Cycle 1: Why Evolution is True

Introduction to Classification of Life

Cellular life is categorized into two main types of cells: eukaryotic cells and prokaryotic cells. **Eukaryotic cells** are more complex and contain a nucleus and membrane-bound organelles. They can be found in plants, animals, fungi, and protists. On the other hand, **prokaryotic cells** lack a nucleus and membrane-bound organelles. They are represented by bacteria and archaea.

Viruses do not consist of cells and are thus *NOT CELLULAR*. Instead, they are composed of a protein shell enclosing nucleic acid genomes, which can be either DNA or RNA. Certain viruses also possess a lipid envelope surrounding their protein structure. Notable examples of viruses include HIV, a retrovirus, and the coronavirus.

Are Viruses Considered Alive?

Yes	No
Viruses can reproduce	Viruses need the host cell to be able to reproduce
Viruses can evolve	Viruses have no metabolic system
Viruses have nucleic acid genome in a protein shell	Viruses have no phospholipid bilayer and cytoplasm
Viruses express genes like cells	Viruses have a lipid envelope

Introduction to Human Immunodeficiency Virus

Zoonotic diseases are infectious diseases that can be transmitted from non-human species to humans. About 75% of new infectious diseases in humans are spilled over from non-human hosts, most likely from closely related species. These diseases tend to be more harmful and severe in humans compared to their original host species, which are known as **reservoirs**.

HIV derives from zoonotic origins; it evolved from **SIV, or simian immunodeficiency virus**, found in monkeys. However, HIV is *no longer classified* as a zoonotic disease, as it has mutated into a human-only strain (i.e. HIV is now specific only to humans.

How HIV Replicates: the Central Dogma

DNA replication is the process by which DNA makes copies of itself. The central dogma describes the flow of genetic information within cells. According to this principle, DNA is transcribed into RNA, and RNA is translated into proteins. However, in certain cases, reverse transcription can occur, where RNA serves as a template to synthesize DNA. This process is significant in the context of HIV, as it allows the virus to integrate its genetic material into the genome of host cells.

How to treat HIV/AIDS?

The treatment of HIV/AIDS primarily involves the use of antiviral drugs, which prevent the replication of the virus. However, the development and discovery of effective antiviral drugs for HIV/AIDS have proven to be challenging compared to antibiotics for bacterial infections. Unfortunately, there is currently no vaccine available for HIV, leaving individuals with a chronic and lifelong infection that lacks a cure.

HIV Life Cycle: Hijacking Immune Cells

Initially, the virion fuses with the host cell, allowing the virus to enter the cell. Once inside, the virus utilizes an enzyme called reverse transcriptase to convert its viral RNA into viral DNA. However, reverse transcriptase is prone to errors, leading to a high mutation rate for the virus. The next step involves the enzyme integrase, which inserts the viral DNA into the DNA of the host cell. This integration ensures the viral genetic material becomes a part of the host's genetic code. The host cell then transcribes and translates the viral DNA, using its own cellular machinery, to produce new virions, which can go on to infect other cells and continue the cycle of infection.

First Drug to treat HIV: AZT

AZT (azidothymidine) is a nucleoside analog that closely resembles thymidine, a building block of DNA. Its mechanism of action involves stopping the replication of the HIV genome. AZT specifically targets the reverse transcriptase enzyme, which is encoded by the POL genes in the HIV genome. By blocking the addition of more nucleotides, AZT hinders the reverse transcriptase from creating a complete DNA copy of the viral RNA. However, prolonged use of AZT treatment can lead to the development of HIV strains that are resistant to the drug. These resistant strains of reverse transcriptase can acquire a proofreading mechanism, enabled by a difference in two nucleotides in their genome. This proofreading ability allows the resistant reverse transcriptase to recognize and remove AZT from the growing viral DNA chain, rendering the drug ineffective in inhibiting HIV replication.

Evolution of AZT Resistance

During the replication of the HIV genome, errors can occur, leading to mutations. These mutations can either confer resistance to AZT or have no impact on its effectiveness. When AZT treatment is administered, many viruses that lack resistance are unable to reproduce. However, a subset of variants can persist and continue reproducing despite AZT, eventually giving rise to drug-resistant HIV. Over time, the viral population undergoes changes as drug-resistant strains become more prevalent. This evolution of AZT resistance demonstrates the principles of natural selection, including variation, heritability, and non-random survival.

