Darwin (1868)**
- According to him, **each part of the animal body produces many minute particles known as gemmules**, which are first collected in the blood and then concentrated in the reproductive organs.
- When the animal reproduces into new individual, these gemmules pass on to it and it has blending of both parents.



Charles Darwin (1809-1882)

Blending inheritance

✓ Individuals inherit a smooth blend of traits from their parents.

Eg. Darwin's pangenesis theory

Example: The height of a person, with one short parent and one tall parent, was thought to always be of some interim value between its two parents' heights.

Limitations:

- the potential for variation would tend to narrow, quite dramatically, with each generation

- It **failed to explain** how traits that seemingly disappeared for several generations often reasserted themselves down the line, unaltered.

Germ Plasm Theory

- **Proposed by August Weismann**: (1892)

- Inheritance only takes place by means of the germ cells—the gametes such as egg cells and sperm cells. Other cells of the body—somatic cells—do not function as agents of heredity.

August Weismann
(1834 –1914)
(German biologist)

Particulate inheritance

Particulate inheritance is a pattern of inheritance discovered by Mendelian genetics theorists, such as William Bateson, Ronald Fisher or Gregor Mendel himself, showing that **phenotypic traits** can be passed from generation to generation through "**discrete particles**" known as **genes**, which can keep their ability to be expressed while not always appearing in a descending generation

What is Genetics?

Ancient Greek "'genesis" meaning "origin"

Genetics is a discipline of biology, that deals with the science of genes, heredity, and variation in living organisms.

It deals with the following aspect of genes,

1. Molecular structure & function- **Molecular genetics**
2. Behaviour (Dominant or recessive)- **Behavioral genetics**
3. Pattern of Inheritance (Autosomal, sex-linked etc.) - **Mendelian genetics/Classical genetics**
4. Variation in the population – **Evolutionary genetics**

Wilhelm Johannsen (1857–1927)

Wilhelm Johannsen

Coined the terms

- **Gene -1909**
- **Genotype- 1903**
- **Phenotype - 1903**

What is genotype?

The **genotype** is the part of the **genetic** makeup of a **cell**, and therefore of any individual, which determines one of its characteristics

What is phenotype?

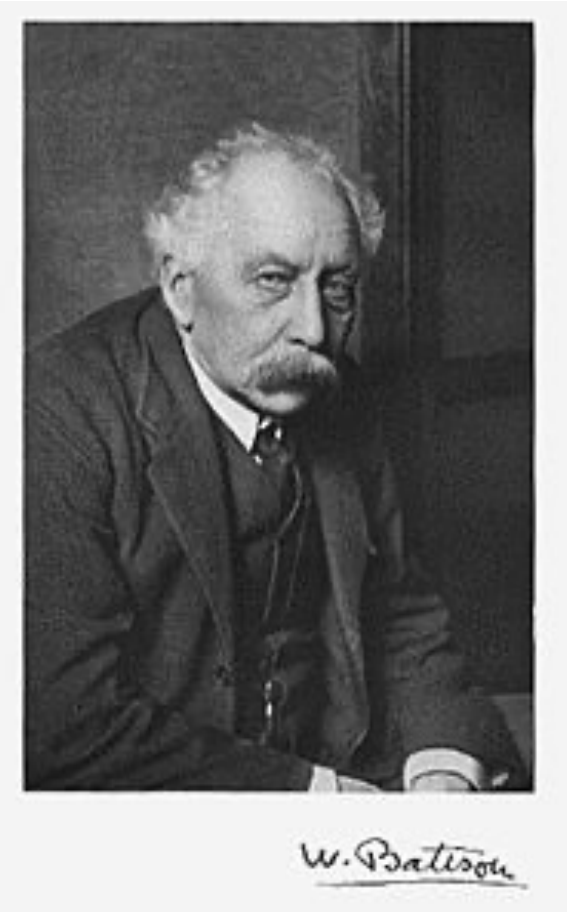
The **phenotype** of an organism is the composite of the organism's observable characteristics or traits.

The term covers the organism’s

- ✓ Morphology or physical form and structure
- ✓ Its developmental processes
- ✓ Its biochemical and physiological properties
- ✓ Its behavior or the products of behavior

William Bateson(1861 – 1926)

- ✓ **Bateson** first suggested using the word "**genetics**“ in 1903
- ✓ from the Greek **gennō** "to give birth" - To describe the study of inheritance and the science of variation



William Bateson

Bateson's contributions to Genetics…

- ✓ **Allele (Allelomorph):**

Bateson together with Edith Rebecca Saunders, in the early days of genetics, used the term **Allele** to describe variant forms of a gene detected as different phenotypes.

- ✓ Book (1894) – "*Materials for the Study of Variation*"

This one of the earliest formulations of the new approach to genetics.

