Natural Viral Engineering in Cognition Based Evolution

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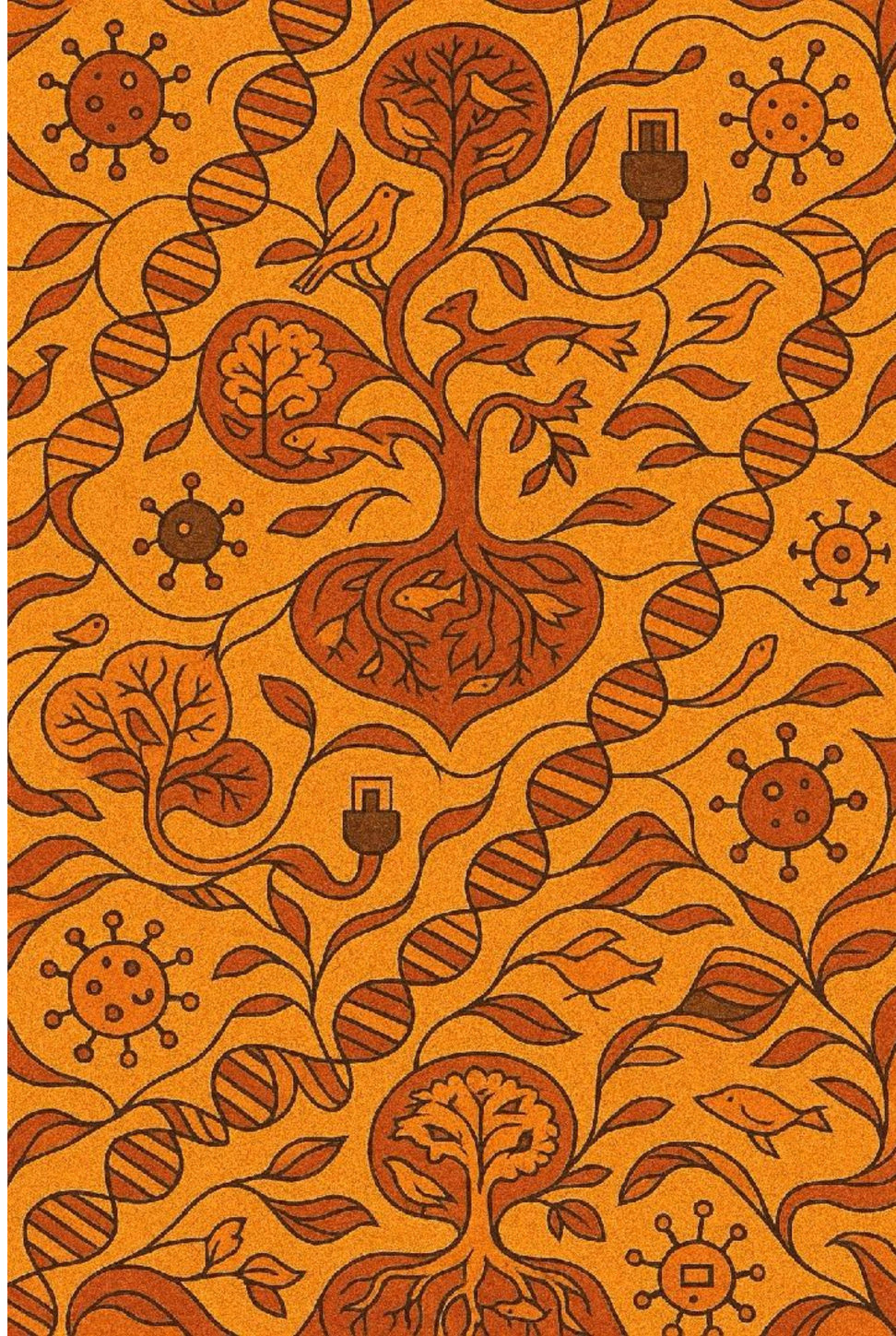
