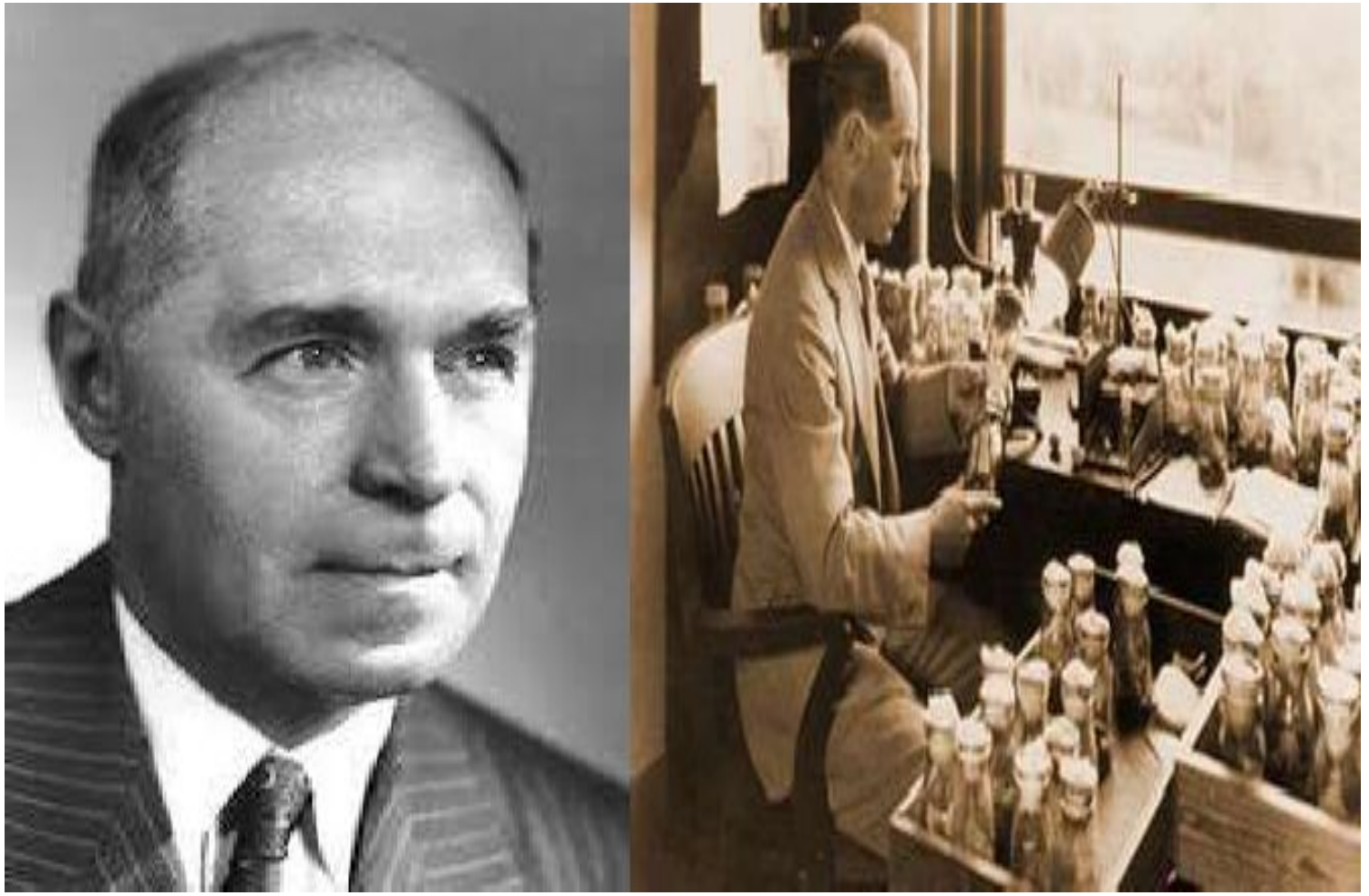
Medical Academy named after S.I.Georgievsky of Vernadsky