Bateson's contributions to Genetics…

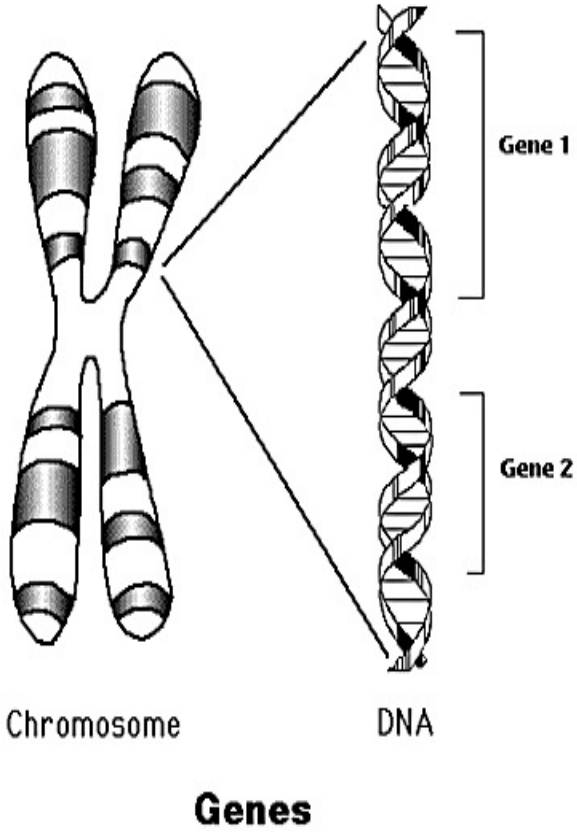
- ✓ Co-discovered genetic linkage along with Reginald Punnett and Edith Saunders
- ✓ Along with Punnett founded the "*Journal of Genetics"* in 1910

"

- ✓ Also coined the term " Epistasis" to describe the genetic interaction of two independent loci
- ✓ He founded The **Genetics Society** in 1919, one of the first **learned societies** dedicated to Genetics

Genetic Information

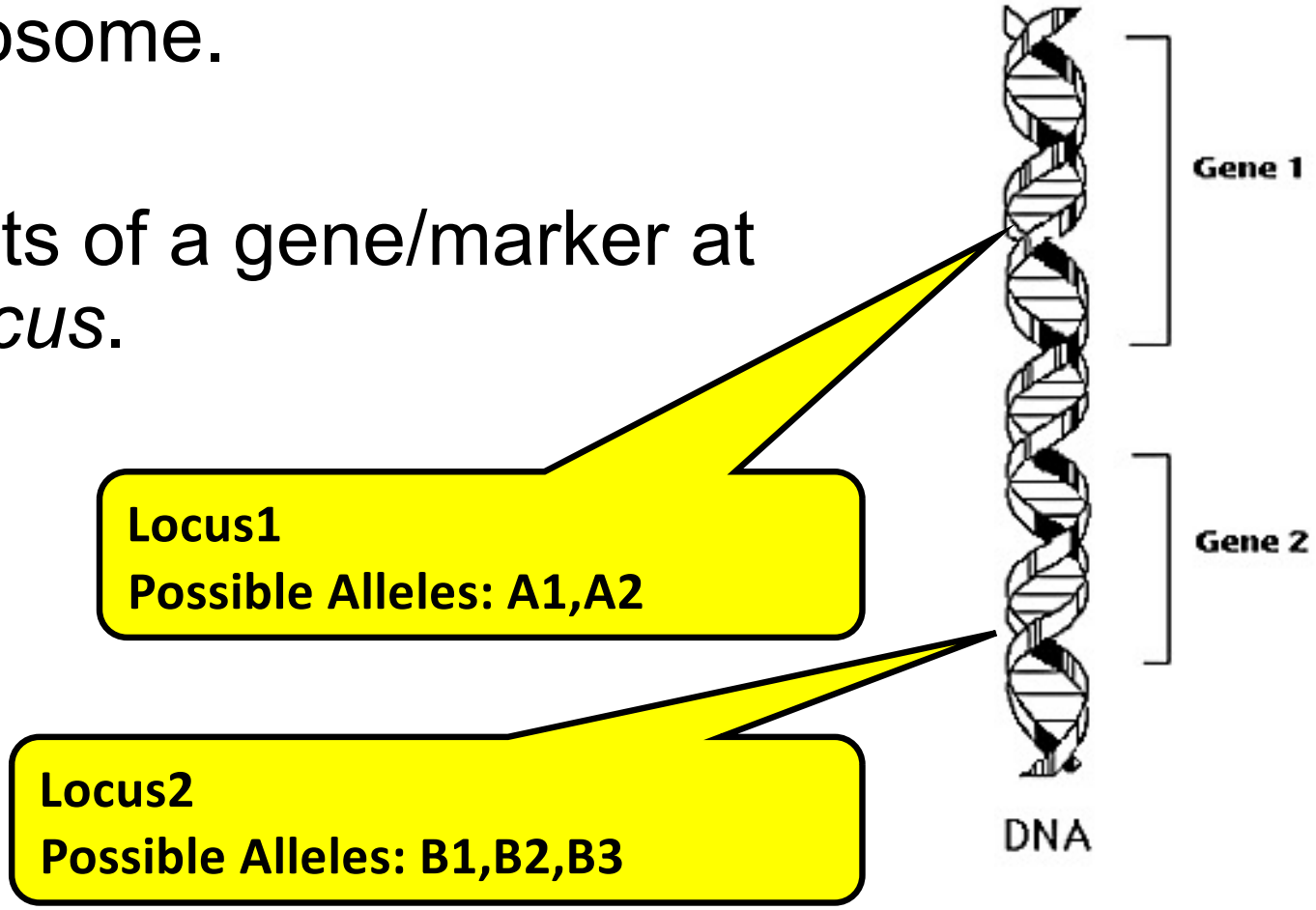
- **Genome** – the collection of genetic information.
- **Chromosomes** – storage units of genes.
- **Gene** – basic unit of genetic information. Genes determine the inherited characters.
- **DNA** - is a nucleic acid that contains the genetic instructions specifying the biological development of all cellular forms of life