“Mutation proposes, selection disposes”

The reverse transcriptase enzyme's high error rate contributes to the occurrence of genetic variation within the viral population. These genetic variants, or mutations, arise randomly and are not influenced by the environment. Interestingly, antiviral drugs can provide advantages to drug-resistant variants, as they selectively target specific viral components. In different environments, certain variants may become more prevalent within the population.

Resistance to many drugs is less likely

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Vaccines are hard to develop because of high mutation rates

The structure of a virus, including HIV, can undergo changes through the emergence of new variants, enabling the virus to evade the immune system. Consequently, developing a vaccine that accounts for all potential variants becomes challenging. Similar evolutionary dynamics have been observed in the case of SARS-CoV-2, the virus responsible for COVID-19. Mutations have given rise to new variants, and those variants that exhibit greater reproductive success have become more prevalent over time.

Introduction to Evolution: a Scientific Theory

A **theory** is an assumption based on limited knowledge. A **scientific theory** is a coherent set of testable hypotheses that attempt to explain facts about the natural world. For instance, the theory of evolution postulates that populations and organisms undergo changes over time and all organisms are related. This theory is testable, falsifiable, and can be contradicted by evidence. Scientific theories are both testable and falsifiable, capable of being contradicted by evidence. This means that they are open to the possibility of being proven incorrect.

A **falsifiable theory** or conjecture points to hypotheses that require testing and the accumulation of evidence. Testing a theory involves the deliberate attempt to falsify it, as falsification ignites critical discussion and further examination. This process often leads to revisions and refinements of the theory in question. A statement or claim is deemed falsifiable when a single observation or piece of evidence has the potential to disprove it, emphasizing that it remains open to the possibility of being incorrect.

A statement that lacks falsifiability often requires a large search of all possibilities to disprove it or pertains to intangible aspects such as opinions. In contrast, a fact represents an indisputable observation that serves as concrete evidence. The strength of scientific theories lies in their ability to explain a multitude of facts. As theories undergo repeated testing without being falsified, they gradually emerge as the most probable explanations for observed phenomena.

Evidence for Evolution: How is the Theory of Evolution Falsifiable?

- *Biogeography*: similar species found in distant places
- *Comparative morphology:* similar structures in species that share a common ancestor
  - Ex. Pig leg, Bat wing, and dolphin flipper
  - Vestigial structures are structures in an organism that must have had a function in an ancestral organism (but may not be used now)
- *Geology:* fossils provide evidence that life in the modern day differed from life in the past

Theory of Evolution by Natural Selection

Natural selection is a mechanism that explains the process of evolution. It operates by taking advantage of the inherent variation in traits within a population. Individuals possessing traits that provide them with a better chance of survival and reproduction, ultimately resulting in higher fitness, are favored by natural selection. Over time, as these individuals pass down their advantageous traits to their offspring, the frequency of these traits gradually increases within the population. This continuous cycle of selection leads to the gradual adaptation and change of species over generations, enabling them to better thrive in their respective environments.

Descent with Modification from a Common Ancestor

Evolution can be understood as the process of descent with modification from a common ancestor. It is driven by variation within populations, with individuals possessing different phenotypes and levels of success. This gradual change, known as gradualism, occurs over numerous generations and is not guided by a specific goal or desire of the population to evolve. Through natural selection, adaptations arise that are well-suited to the environment, although not always perfect. Factors such as limited genetic variation and changing environments contribute to the diverse range of life forms we observe today. All life on Earth is believed to stem from a common ancestry, potentially originating from a primitive entity capable of self-replication over 3.5 billion years ago. Over time, this primitive entity changed and diversified, leading to the development of new cells and the subsequent branching out into various forms of life. Natural selection stands as the primary mechanism driving most of the evolutionary changes observed in the biological world.

Quick Recap/Final Notes

- Evolution can be fast
- All living things evolve similarly, non-living: viruses can evolve too
- HIV Evolution displays concepts of heredity, diversity, natural selection, mutation, and variation
- It also shows how humans can be an evolutionary force