CRIMEA FEDERAL UNIVERSITY

- TOPIC – EVOLUTION
- SUBJECT – MEDICAL BIOLOGY

MUTATIONS AND ITS ROLE IN HUMAN POPULATION

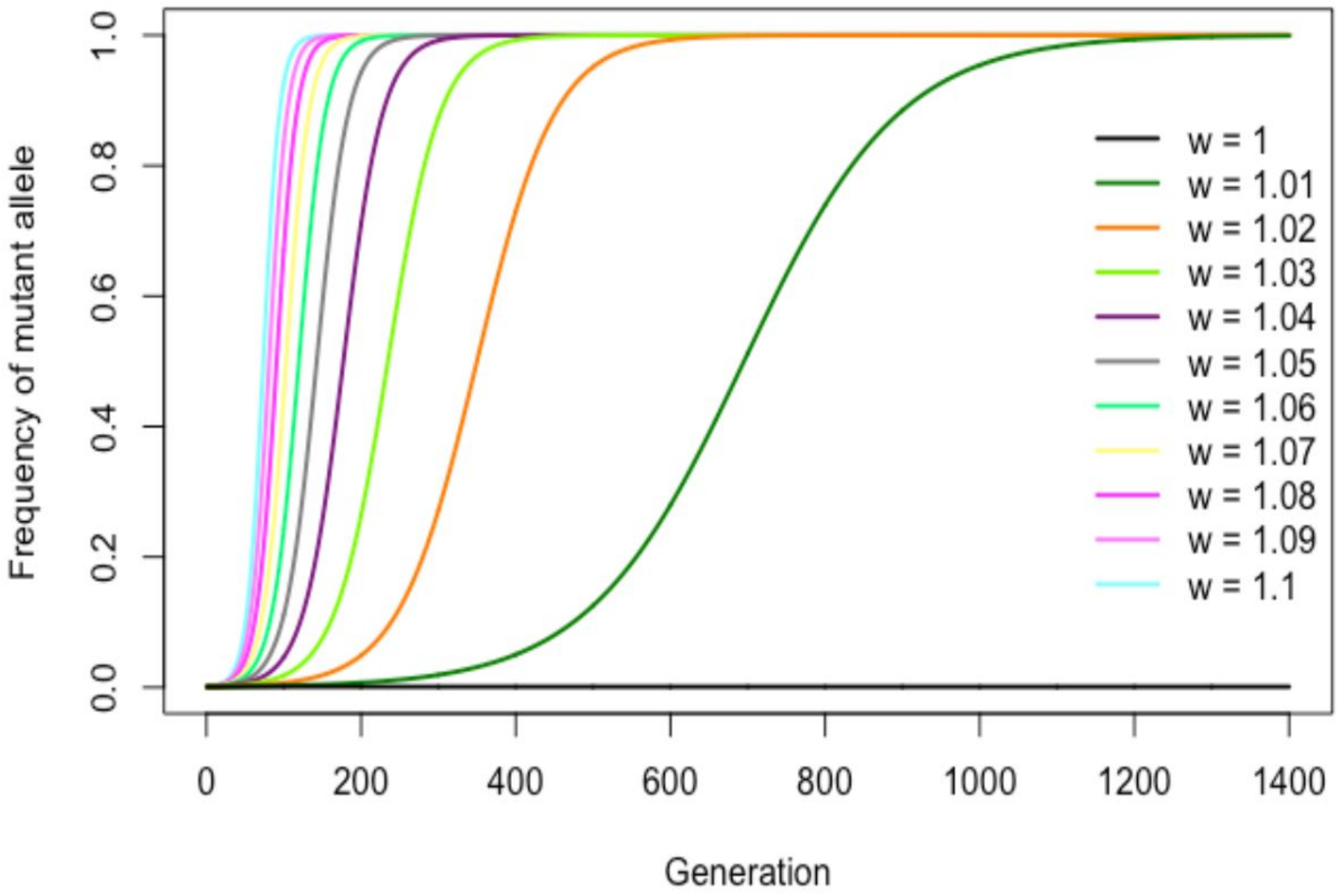
NAME – AMIT KUMAR
LA1-191 B



H. J. Muller, who first demonstrated the mutagenic effect of X-rays in 1927. Prof. Muller made many contributions to our understanding of basic genetics through his extensive research. He was awarded the Nobel Prize in 1949.

ABSTRACT

Spontaneous mutation in man was reviewed in this series almost a decade ago (Vogel and Rathenberg, 1975). These authors remarked that mutation rates in general, and human rates in particular, had not been the subject of the extensive, systematic study that might be expected from the importance of the subject. That statement is still true. As mentioned by Vogel and Rathenberg, estimates of human mutation rates depend on large epidemiologic studies of a type that were more popular in the 1940s and 1950s than since. As a result, the values given in still earlier reviews (Penrose, 1961; Crow, 1961) do not differ importantly from those of more recent reviews, including the present one.