http://www.accessexcellence.com/AB/GG/

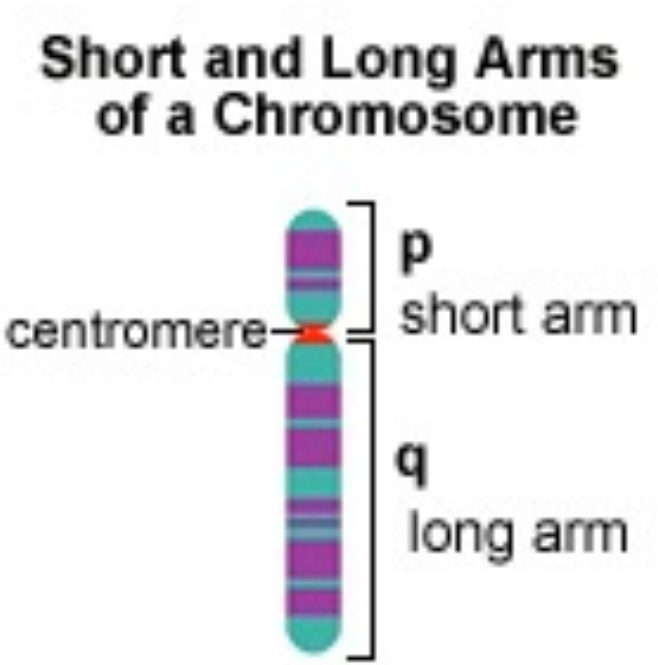
Chromosome Logical Structure

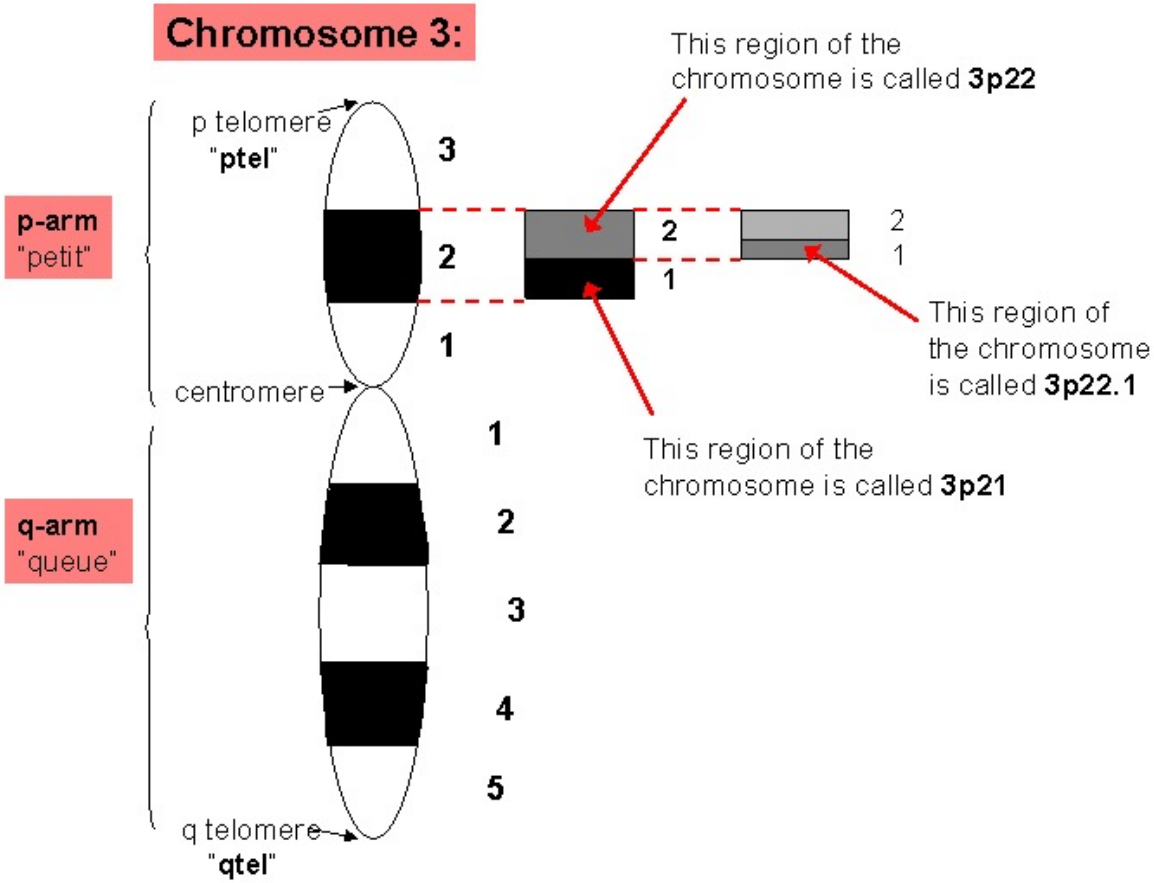
- **Locus** – location of a *gene/marker* on the chromosome.
- **Allele** –variants of a gene/marker at a particular *locus*.