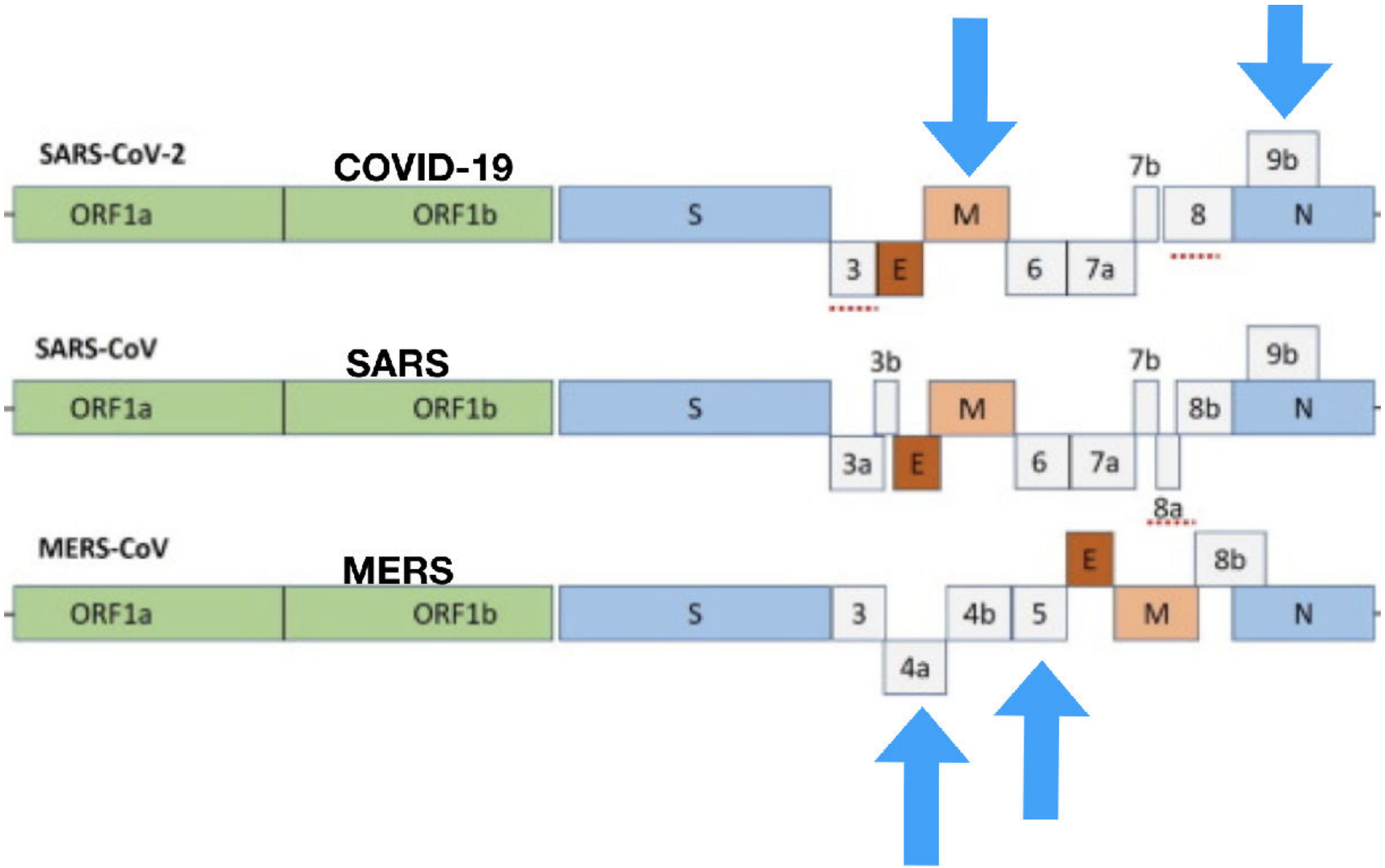
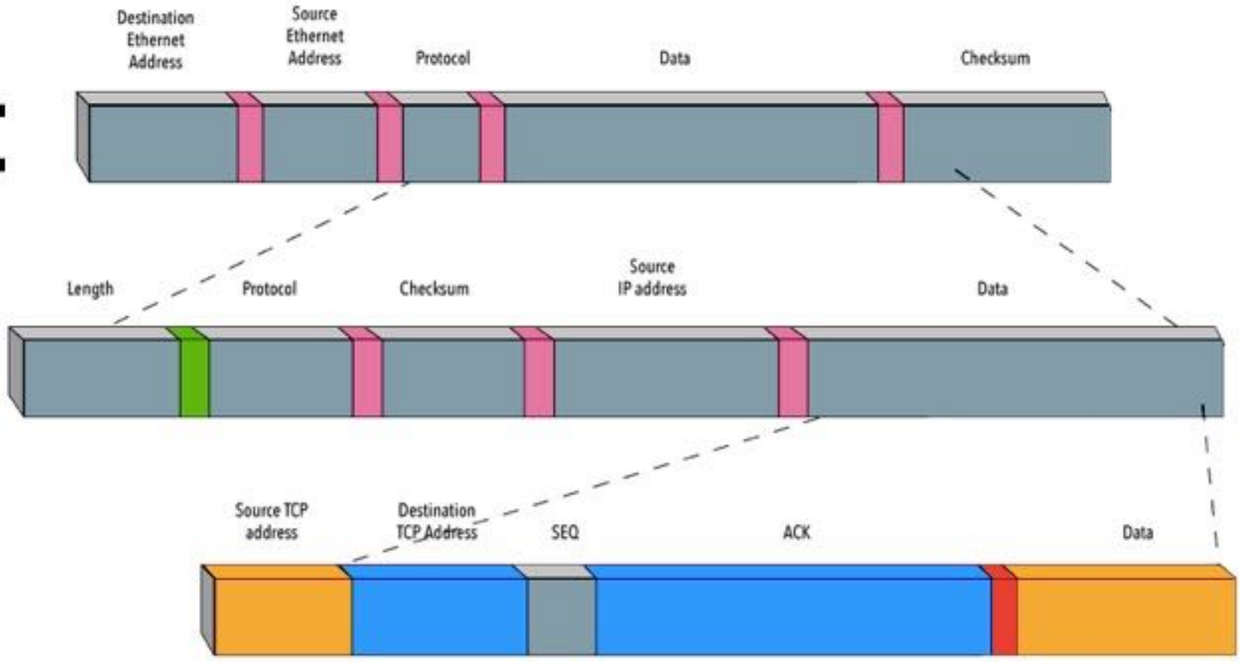


