Faith & Science
CONFERENCE

MUTATIONS AND POPULATION GENETICS

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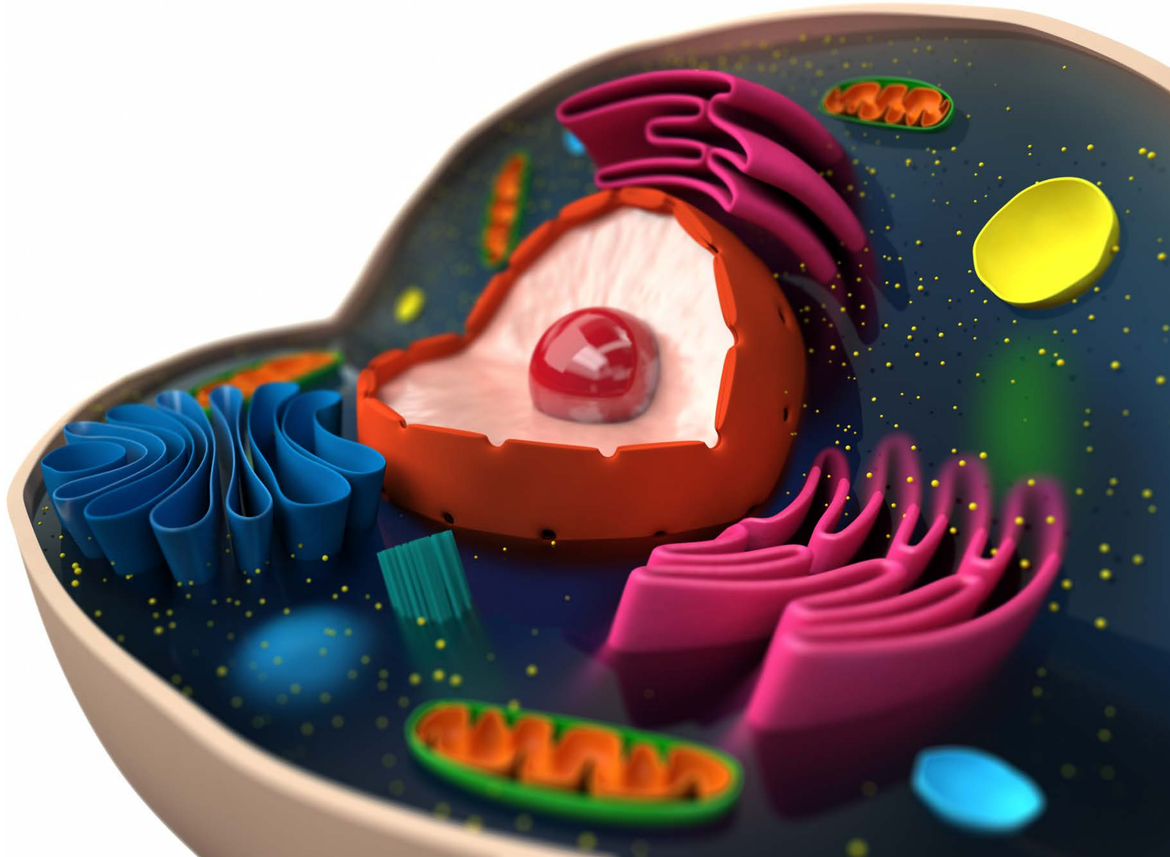


MUTATION

- For an organism to become more complex it requires more genes and therefore more DNA.
- Mutations don't provide more DNA. They change existing DNA, usually adversely.
- The model is that some of these changes can create new genes i.e. *de novo* genes.

"The classic model of evolution is based on duplication, rearrangement, and mutation of genes with the idea of common descent." ***https://en.wikipedia.org/wiki/Orphan_gene***