What is a Locus?

A locus (plural loci) is the specific location of a gene, DNA sequence, or position on a chromosome

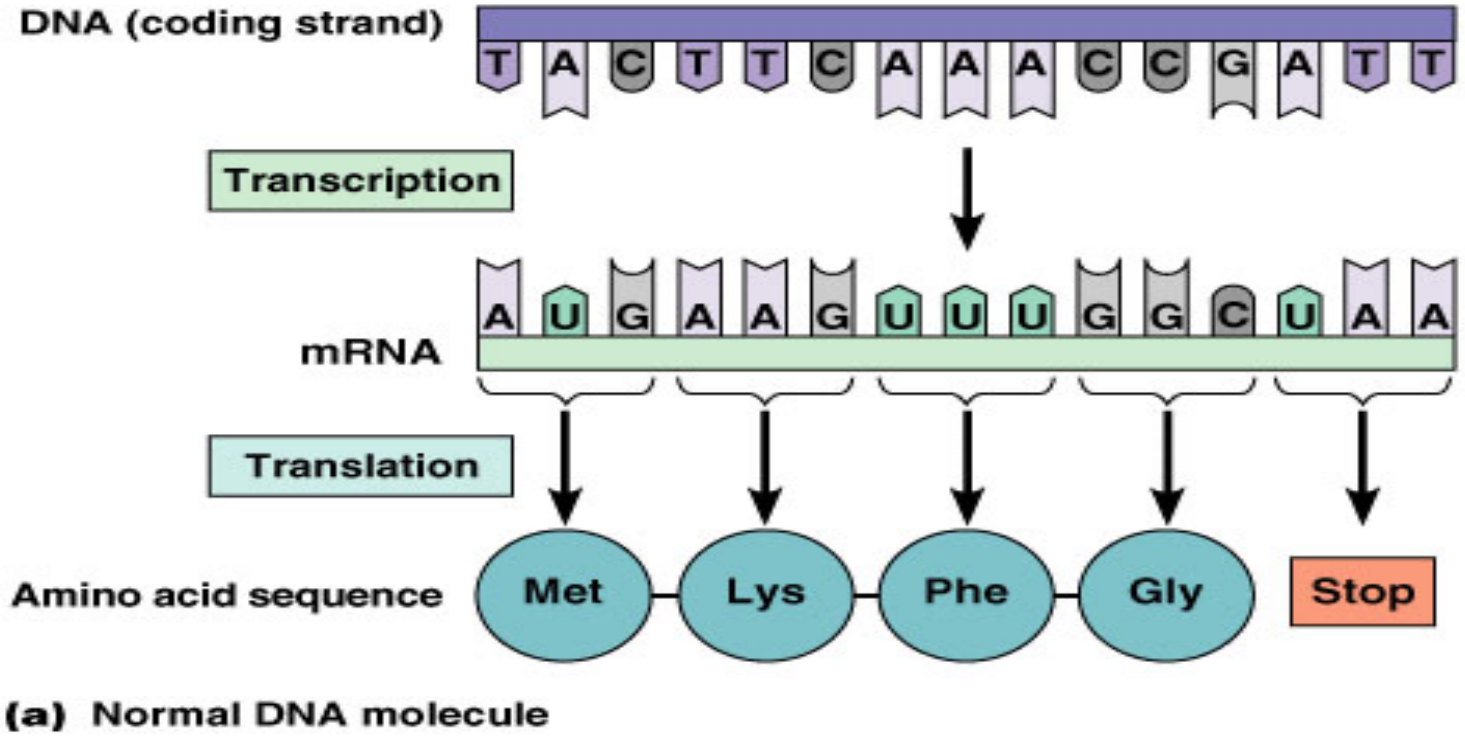




What is an Allele ?