1 week into COVID: Conversation

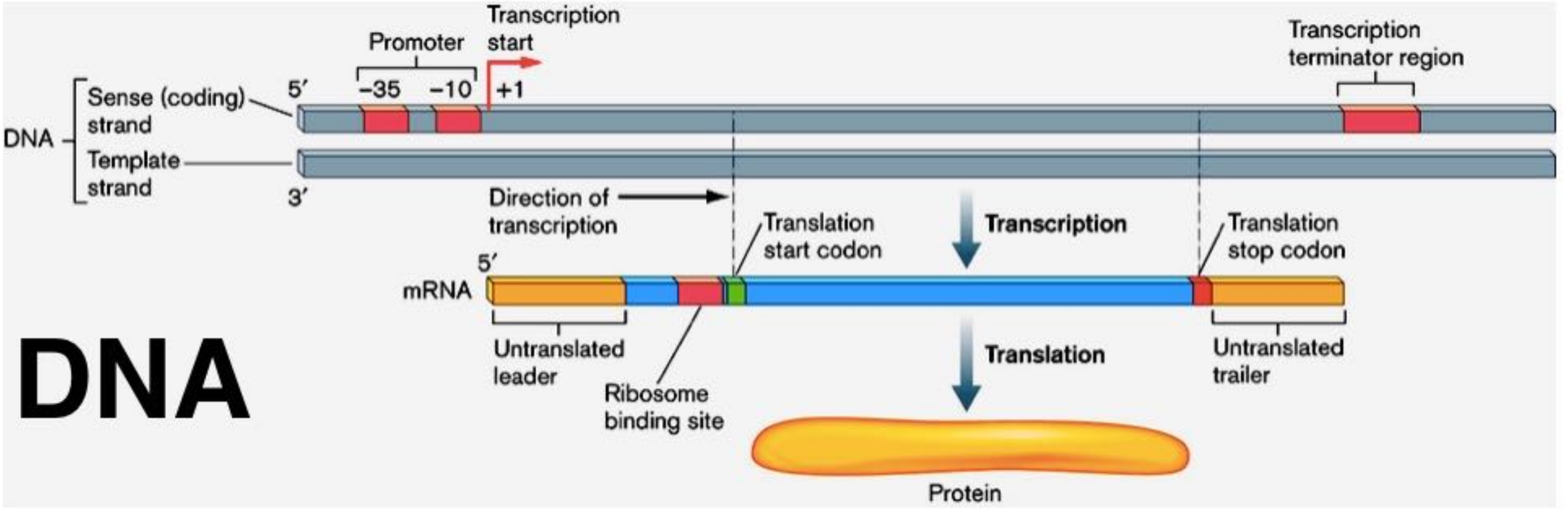
MERS vs. SARS vs. COVID19



Ethernet



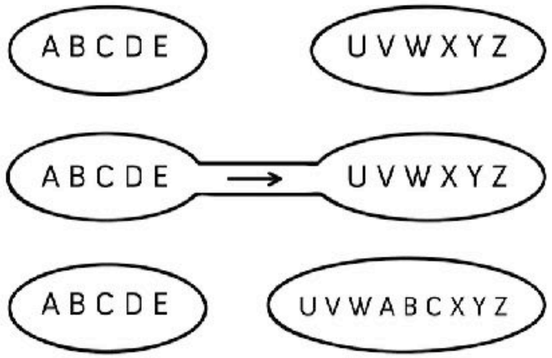
DNA



An MD, 3 virologists, a geneticist, a cell biologist and a cognitive psychologist walk into a bar…

TRANSPOSITION

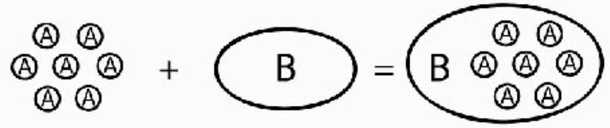
HORIZONTAL GENE TRANSFER



EPIGENETICS

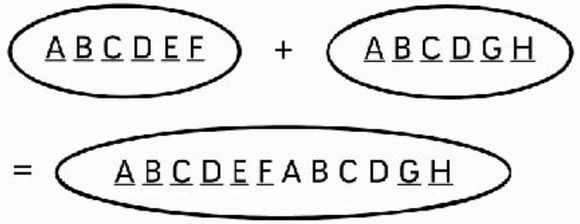
SYMBIOGENESIS - HOST/PARASITE

BACTERIA IN YOUR GUT

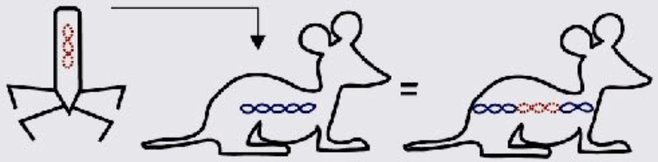


SYMBIOGENESIS - SYSTEM IN A SYSTEM

HYBRIDIZATION



RETROVIRUS



“Cells are Engineers”

-James A. Shapiro, *Evolution: A View from the 21st Century*

Viruses: Global “Open-Source Repository” of genetic tools

- Virus Evolution is host-mediated engineering, not random copying errors.
- Viruses lack the machinery to re-engineer their genomes. They rely on host cell for replication, variation, and innovation.
- Code exchanged across life forms, not rogue elements mutating at random.

William Miller, Arthur Reber, Perry Marshall & František Baluška (2023)
Cellular and Natural Viral Engineering in Cognition-Based Evolution
Communicative & Integrative Biology DOI: 10.1080/19420889.2023.2196145