MUTATION

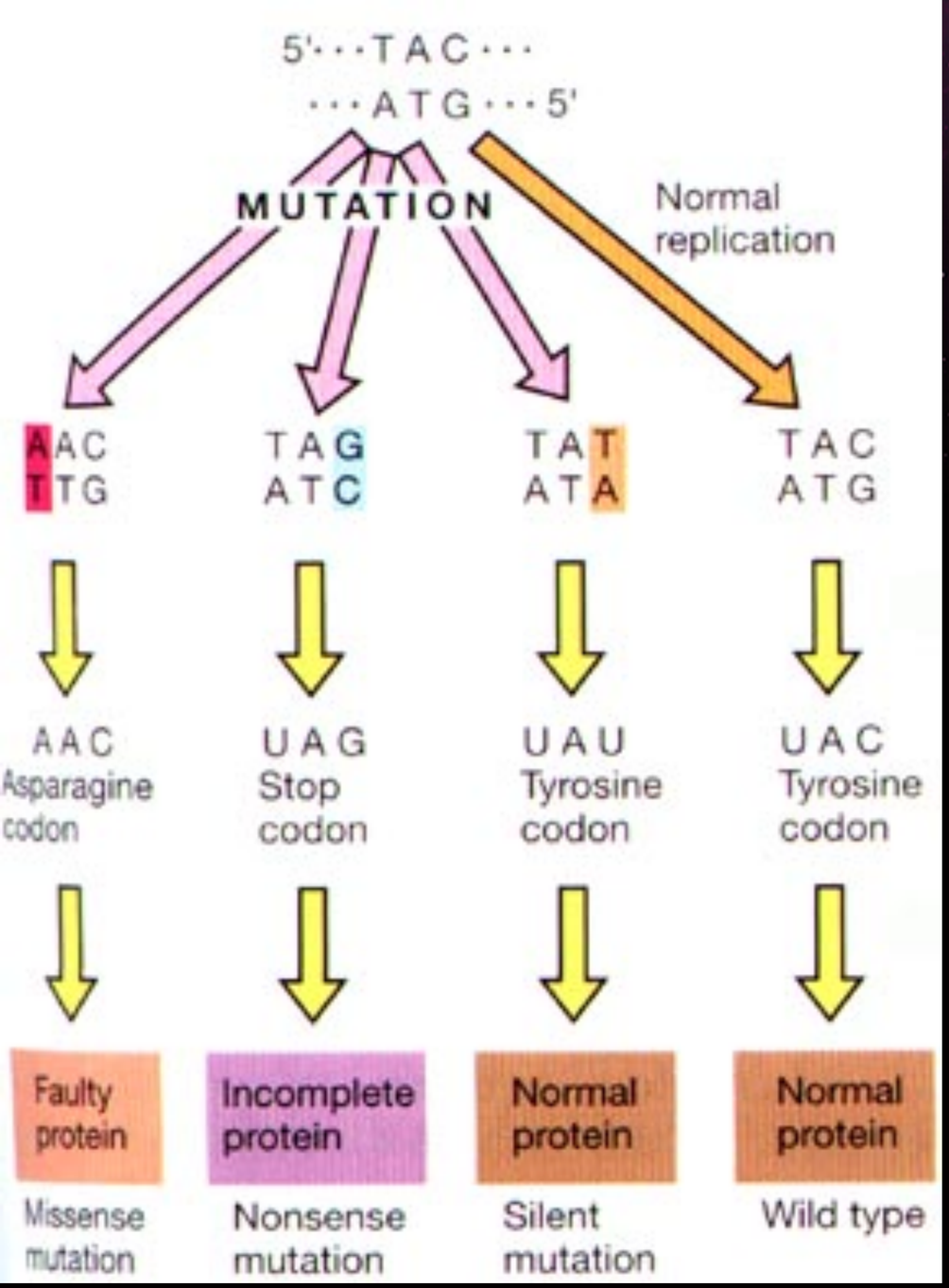
- *"-- alteration of the nucleotide sequence of the genome of an organism"*

  https://en.wikipedia.org/wiki/Mutation

- *"For life to exist with stability, it is essential that the nucleotide sequence of genes is not disturbed to any great extent."*

  Prescott *et. al.* Microbiology 4th Ed. p.262.

- E.g. of mutations:



1. POINT MUTATIONS

1. NORMAL PROTEIN
2. SILENT

   Different codon but still same amino acid
3. NONSENSE

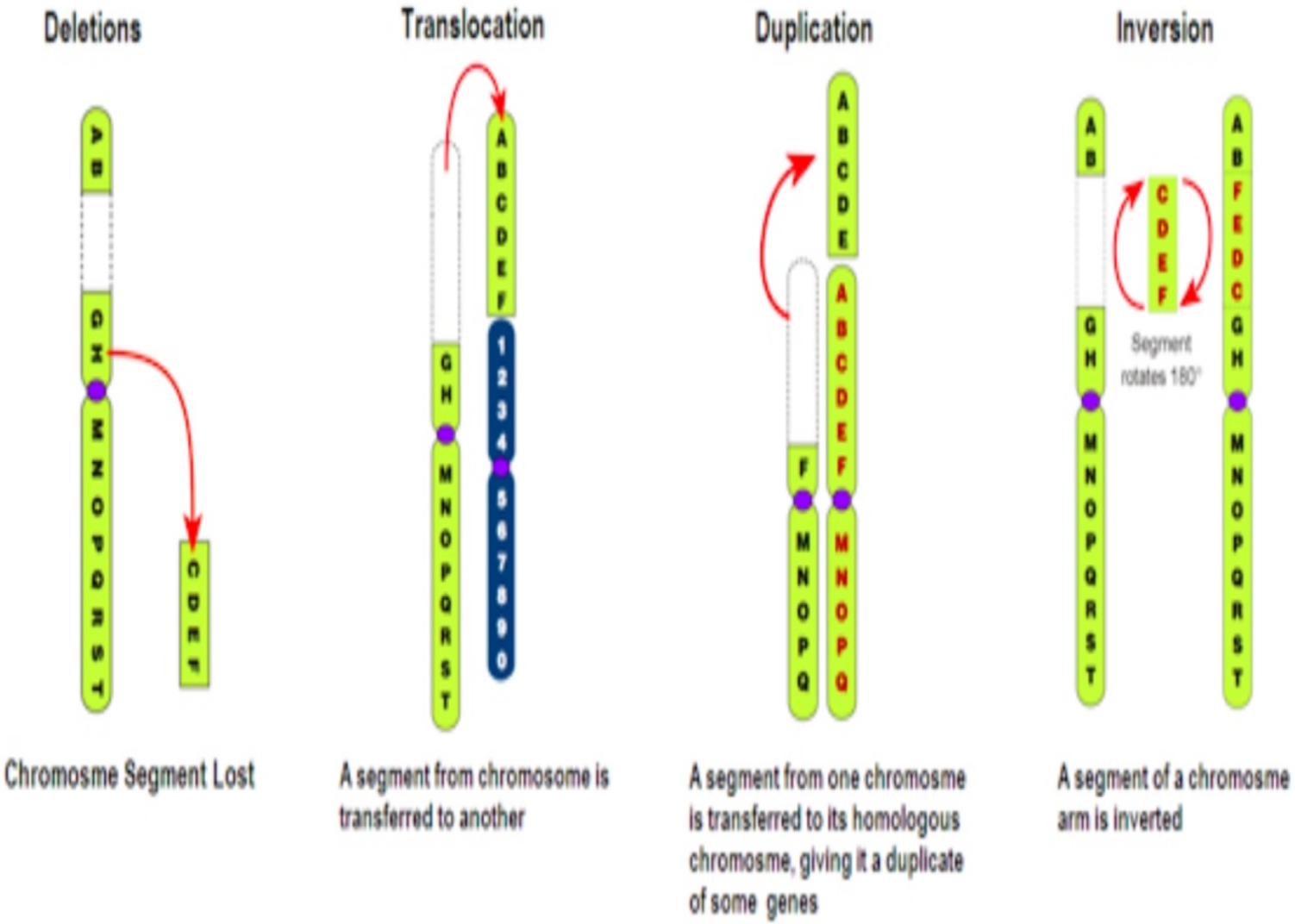
   Stop codon – incomplete protein
4. MISSENSE

   Functional or non-functional

https://www.onlinebiologynotes.com/mutation-and-types-of-mutation/

2. FRAME SHIFT

DNA	AAC TGA CGA CTA	ORIGINAL
mRNA	UUG AGU GGU GTU	
aa	Leu Thr Ala Asp	
	A ↑	
DNA	AAC TGC GAC TA	DELETION
mRNA	UUG ACG CUG AU	
aa	Leu Thr Leu	
	T ↓	
DNA	AAC TTG ACG ACT A	INSERTION
mRNA	UUG AAC UGC UGA U	
aa	Leu Asn Ala Stop	



3.MULTIPLE BASES

1. DELETIONS
2. TRANSLOCATION
3. DUPLICATION
4. INVERSION

https://socratic.org/questions/what-are-four-types-of-chromosomal-mutations

- E.g. of mutations:
  1. Point mutations.
  2. Frame shift mutations.
  3. Multiple bases affected.
  4. Mobile genetic elements – MGEs. “Jumping genes”
     - Can move from one site to another – don’t code any other function.
     - Can transpose a gene to another site. (IS)
     - Carry additional information. E.g. drug resistance, virulence.(Tn)
     - Insert into a gene and inactivate it.
     - Insert down stream and inactivate a gene.