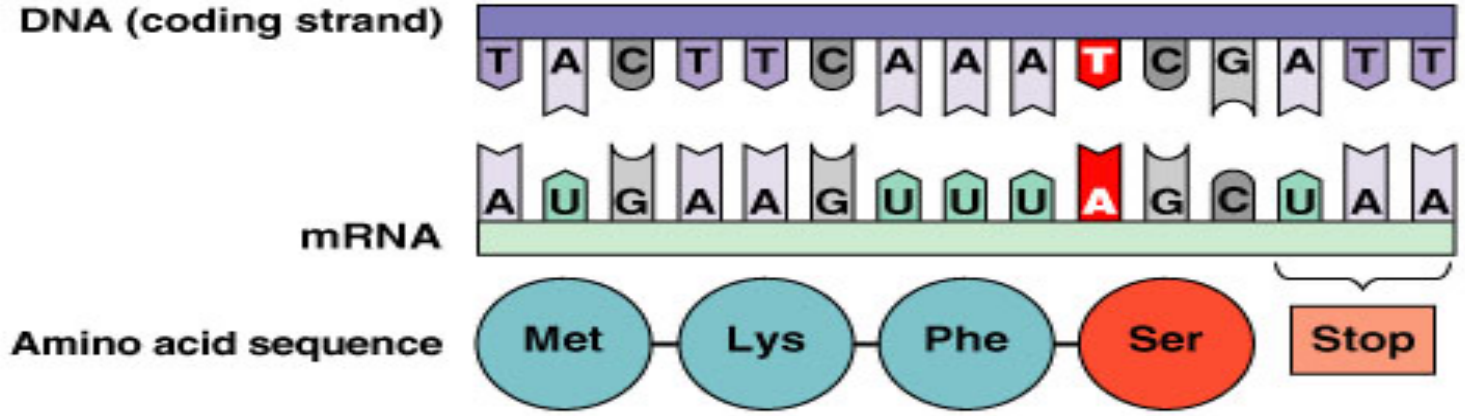
An allele is different forms of the DNA sequence of a particular gene (variants of a gene)

GENE



(a) Normal DNA molecule

Allele



(b) Missense mutation

Wild type vs Mutant

In genetics, the wild-type organisms serve as the original parent strain before a deliberate mutation is introduced (for research) so that geneticists can use them as reference to compare the naturally occurring genotypes and phenotypes of a given species against those of the **deliberately mutated counterparts**.

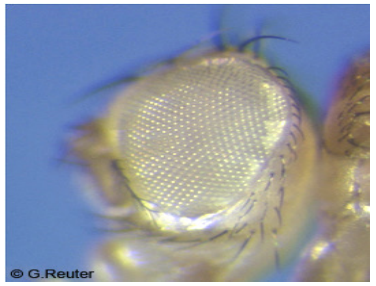
Wild type vs Mutant

- ✓ **Wild type** (or wildtype abbreviated WT) *refers to the phenotype of the typical form of a species as it occurs in nature*.