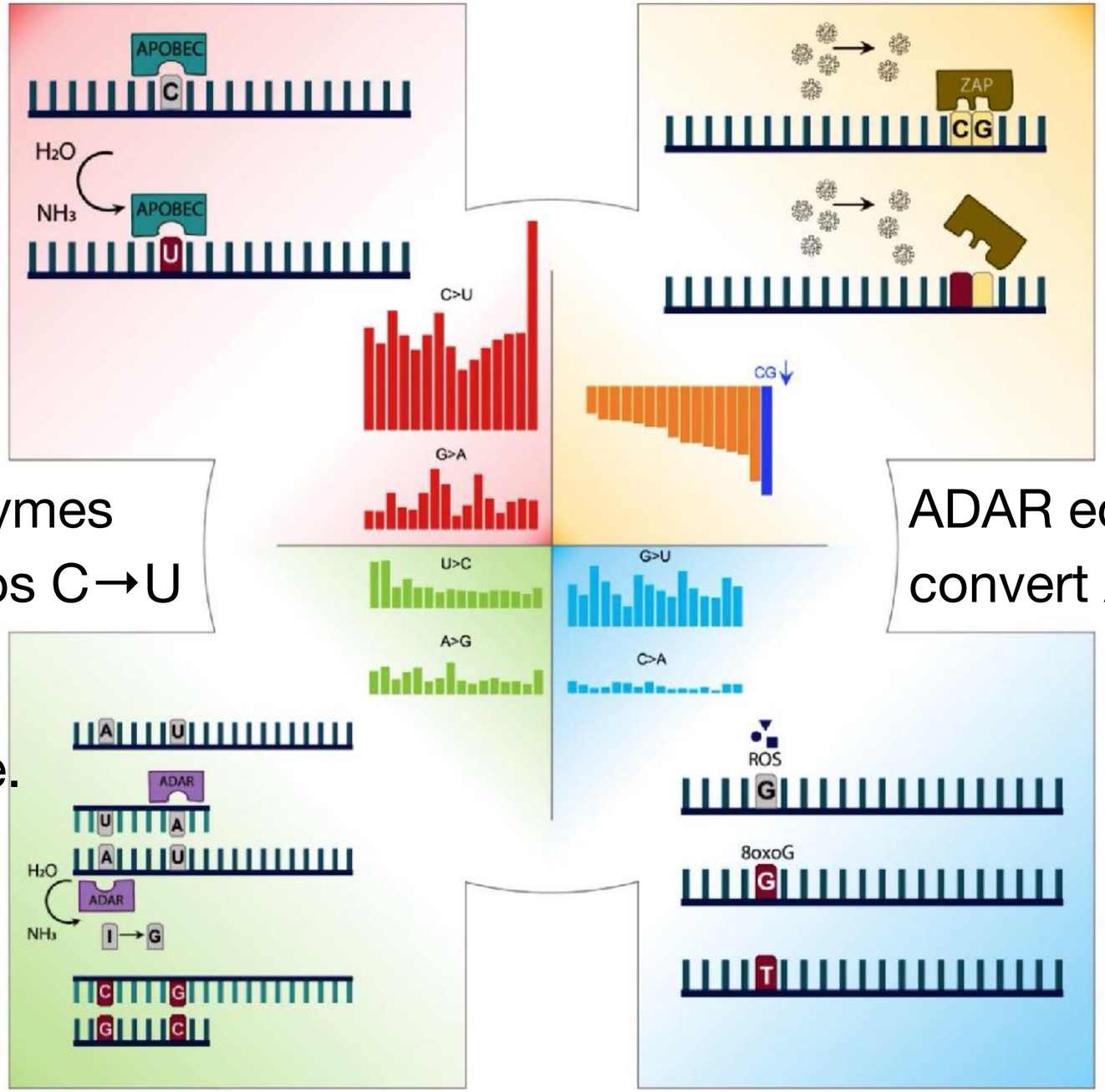
Mutation frequencies in SARS-CoV-2:

Viruses do have RNA polymerase editors, but the edits lack their signature.

APOBEC editor enzymes remove amino groups C→U

ADAR editor enzymes convert A→G

Host driven edits dominate.



Azgari C, Kilinc Z, Turhan B, Circi D, Adebali O.
The Mutation Profile of SARS-CoV-2 Is Primarily Shaped by the Host Antiviral Defense.
Viruses. 2021; 13(3):394. https://doi.org/10.3390/v13030394

Most mutations are in line with host enzymes—not random polymerase errors

These editing enzymes are part of the cell's innate immune defense. They are the molecular tools that enable Natural Genetic Engineering in the host genome (Transposition, Somatic Hypermutation, and Retroviral Silencing)

- Enzymes actively edit viral RNA within infected host cells.
- Edits are non-random, context-sensitive (targeting motifs like UC or AU), and **often occur in functionally relevant regions such as the spike protein** receptor-binding domain.
- Most virus mutations match host enzymatic editing signatures, not errors from the virus's own RNA polymerase (proofreading ability via nsp14).
- Our cells are actively trying to "re-engineer" the virus as part of our immune defense.
- **The virus is re-engineered by the host. Not by itself, not by accident.**