Frequency of mutant allele
0.0
0.2
0.4
0.6
0.8
1.0
0
200
400
600
800
1000
1200
1400
Generation
w = 1
w = 1.01
w = 1.02
w = 1.03
w = 1.04
w = 1.05
w = 1.06
w = 1.07
w = 1.08
w = 1.09
w = 1.1

INTRODUCTION

- Mutation in a broad sense include all those heritable changes which alter the phenotype of an individual.

- Thus mutation can be defined as a sudden heritable change in the character or nucleotide sequence of an organism which is not due to either segregation or recombination.

- The term **mutation** was first used by **Hugo de Vries** to describe the sudden phenotypic changes which were heritable, while working with *Oenothera lamarckiana.*

- However the systematic studies on mutations were started in 1910 by **T.H. Morgan** who used *Drosophila melanogaster* for his studies.

- In 1927, **H.J. Muller** demonstrated for the first time the artificial induction of mutations by using x-rays in *Drosophila.*

Hugo De Vries, around 1920.

Photo courtesy of
Cold Spring Harbor Laboratory Archives.

INTRODUCTION

- Similarly in 1928, **L.J. Stadler** demonstrated an increase in the rate of mutations due to x-rays in barley and maize.

- Induction of mutations by chemicals in fungus *Aspergillus* was demonstrated by **R.A. Steinberg** in 1939.

- **C. Auerbach and J.N. Robson** in 1946 used chemicals to induce mutations in *Drosophila*.

- The first plant breeding programme using mutations (mutation breeding) was initiated in 1929 in Sweden, Germany and Russia.

- In India it was initiated in early **1930s**.

Terminology

- **Muton:** The smallest unit of gene capable of undergoing mutation and it is represented by a nucleotide.
- **Mutator gene:** A gene which causes another gene or genes to undergo spontaneous mutation.
- **Mutable genes:** Genes which show very high rates of mutation as compared to other genes.
- **Mutant:** An organism or cell showing a mutant phenotype due to mutant allele of a gene.
- **Mutagen:** A physical or chemical agent which induces mutation.
- **Hot spots:** Highly mutable sites with in a gene.
- **Gene mutations or point mutations:** The changes which alter the chemical structure of a gene at molecular level.

Classification of mutations:

1. **Based on direction of mutations :**
   a) **Forward mutation :** Any change from wild type allele to mutant allele.
   b) **Backward mutation or reverse mutation:** A change from mutant allele to wild type.
2. **Based on source / cause of mutations :**
   b) **Spontaneous mutation**: Mutation that occur naturally.
   c)**Induced mutation:** Mutation that originates in response to mutagenic treatment.
3. **Based on tissue of origin :**
   b) **Somatic mutation:** A mutation in somatic tissue.
   c) **Germinal mutation:** A mutation in germline cells or in reproductive tissues.

Classification of mutations

4.Based on trait or character effected :

a)Morphological mutation: A mutation that alters the morphological features of an individual

b) Biochemical mutation: A mutation that alters the biochemical function of an individual.

5.Based on visibility or quantum of morphological effect produced :

c)Macro-mutations: Produce a distinct morphological change in phenotype (which can be detected easily with out any confusion due to environmental effects) Eg : colour of flowers, height of plant etc.

d) Micro-mutations: Mutations with invisible phenotypic changes, (which can be easily confused with effects produced due to environment).

6.Based on the site of mutation or on cytological basis :

e)Chromosomal mutations: Mutations associated with detectable changes in either chromosome number or structure.

f) Gene or point mutations: Mutations produced by alterations in base sequences of concerned genes.

c)Cytoplasmic mutations: Mutations associated with the changes in chloroplast DNA (cpDNA) and mitochondrial DNA (mtDNA).

Characteristic features of mutations:

1. Mutations are mostly recessive and very rarely dominant.
2. Most mutations have harmful effects and very few (less than 0.1 %) are beneficial.
3. They may be due to a change in a gene, a group of genes or in entire chromosome.
4. If gene mutations are not lethal, the mutant individuals may survive.
5. If mutation occur at both loci simultaneously, the mutants can be identified in M1 generation. However, if it is restricted to one locus only, (dominant to recessive) the effect can be seen only in M2 generation.