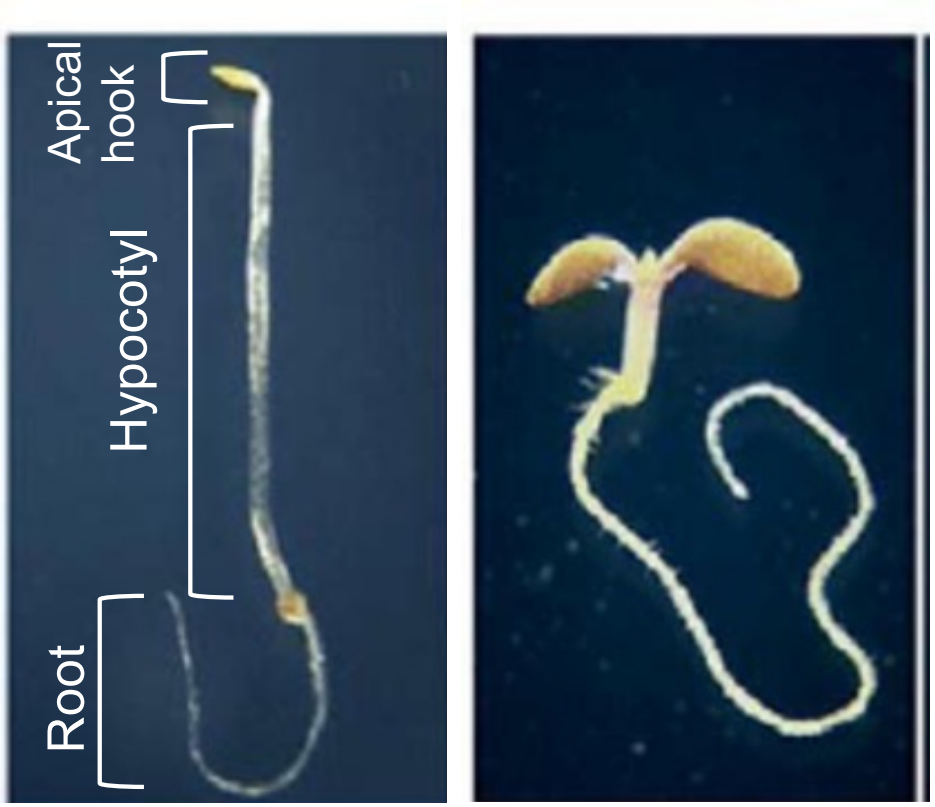
Large number in the population.

- ✓ A mutant is an individual, that exhibits a new character or trait not found in the wild type.

Less frequent in the population



Arabidopsis thaliana (Arabidopsis)



