# GEN PHILIC

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Genetic Variations | Evolution



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## Change is the Only Constant

*Insight into evolution and genetic variations*

"Nothing in biology makes sense except in the light of evolution"

~ Theodosius Dobzhansky

I'm sure when some of you think of the word 'evolution', you associate it with the phrase 'humans evolved from monkeys'. Well, that is an extremely vague understanding of the concept. Let's try and delve a bit more into the depth. According to John Endler, a noted evolutionary biologist, 'Evolution may be defined as any net directional change or any cumulative change in the characteristics of organisms or populations over many generations'. It explicitly includes the origin as well as the spread of alleles, variants, trait values, or character states and it is driven by natural selection, mutation, genetic drift and gene flow.

In simple terms, evolution is the change in the gene frequencies/allele frequencies from one generation to another. These traits (shown by expression of specific genes) are passed on to the offsprings via the process of reproduction. And so, mutations in these genes can produce new or altered traits, resulting in heritable differences (genetic variation) between organisms. New traits can also be derived from transfer of genes between populations, as in migration, or between species, in horizontal gene transfer.

### ➢ Darwin's theory or 'Darwinism'

The main concept of Darwinism is Natural Selection. Nature preferably selects mutations that are heritable and which essentially make survival easier so that individuals (generally in a population) possessing these variations are able to reproduce and give birth to more and more number of progeny. This is known as natural selection. It is evident that evolution and natural selection go hand in hand. If you think of evolution as a vehicle then natural selection is a fuel to that vehicle. Wondering about the destination? It is adaptation to the surroundings.

The theory of evolution by natural selection was proposed roughly simultaneously by both Charles Darwin and Alfred Russel Wallace, and set out in detail in Darwin's 1859 book 'On the Origin of Species'.

Some key characteristics of his theory include:

- All successful organisms have a comparatively high Biotic potential or reproductive rate, which means these organisms produce a large number of offsprings that can probably survive. Out of all the offsprings, only some individuals survive and reach adulthood, and they reproduce at different rates. This phenomenon is essentially called 'Differential Reproduction'.
- Only those organisms will survive which are the fastest and hence there is a 'Struggle for existence'. This concept was asserted by Darwin as 'Natural selection'.

### Interesting facts:

1. Darwin did not come up with the phrase "survival of the fittest" to summarise his theory. Rather, the philosopher Herbert Spencer coined the phrase.

2. We didn't evolve from apes. Contrary to the popularised notion of mankind 'arising' from apes, modern humans – Homo sapiens – did not evolve directly from the apes alive today, but rather we share a common ancestor. Our evolutionary paths diverged from those of chimpanzees and gorillas about six million years ago. Though we do share over 90% of our DNA with them, apes are distant cousins, not great-great-great (etc.) grandparents.

3. Lip twitching when angry is an evolutionary leftover. It is the first part of baring teeth at an intruder and can also be seen in wolves, bears and chimpanzees.

4. There are more than 2 million SNPs in human genome!

5. DNA chip technology (DNA microarray technology) is a revolutionary new tool designed for identifying mutations in certain genes or survey expression of tens and thousands of genes in a single experiment.


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**So evolution can be called as a 'change' in the genetic composition of a population which is brought about by natural selection which in turn acts upon the variability in population.**

In the 1930s, Darwinian natural selection was combined with Mendelian inheritance to form the modern evolutionary synthesis, in which the connection between the units of evolution (genes) and the mechanism of evolution (natural selection) was made.

➢ **Genetic Variation**

We know that 99.9% of everyone's genome is similar. Then what makes all of us so astonishingly different from each other? Its all by the courtesy of genetic variations. Genetic variations are differences or diversity in gene frequencies which make individuals to look different from one another.

**Polymorphism** is variation at genetic level. It is important to understand that allelic sequence variation has been traditionally described as DNA polymorphism if more than one variant (allele) at a locus occurs in the human population with a frequency greater than 0.01. And similarly, if in a population, an inheritable mutation is observed at high frequency, it is conveniently referred to as DNA polymorphism. Moreover, mutations, specifically in the non-coding DNA sequences keep on accumulating through generations and therefore form one of the basis of variability/polymorphism.

Almost 90% of the human genome variation fall in the category of 'Single nucleotide polymorphisms' (a type of DNA Polymorphism) or SNPs. SNPs are variations in just one nucleotide or base in the DNA (nucleotides or bases are building blocks of DNA). For instance, only a 'T' (thymine) might get replaced with a 'G' (guanine), a 'C' (cytosine) can be replaced with an 'A' (adenine) or any such replacement. SNPs (pronounced 'snips') generally occur throughout a person's DNA, once in every 1000 nucleotides on an average.