6. Macro-mutations are visible and can be easily identified, while micro - mutations
   can not be seen with naked eye and need special statistical tests.
7. Many of the mutants show sterility.
8. Most mutants are of negative selection value.
9. Mutation for altogether new character generally does not occur.
10. Mutations are random i.e. they can occur in any tissue or cell of an organism.
11. Mutations can be sectorial. mutated sector show mutant characters.
12. Mutations are recurrent i.e. the same mutation may occur again and again.
13. Induced mutations commonly show pleiotropy often due mutation in closely linked genes.

Spontaneous mutations:

- Spontaneous mutations occur naturally without any apparent cause.
- There are two possible sources of origin of these mutations.
- ✔ 1. Due to error during DNA replication.
- ✔ 2. Due to mutagenic effect of natural environment Eg : UV rays from sunlight
- ✔ Mutations can affect any structure or process; hence the range of mutational possibility extends over the entire gamut of morphology, physiology, biochemistry, and behavior. The magnitude or severity of effect ranges from trivial to catastrophic. There are two obvious limitations to the observation of mutant effects. First, the mutant phenotype may be below the threshold of detection. Sometimes this difficulty can be circumvented by technical improvements; in some cases this is simply a more refined phenotypic measurement. In other cases something closer

Induced mutations:

- **Induced mutations:** Mutations can be induced artificially through treatment with either physical or chemical mutagens.
- The rate of induced mutations is very high.
- The induced mutations did not differ from spontaneous mutations in expression.

Artificial induction of mutations

- **Mutations can be induced artificially using some agents-**

1. Physical mutagens or radiations
2. Chemical mutagens

Physical mutagens

a) **Ionizing radiations:** They work through the release of ions. They have deep penetrating capacity. Eg : x-rays, g-rays, a -particles etc.

b) **Non-ionizing radiations :** They function through excitation and have a very low penetrating capacity. They are used for studies on bacteria and viruses. Eg : UV rays.

- **Sources of physical mutagens:**

- Gamma garden
- Gamma green house
- Vertical gamma irradiation facility
- Horizontal gamma irradiation facility
- X-ray machine
- Isotopes
- Small portable irradiators, accelerators and cyclotrons
- Nuclear reactors

Chemical mutagens

a) Alkylating agents:

- ✔ This is the most powerful group of mutagens.
- ✔ These are the chemicals which are mainly used to induce mutations in cultivated plants.
- ✔ They induce mutations especially transitions and transversions by adding an alkyl group (either ethyl or methyl) at various positions in DNA.
- ✔ Alkylation produces mutation by changing hydrogen bonding in various ways.
- ✔ Eg: Dimethyl sulphonate (DMS), Ethyl methane sulphonate (EMS), Nitrosomethyl Urea (NMU), Nitrosoethyl Urea (NEU), Methyl methane sulphonate (MMS).

b) Base analogues:

- ✔ These are chemicals which are very similar to DNA bases, such chemicals are sometimes incorporated in DNA in place of normal bases during replication.
- ✔ Thus they can cause mutation by wrong base pairing.
- ✔ An incorrect base pairing results in transitions or transversions after DNA replication.
- ✔ Eg: 5– bromouracil, 3-bromodeoxy uridine, 2 -amino purine.

Chemical mutagens cont...

c) Antibiotics:

- A number of antibiotics like mitomycin and streptomycin have been found to possess chromosome breaking properties.
- Their usefulness for practical purposes is very limited.

d) Acridine dyes:

- These are positively charged and they insert themselves between two base pairs of DNA.
- This is known as intercalation. Replication of intercalated DNA molecules results in addition or deletion of one or few base pairs which produces frame shift mutations.
- Acridine dyes Eg: proflavin, acriflavin, acridine orange, etc. are very effective mutagens.

e) Miscellaneous:

- Hydoxyl amine produce chromosomal aberrations.
- Nitrous acid (deaminating agent) has strong mutagenic activity in a variety of viruses and micro organisms.
- But not useful in higher plants.

Molecular basis of mutations

- The term mutation is presently used to cover only those changes which alter the chemical structure of the gene at molecular level.
- Such changes are commonly referred to as "point mutations".
- Point mutations involve a change in
- The base sequence of a gene which results in the production of a mutant phenotype.
- Point mutations can be subdivided into the following three classes on the basis of molecular change associated with them.

✔ 1. Base substitution
✔ 2. Base deletion
✔ 3. Base addition


Thank you