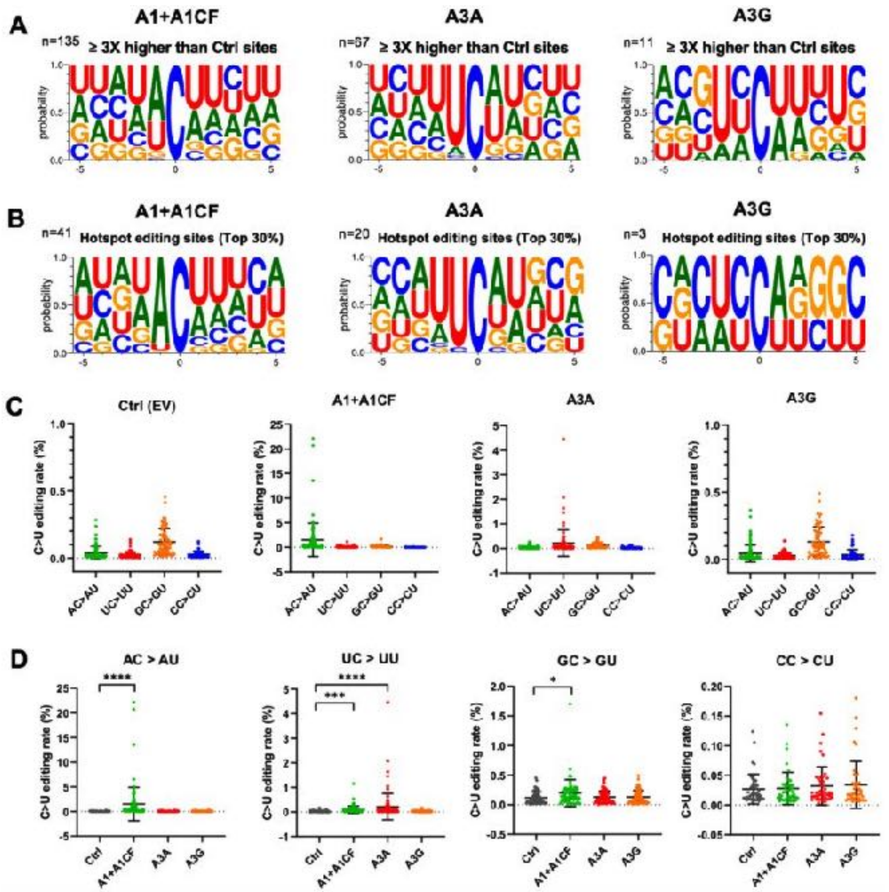
APOBEC-mediated Editing of SARS-CoV-2 Genomic RNA Impacts Viral Replication and Fitness

"APOBEC3A-editing of SARS-CoV-2 promotes viral replication/propagation, suggesting that **SARS-CoV-2 utilizes** the APOBEC-mediated mutations for **fitness** and evolution.

Unlike the unpredictability of random mutations, this study has significant implications in predicting the potential mutations…

thus offering a basis for guiding future antiviral therapies and vaccines against the escape mutants."

96% of edits occur in coding exon regions, many nonsynonymous. Functionally significant.