MUTATIONS

- Occur spontaneously.
- Rates vary for genes and DNA sequences.
- Rates vary for organisms.
- Humans - $\sim 1.1 \times 10^{-8}$ per site/generation.
- Unicellular organisms $\sim 3 \times 10^{-3}$ per genome/cell.
- Lowest rate, in a *Paramecium* - $\sim 2 \times 10^{-11}$ per site/generation.
- Organisms have repair mechanisms.
- Ironically mutations can occur doing repair.

https://en.wikipedia.org/wiki/Mutation_rate

MUTATIONS

- In somatic cells - usually can’t be inherited.
- In germ cells of reproductive organs of multicellular organisms - can be inherited.

https://en.wikipedia.org/wiki/Mutation_rate

MUTAGENS

- *"a substance or preparation capable of inducing mutation."*[1]
- *"a physical or chemical agent that changes the genetic material, usually DNA, of an organism and thus increases the frequency of mutations above the natural background level."* [2]
- Some directly mutagenic, some converted to mutagens in organism and some with other compounds.
- Many a result of human activity so not relevant to past mutational events. May be for current & future.
- Natural mutagens.

1. https://www.dictionary.com/browse/mutagen
2. https://en.wikipedia.org/wiki/Mutation_rate

MUTAGENS

- Natural mutagens:
  1. UV;[1]
  2. Mycotoxins e.g. aflatoxins – *A. flavus;*[1]
  3. Plant pyrrolizidine alkaloids.[2]

1. https://en.wikipedia.org/wiki/Mutagen
2. https://www.ncbi.nlm.nih.gov/pubmed/29524571

MUTATIONS

➤Why?

- Such a serious design flaw;
- Such an error prone system in such an incredible system;
- To allow organisms to adapt to changes;
- To enable organisms to evolve to more complex forms.

“Believe it or not, a certain amount of sloppiness is built into the system. Without mutation there would be no variation, and without variation there would be no evolution.” [1]

1. ttps://learn.genetics.utah.edu/content/basics/mutation

How to study significance?

- Look at what happens in populations.
  - **Organisms with slow growth rates more difficult to study.**

    Humans - 22-23 years. Not all humans procreate and they vary in the number of offspring they have.
  - **Faster - easier.**

    Drosophila - 10-12 days.

- **Unicellular - easiest.**
  - Yeasts. Doubling time ~90 min.
  - Bacteria. Doubling time ~20 min. Start with 1000 orgs/ml and in 4 hrs ~4m/ml

  Can study many generations over a very short time. However, conditions are artificial.

Observations of populations under natural conditions:

- Moths in industrial revolution;

- Examples from my own experience:
  - Mutation to antibiotic resistance;[1]
  - Removal of antimicrobial use in a hospital;
  - CA-MRSA – chromosomal;[2]
  - Mupirocin resistance – acquired.[3]

If the selective pressure isn't maintained, the normal metabolically efficient organism predominates.

1. https://www.icr.org/article/evolution-antibiotic-resistance/
2. J. Antimicrob. Chemother. (2009): 64(4), 684
3. MJA (1994): 161(6), 397.

"For life to exist with stability, it is essential that the nucleotide sequence of genes is not disturbed to any great extent. However, sequence changes do occur and often result in altered phenotype. These changes are largely detrimental and important in generating variability and contribute to the process of evolution."

Prescott *et al* Microbiology 4th Ed. p. 262

"--- it is now generally thought that the majority of mutations are mildly deleterious, that many have little effect on an organism's fitness, and that a few can be favorable."

https://en.wikipedia.org/wiki/Mutation_rate

"Generally speaking, however, it remains debated whether duplication and divergence or de novo *gene birth represent the dominant mechanism for the emergence of new genes [63, 65, 73, 75–77], in part due to the fact that* de novo *genes are likely both to emerge and to be lost more frequently than other young genes (see below)."*

"If de novo gene birth is frequent, it might be expected that genomes would tend to grow in their gene content over time; however, the gene content of genomes is usually relatively stable [6]. This implies that a frequent gene death process must balance de novo *gene birth, and indeed,* de novo *genes are distinguished by their rapid turnover relative to established genes."*

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6542195

The theory on the evolution of mutation rates identifies three principal forces involved:

the generation of more deleterious mutations with higher mutation,

the generation of more advantageous mutations with higher mutation,

and the metabolic costs and reduced replication rates that are required to prevent mutations."

https://en.wikipedia.org/wiki/Mutation_rate

Basic problems:

1. Alteration of existing DNA to make a new gene means loss of a functional gene;
2. Therefore have to acquire additional DNA to be mutated;
3. Energy wise organisms maintain a stable genome;
4. How many changes do you need to a gene sequence in order for it to encode a completely new phenotype?;
5. Need a high mutation rate to make a lot of changes;
6. This imposes an energy cost which cells avoid.

Making a small change in existing genetic information in order to adapt to a new environment doesn't incur these problems.

How one interprets this data will depend on one's point of view.

- Adaptability of an organism is desirable and a good design feature.
- A chance mechanism that has enabled organisms to evolve.

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