Apart from SNPs, polymorphism can exist in the form of large-scale variations too. This means that there might be hundreds and thousands of base pairs of DNA that is different in different people, and not only differing at a single nucleotide/base. Although, mutations are considered to be the ultimate cause of these genetic variations, mechanisms like genetic drift contribute too. Generally, there are 3 main causes of Genetic variations:

1) **Mutations** – Changes in a DNA sequence which may result from errors in DNA replication during cell division. Mutations include point mutations (replacement of a base with another), frameshift mutations (these mutations shifts the way the sequence is read). Frameshift mutations occur due to certain insertions and deletions (of base pairs) in a particular sequence.

2) **Recombination** – The crossing over during meiosis in sexual reproduction gives rise to new combinations of characters/traits which the result into variations.

3) **Intermingling of two widely separated populations** — Every population possesses a unique set of traits from years together. So mating between two widely distant populations (which have different geographic origins) would necessarily result into generation of new traits (due to crossing-over events i.e. recombination). Accumulation of these new traits will eventually give rise to variations in the population.

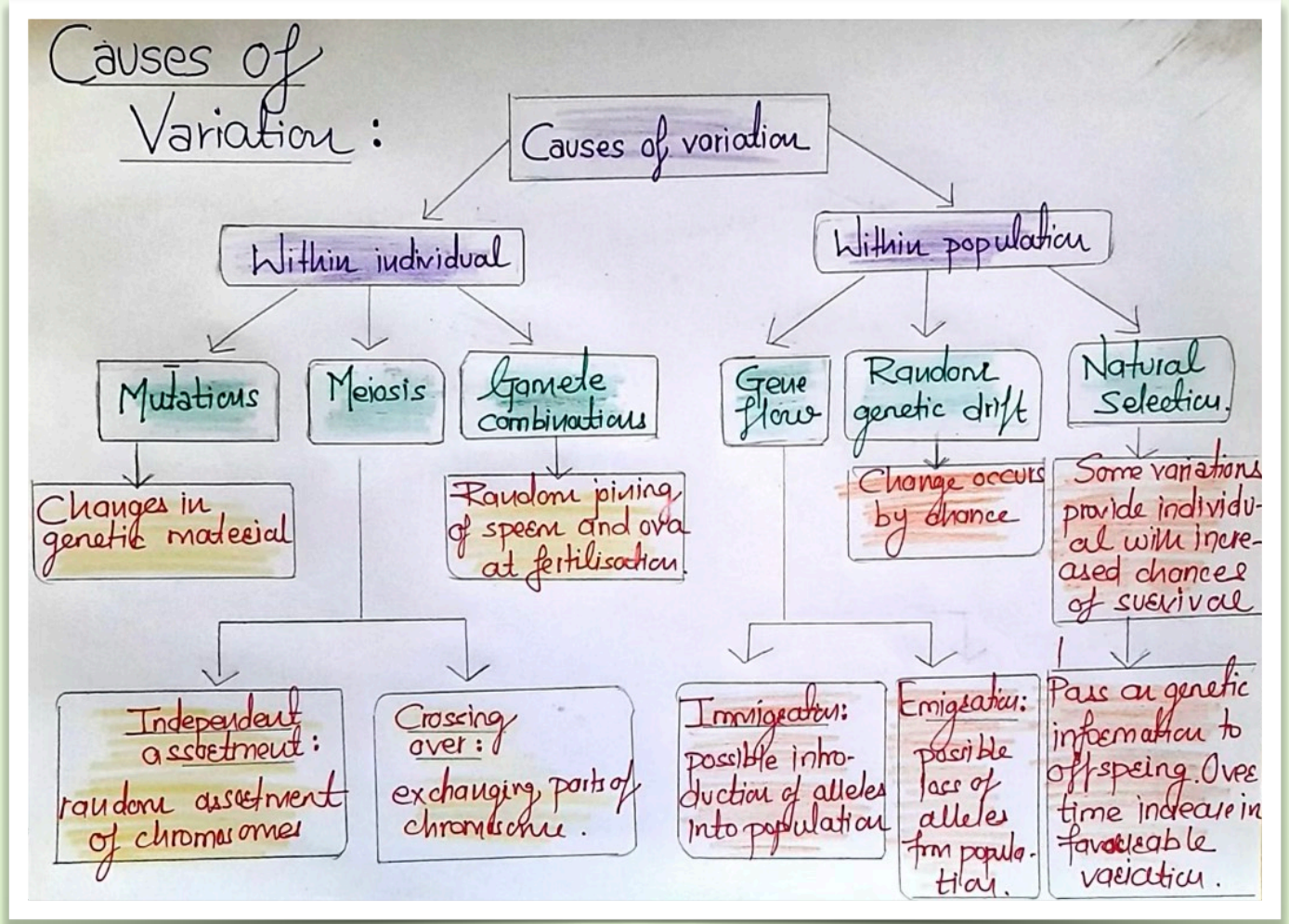


Illustration 1 :

Mutations and variations are thought to be interlinked in many ways. Nevertheless, there are some key differences between mutations and variations. Variations are small and directional and are generally incapable of bringing about a large sudden change, in short, they can bring the change only when they accumulate. Whereas, mutations on the other hand, are large, directionless and can induce a sudden change.

➢ **Are variations good or bad?**

Some variations can modify the amino acid sequence of the resulting protein but will produce no significant change in its function. Another variation (for example, a silent mutation) would not even change the sequence of amino acids. Furthermore, since coding sequences consist of only a small percentage in the genome (sequences that are ultimately translated into protein), the differences or variations that occur in the vast majority of the DNA have no impact.

Some variations are seen to be associated with diseases. The classic example is of the single-gene disorder Sickle cell anaemia (in which a point mutation leads to the replacement of the amino acid Glutamate by Valine in the polypeptide sequence). The more common diseases would result from the interaction of multiple genes and environmental variables. Such diseases are termed polygenic and multifactorial. Some genetic variation, however, can be positive, providing an advantage in changing environments. For example, people who are heterozygous for sickle cell anaemia are provided a selective advantage in areas where malaria is endemic, as they are less susceptible to this disease.

➢ **How is the understanding of human genetic variation affecting medicine?**