Wild-type *cop1* mutant

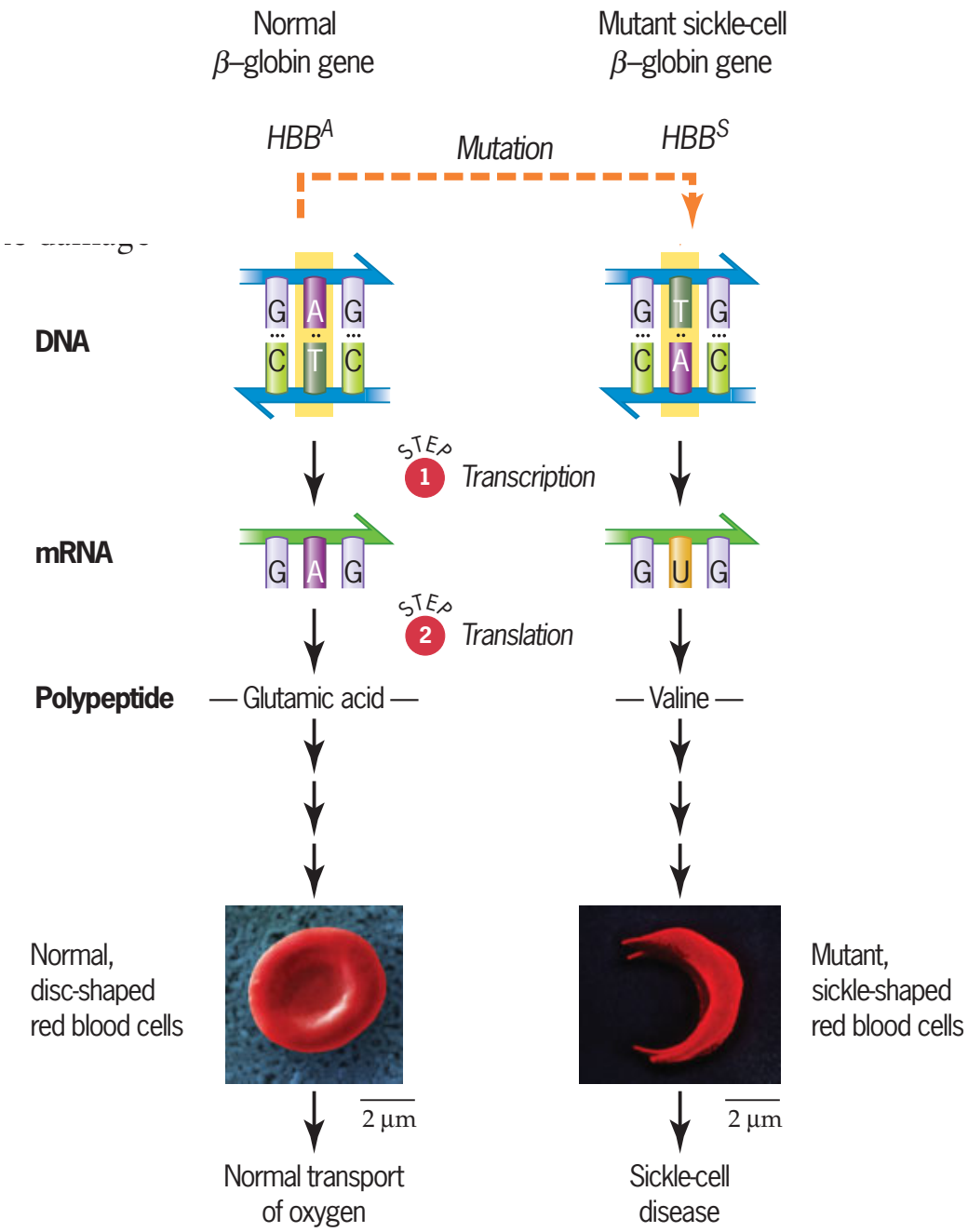
Dark grown seedlings

Wild-type *cop1* mutant

Dark grown seedlings

✓ ***cop1*** **mutant phenotype is due a point mutation in the *COP1* gene, *CONSTITUTIVE PHOTOMORPHOGENIC 1 (COP1)***

Wild-type vs mutant

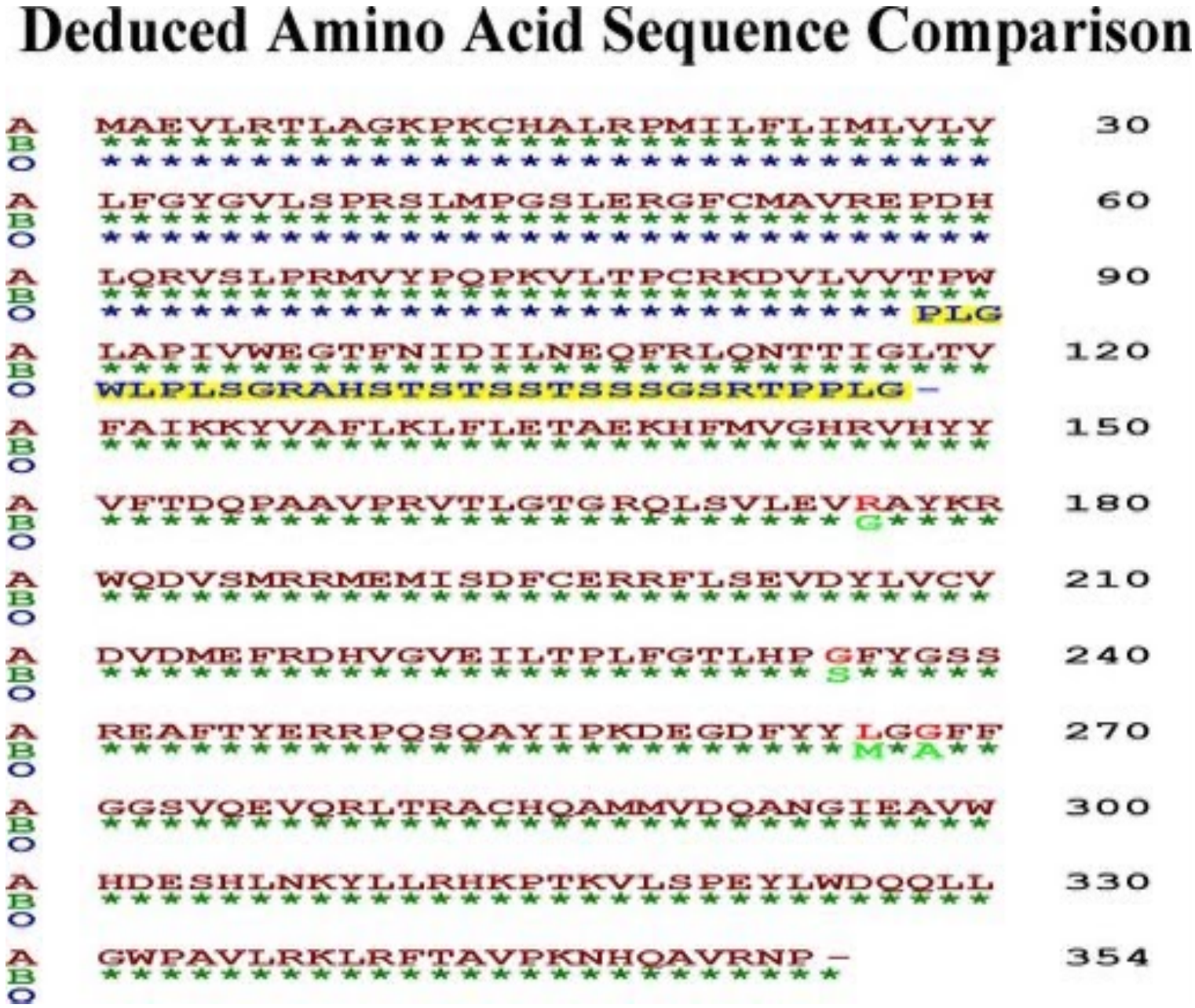


■ **FIGURE 1.9** The nature and consequence of a mutation in the gene for human β-globin. The mutant gene (*HBB*^{S} top right) responsible for sickle-cell disease resulted from a single base-pair substitution in the β-globin gene (*HBB*^{A} top left). Transcription and translation of the mutant gene produce a β-globin polypeptide containing the amino acid valine (center right) at the position where normal β-globin contains glutamic acid (center left). This single amino acid change results in the formation of sickle-shaped red blood cells (bottom right) rather than the normal disc-shaped cells (bottom left). The sickle-shaped cells cause a severe form of anemia.