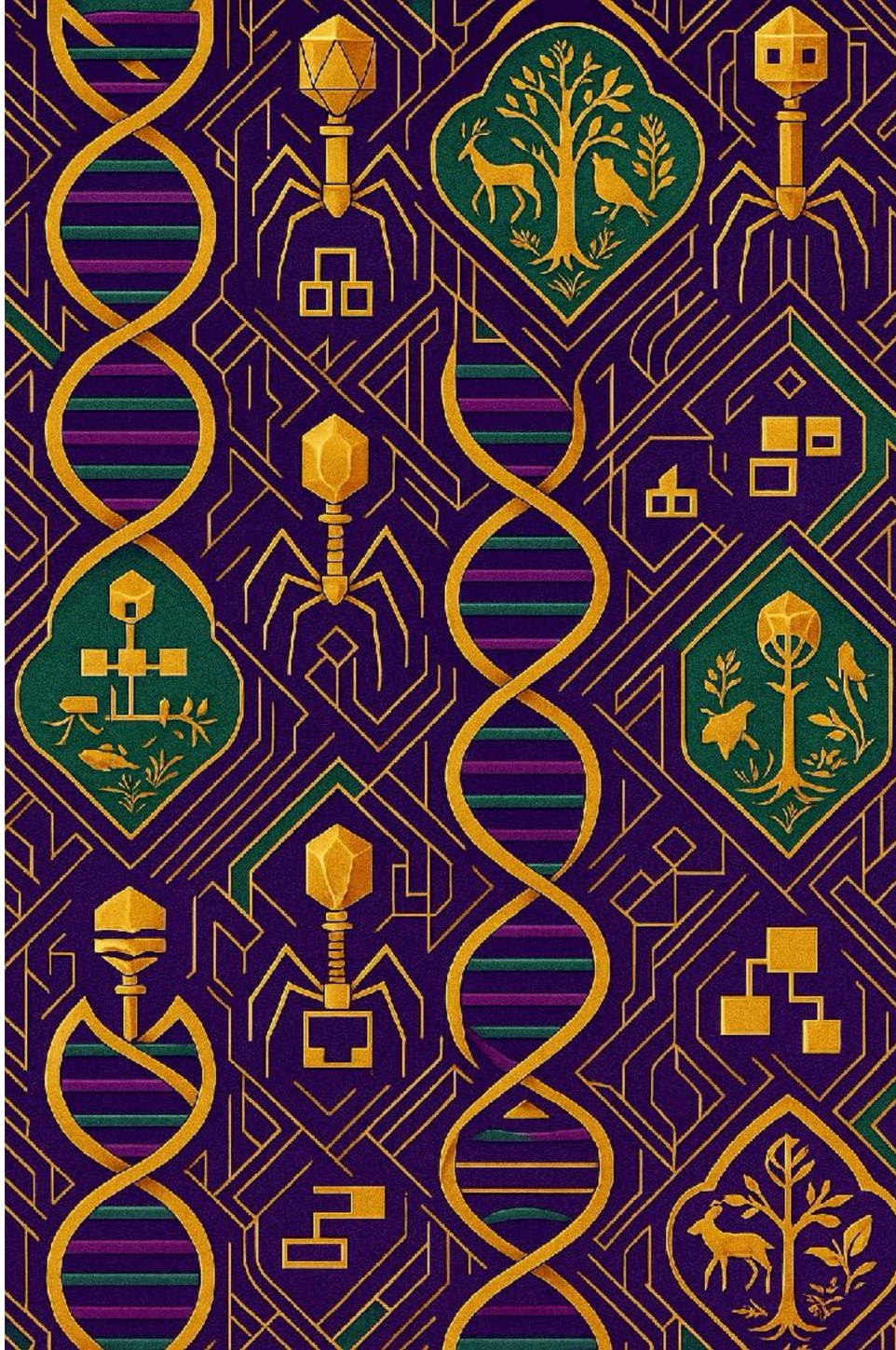
APOBEC-mediated Editing of SARS-CoV-2 Genomic RNA Impacts Viral Replication and Fitness
Kyumin Kim, Peter Calabrese, Shanshan Wang, Chao Qin, Youliang Rao, Pinghui Feng, Xiaojiang S. Chen
bioRxiv 2021.12.18.473309; doi: https://doi.org/10.1101/2021.12.18.473309

Virus uses our body's editing efforts to its own advantage

- When our APOBEC enzymes edit SARS-CoV-2 RNA, they affect its replication and fitness

- The virus responds by engineering its own changes. Our own defense mechanism can help the virus evolve.

- **Guess your opponent's next move:** Predict how the virus may change in the future. If we can predict the next "escape mutants" we can take countermeasures.



Alpha, Delta, Omicron COVID strains came from host-initiated edits

- Omicron’s sudden emergence with dozens of coordinated mutations sparked hypotheses including cryptic circulation, chronic infection, animal reservoirs, and directed editing.

Markov, P.V., Ghafari, M., Beer, M. *et al.* The evolution of SARS-CoV-2. *Nat Rev Microbiol* **21**, 361–379 (2023). https://doi.org/10.1038/s41579-023-00878-2

- Host tries to destabilize viral RNA through hypermutation, thereby weakening the virus.
- Edits often reduce viral fitness but can also produce novel variants.
- Host favors less lethal viral strains (to preserve the host) and more transmissible strains.
- Leads to the gradual extinction of harmful strains.
- The host actively repurposes viral genetic elements for its own biological functions.