The presence of particular gene variants in different individuals is drastically changing the way drugs are prescribed and developed.

**Pharmacogenomics** is a rapidly growing and developing field. The primary focus of pharmacogenetics is on crucial genetic differences that cause drugs to work well in some individuals and not so well, or with dangerous adverse effects, in others. For example, in Alzheimer disease, the consequence of three genetic variants of the ApoE (Apolipoprotein E) gene a person carries will decide how differently the person will respond to a specific drug as compared to others.

Eventually, in the future, genetic tests would be used to match drugs to an individual patient's body chemistry and gene behaviour, so as to prescribe the safest and most effective drugs and dosages.

The overall understanding of human genetic variations, its phylogeny, etc has managed to throw light on the importance of mutations in disease biology and medicine. Moreover, the genetic and environmental bases for multi-factorial diseases will lead to the introduction and development of novel interventions that likely will have a significant effect on the practice of medicine in the next century.

*Article by: Sanskruti Deshmukh*
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*And (along with illustrations) Aqsareha Mujawar*
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# Nemo- Our founding father?

## *Anatomical clues of evolution from fish*

Often we've heard apes are our cousins. What if I tell you, we evolved from fish? Michael Phelps? Perhaps. Me? NO! Every part of the whole that we call our "body" is a version of what's seen in fish.

Human faces, though varied, have similarities; two eyes, nose, lips, philtrum. Philtrum is the little groove on the top lip beneath the nose which we see everyday and forget. That is a bridge to our fishy past.

A growing human embryo has striking similarity to other mammals, birds, amphibians- all of which evolved from fish. Your eyes, as in a fish, start out at sides of your head! The top lip, jaw and palate started their journey of development as gill-like structures on your neck. The mid lip, nostrils traveled down from the top of your head. All of this, yet there is no scar in sight; the fusion of tissue and muscle is flawless there. However, a tiny remnant and evidence of all this rearrangement is captured at the middle of your top lip - your philtrum.

We're aware of the fact that the human brain constitutes a forebrain, midbrain and hindbrain that flows into the spinal cord. Despite being very different in structure and form this fundamental architectural similarity is seen in sharks!

Next time you get the hiccups that just won't go away, blame your fish ancestors. A hiccup is caused by a spasm of the diaphragm followed by an involuntary gulp.

In fish the nerves that activate breathing have a short journey: from the brain stem ➡️ throat ➡️ gills. In humans, our brain stem has to send messages to throat, chest then diaphragm. This complex arrangement may at times cause the nerves to spasm, initiating hiccups.