Example of Alleles : ABO system

- ABO gene encodes an enzyme –*Glycosyl transferase*. (Chromosome 9)
- Modifies the oligosaccharide on cell surface glycoprotein
- *A* allele adds N-acetyl galactosamine
- *B* allele adds galactose
- *o* allele is deletion which lacks the glycosyl transferase activity.

ABO allele


Deduced Amino Acid Sequence Comparison
A MAEVLRTLAGKPKCHALRPMILFLIMLVLV 30
B ********************************
O ********************************
A LFGYGVLSPRSLMPGSLERGFCMAVREPDH 60
B ********************************
O ********************************
A LQRVSLPRMVYPQPKVLTPCRKDVLVVTPW 90
B ********************************
O ********************************PLG
A LAPIVWEGTFNIDILNEQFRLQNTTIGLTV 120
B ********************************
O WLPLSGRAHSTSTSSTSSSGSRTPPLG-
A FAIKKYVAFLKLFLETAEKHFMVGHRVHYY 150
B ********************************
O
A VFTDQPAAVPRVTLGTGRQLSVLEVRAYKR 180
B ********************************G****
O
A WQDVSMRRMEMISDFCERRFLSEVDYLVCV 210
B ********************************
O
A DVDMEFRDHVGVEILTPLFGTLHPGFYGSS 240
B ********************************S*****
O
A REAFTYERRPQSQAYIPKDEGDFYYLGGFF 270
B ********************************M*A**
O
A GGSVQEVQRLTRACHQAMMVDQANGIEAVW 300
B ********************************
O
A HDESHLNKYLLRHKPTKVLSPEYLWDQQLL 330
B ********************************
O
A GWPAVLRKLRFTAVPKNHQAVRNP- 354
B ***************************
O

Wildtype and mutant allele

The allele that encodes the phenotype most common in a particular natural population is known as the **wild type** allele.

It is often designated, in genetic shorthand, as "+/+" or WT

Any form of an allele **other than the wild type** is known as a **mutant** form of that allele.

Orange tiger

Wildtype (+/+)

White tiger

white tiger (-/-)

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Volume 23, Issue 11, p1031–1035, 3 June 2013

Report

Switch to Standard View

The Genetic Basis of White Tigers

Xiao Xu, Gui-Xin Dong, Xue-Song Hu, Lin Miao, Xue-Li Zhang, De-Lu Zhang, Han-Dong Yang, Tian-You Zhang, Zheng-Ting Zou, Ting-Ting Zhang, Yan Zhuang, Jong Bhak, Yun Sung Cho, Wen-Tao Dai, Tai-Jiao Jiang, Can Xie, Ruiqiang Li, Shu-Jin Luo

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DOI: http://dx.doi.org/10.1016/j.cub.2013.04.054

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Summary Full Text Images/Data References Related Articles Comments

Highlights

- Whole-genome sequencing enables mapping of the white tiger mutation
- A single amino acid change in transporter SLC45A2 causes the white tiger phenotype

- ✓ A single amino acid change in ***SLC45A2*** gene (it codes for transport protein) causes the white tiger phenotype
- ✓ The resultant single amino acid (A477V) introduces an **alanine** to **valine** substitution, which apparently block the transporter channel cavity and thus affect melanogenesis.
- ✓ The gene variant found in the white tiger primarily inhibits the synthesis of red and yellow pigments.

Symbols and Terminology

Wild type- *For a given pair of alternate trait that is more* ***frequent*** *in a population (+/+)*

Mutant*- Alternate form of trait* ***rare*** *in natural population.*

i) ***Dominant Allele****: Upper case letter (A)*

ii) ***Recessive Allele****: Lower case letter (a)*

Another example,

***COP1*: *CONSTITITIVE PHOTOMORPHOGENIC 1* (Gene)**

COP1: CONSTITITIVE PHOTOMORPHOGENIC 1 (protein)

cop1*: *mutant

***C*: Dominant allele**

***c*: Recessive allele**

***CC*: Homozygous dominant (+/+, Wild-type)**

***cc*: Homozygous Recessive (-/-, mutant)**

***Cc*: Heterozygous (+/-)**