Ancient tadpoles used this to guide air to the lungs particularly, as the passage closed immediately while gulping water, which is then further directed to the gills, thus maintaining the characteristic feature of an amphibian.

For humans apart from being a tiny inconvenience it provides a crucial evidence for our inner fish.

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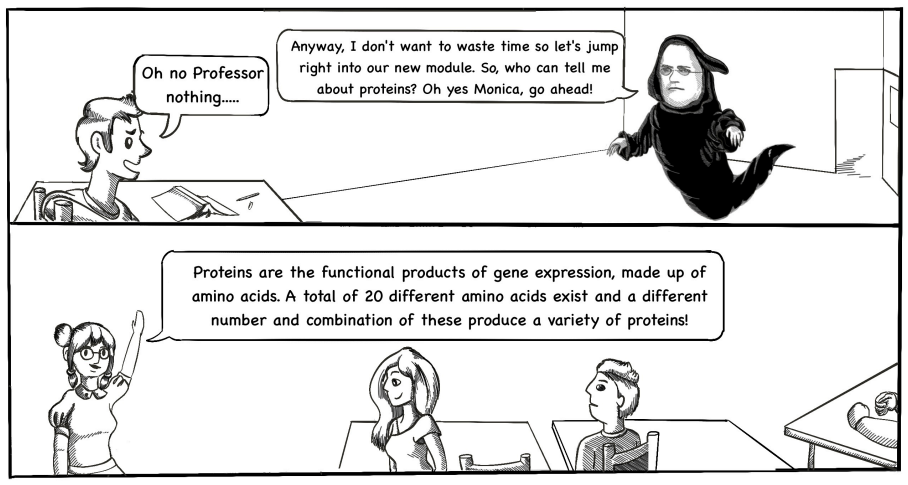
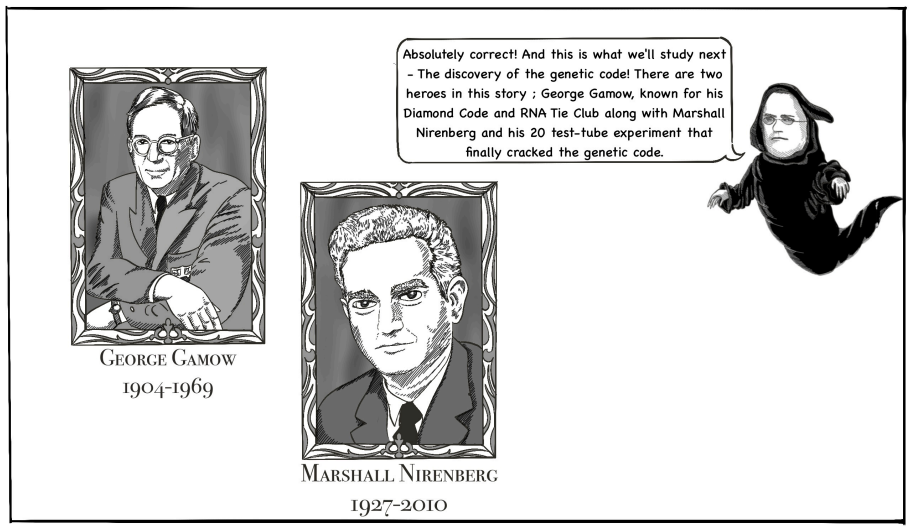
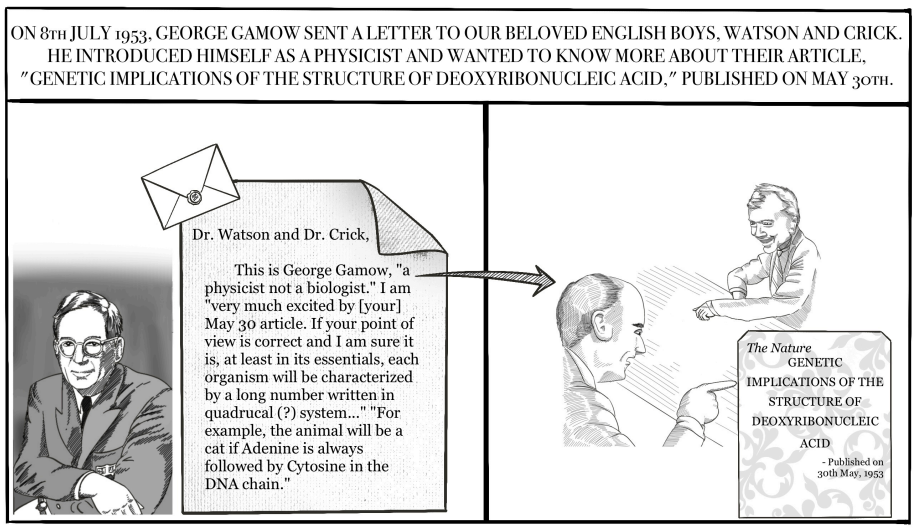
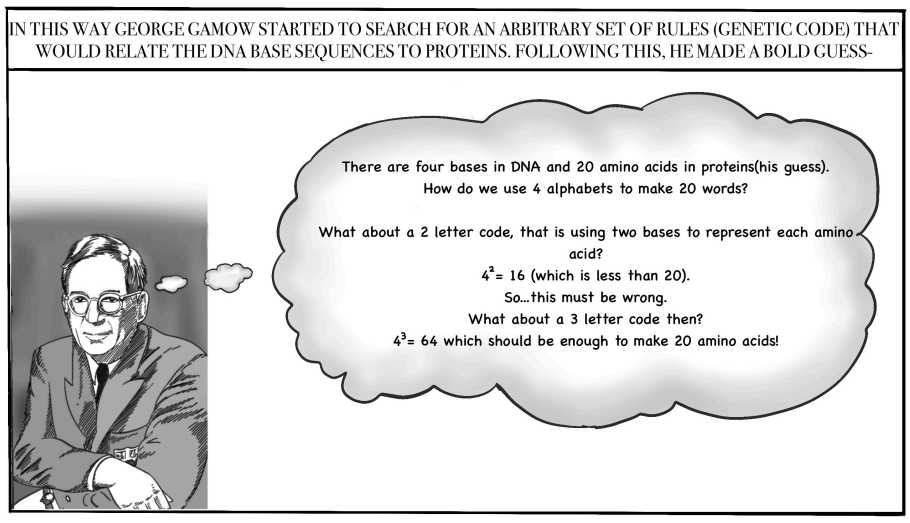
# Back to the Basics with Friendly Ghost Grandpa Mendel!

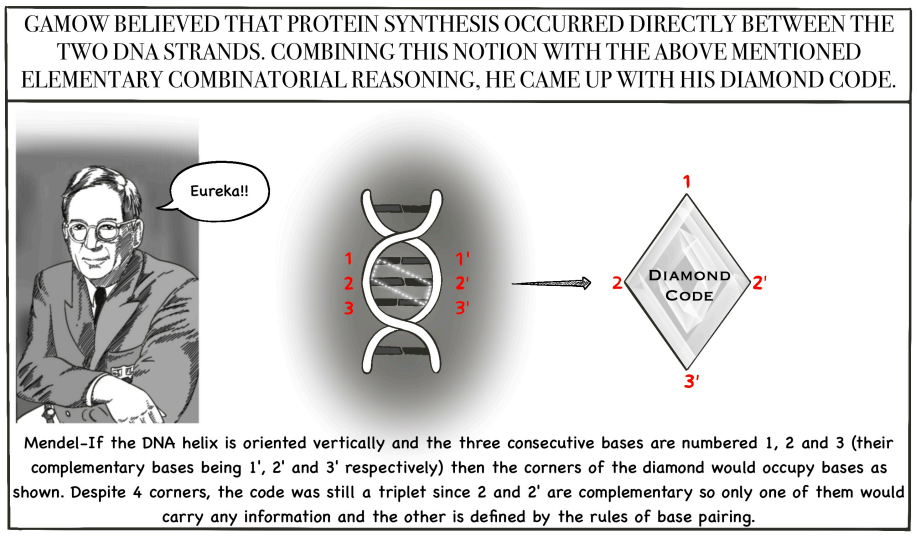
You know the legendary Gregor Mendel. You might not know the legends in the race to find messengers of life! Come, discover the story with Mendel himself, and see where the journey takes you!
(Note : Read left to right)





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# The Race to be the Smartest Animal

## *Genetic Evolution of the Human Brain*

One of the major characteristics of human evolution is the rapid increase in brain size and the complexity which has made our species so successful and distinctive. Humans have the largest brains in proportion to their body when compared with any living creature and also the most sophisticated. The genetic changes that underlies the human brain evolution and has made it the way it is today spans a wide range from single nucleotide substitutions to large scale structural alterations of the genome.

One of the major aspects of evolution of the human brain is its advanced cognitive capacity which has made humans capable of tool use, language, science and art. The volume of the human brain has tripled since the divergence from chimpanzees. This has led to changes in relative proportions of the areas of the brain. For example, the cerebral cortex has become more pronounced with the pre-frontal cortex expanding in

size, an area which has a crucial role in regulating social behaviour. Another prominent change is in the wiring that affects how brain cells communicate with each other and the rest of the body.

An important human gene SRGAP2 in Chromosome 1 has provided evidence for molecular mechanisms that links to its role in the evolution and development of the human brain. Humans have at least three similar copies of the SRGAP2 gene whereas non-human primates only have one and this gene duplicated in the human lineage about 3.4 million years ago. This gene played a major role in expansion of the cortex leading to human brain specialisations like development of language, social cognition and problem solving. It has also played an important role in the development of dendritic spines; whose function is to transmit nerve impulses. It helps in the maturation of dendritic spines which has led to plasticity i.e. the ability to alter neural connections in response to new experiences in humans.

The suspected gene that drove the growth of the human brain and increased its size is called the NOTCH 2NL genes. These genes are only present in humans today. Evidence of this gene has been found from the extinct cousins of the Homo sapiens, in the DNA of the Neanderthals but not in chimpanzees. These genes basically control the growth rate and differentiation of the brain stem cells causing the growth of more neurons and brain tissue which has led to increase in the size of the brain in modern humans.

Language is probably one of the key characteristics that distinguishes humans from other animals. A great amount of information about the evolution of language has been unveiled from the study of the FOXP2 gene, also termed as the master gene for language, mutations in this gene interfere with the part of the brain responsible for language development. One of the key roles of this gene is in the growth and connections of nerve cells during learning and development. It also regulates the brain's ability to learn sequences of movements which in humans has translated into complex muscle movements, needed to understand and produce the sounds for speech.

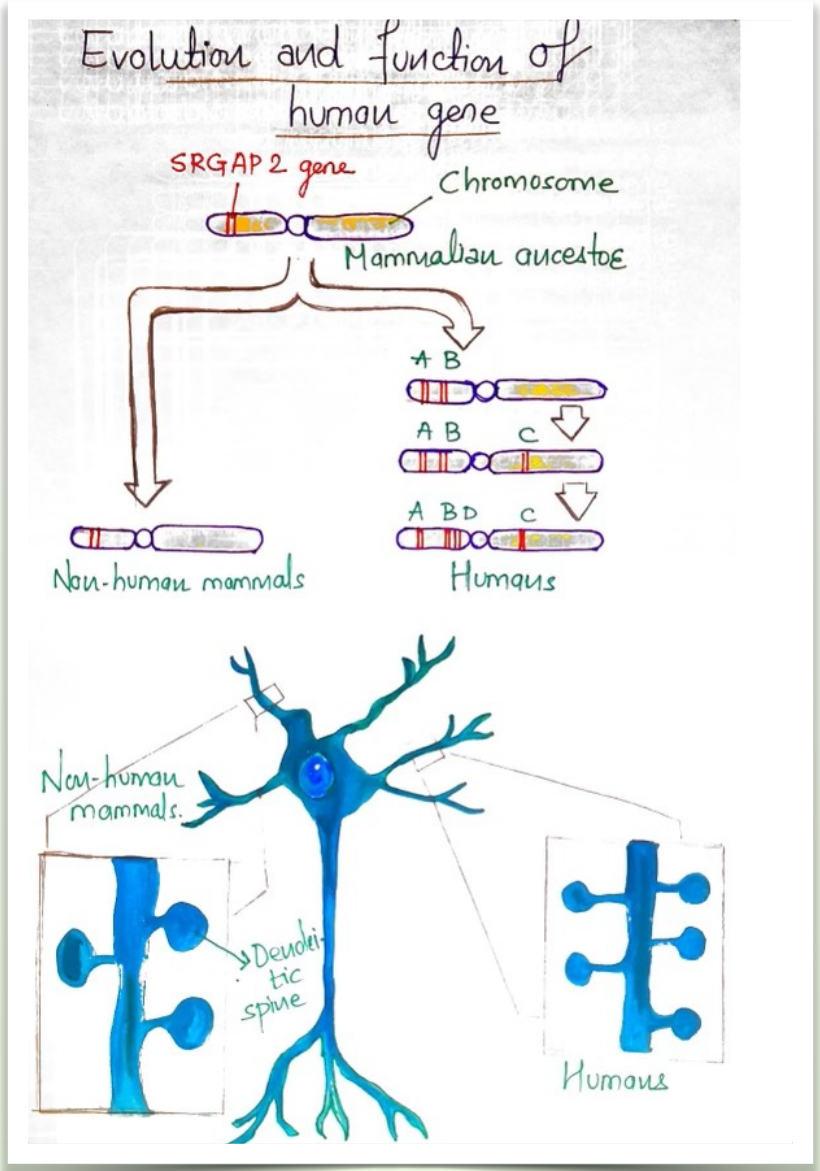


Illustration 2:

*Illustration by : Aqsareha Mujawar*
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One of the primary reasons why the evolution of the human brain is being studied so extensively since the past few years is because researchers hope to identify the biological basis of distinct behaviours that set humans apart from other animals. Also, there is a notion that the human brain is 'superior' to the brains of the other less-evolved groups. The human brain has also undergone a lot of adaptive changes over a period of at least a few million years, the difference being that, these changes are more pronounced and effective than of other non-human primates.

In the recent years, comparative genomics has proved to be the most useful tool in investigating the genetic basis of the human brain evolution and has provided much insight regarding brain-related genes during human evolution.

*By Sifa Lalani*
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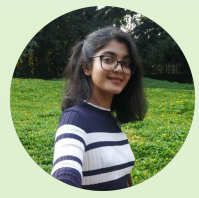
*And Pragyananda Choudhury*
*S. Y. BSc. Biotechnology*



# Transposons Are Not So Evil After All!

*Transposons and evolution*

Traditionally thought of as bad, selfish or 'junk' for causing mutations, deletions and inappropriate insertions, these transposable elements (TEs) or 'jumping genes' actually have a new side to them-a good one!

They play a huge role in evolution and genetic diversity. Their 'jumping' around creates new genotypes and phenotypes and if this phenotype is an evolutionarily favourable one, it can contribute to a varied genetic pool.

Exon shuffling, creation of new genes and pseudogenes, genetic mosaicism, affecting gene regulatory networks are some of the ways in which TEs impact evolution and diversity.

Heightened immunity in Arabidopsis plant, pigmentation in medaka fish, stress tolerance are some of the reasons why transposons aren't completely useless.

Transposable elements (TEs) are of importance to humans, particularly with reference to the placenta.

**Placental Evolution**

The placenta, a characteristic feature of eutherian mammals owes its evolution in part to transposons. A research was conducted at Yale involving humans, armadillos (placental) and opossum (non-placental). It was found that 1532 genes were expressed in humans and armadillos

whereas they were silenced in the opossum. The 199 genes that were silenced in placental mammals, were expressed in opossums. When the first mammals came into the picture, many genes related to egg shell formation had to be turned off and many others had to be expressed for live births, maternal-foetal communication, uterine development, all of which are crucial to mammalian pregnancy.

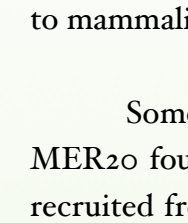
Some of the expressed genes in placental mammals were regulated by the transposon-MER20 found in eutherian mammals. Further, it was seen that these 1532 genes were in fact recruited from other organs. Therefore, they had to evolve accordingly. They had to evolve a mechanism to respond to progesterone (a very important hormone in pregnancy). This was made possible by MER20 transposons. MER20 had a progesterone binding site so whenever they inserted themselves next to a gene they passed on this progesterone-affinity to it.

Moreover, MER20 recruits cAMP signalling pathway into the endometrial stromal cells (ESC).

This is important for pregnancy because cAMP pathway is involved in decidualization process i.e changes in the cells of endometrium.

Prolactin is another important hormone in pregnancy. In humans the promoter for this hormone contains a transposable element MER39 but MER39 is primate specific. In other animals like mouse and elephant, MER77 and LINE retrotransposons respectively, were involved. This is the first reported case of convergent evolution of gene expression involving TEs.

Placenta is said to be the most diverse organ among mammals which makes research a bit difficult but new developments and perspectives would make the picture clearer in the future.



*by Isha Navare*
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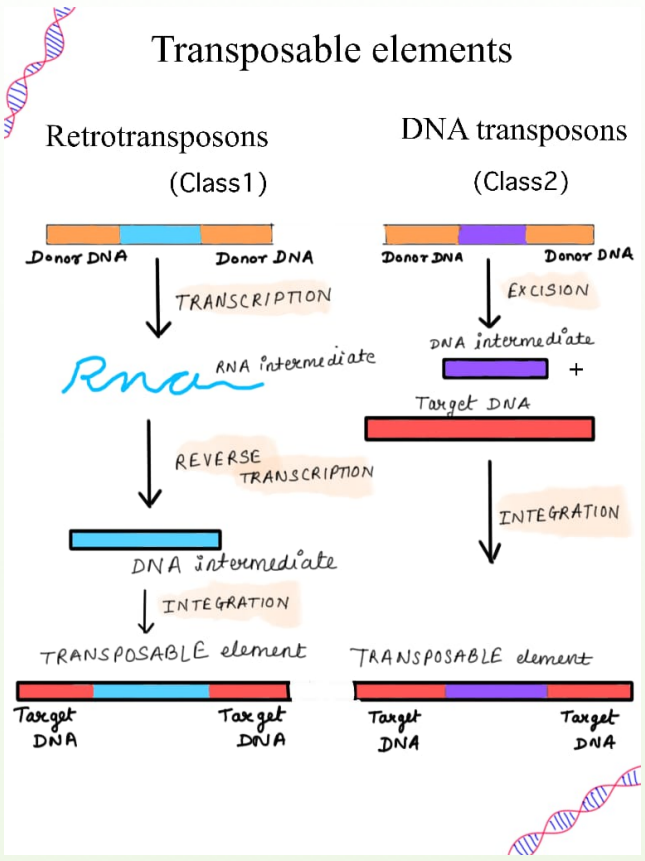


Illustration 3:

*Illustration by : Samidha Dabrase*
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# The Merry Game-te Corner

## Code Decode

**Fill in the blanks and unjumble the highlighted letters to decode the word of this issue.**

i. Alteration in the nucleotide sequence of the genome: _ _ _ _ _ _ _ _

ii. The difference in DNA among individuals: _ _ _ _ _ _ _ _ _

iii. A group of living organisms consisting of similar individuals capable of exchanging genes or interbreeding: _ _ _ _ _ _ _

iv. Ernst Haeckel, in 1866 coined this to describe the "economies" of living forms: _ _ _ _ _ _ _

v. The Father of Evolution who wrote 'Origin of Species': _ _ _ _ _ _

Word of the Issue: _ _ _ _ _ _ _ _ _

## Heredity Hunt

**Find the words listed in the word search below:**

| | |
|---|---|
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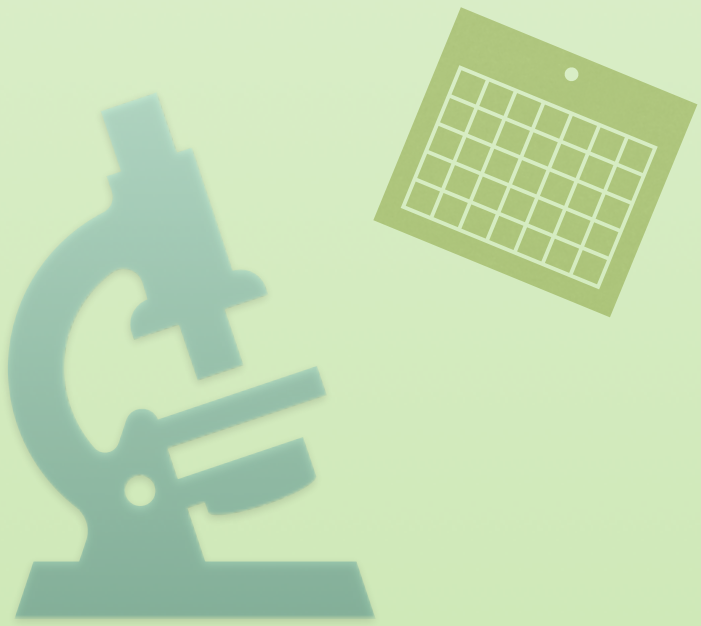
| GENERATION | EVOLUTION |
| RANDOM | SPECIES |
| MATING | TRANSPOSON |
| VARIATION | DARWIN |



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## Gags By Gregor

Q. My friend's job involves cloning the DNA of trains so what do we call him?
A. A genetic engineer.

*Created by : Divya Bhardwaj*
*S. Y. BSc. Biotechnology*

## How did you find it? Any feedback? Suggestions?

We would like to know what you thought of this issue of Genophilic, any suggestions are welcome.

Our next issue will be on the topic 'Experiments in Genetics ', and we would appreciate any contributions on said topic.

Contact us on : editor.genophilic@gmail.com

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