Bad Guy Becomes Good Guy

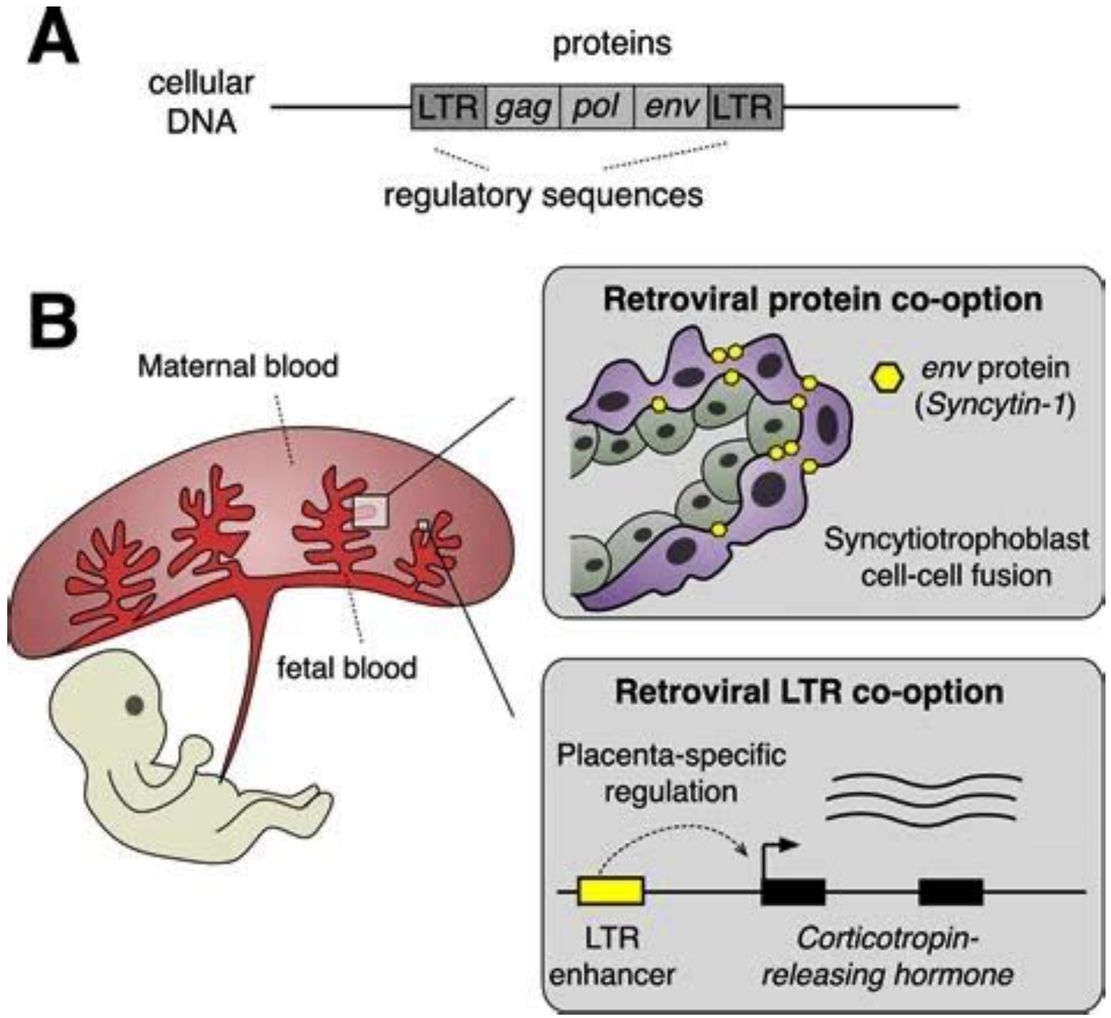
Syncytin and the Viral Origin of the Placenta

Virus infects germline → becomes part of lineage → Envelope “env” gene preserved

The endogenous retrovirus (with gag-pol-env structure) integrated itself into the host genome

Host initiated vertical inheritance:

env becomes Syncytin, expressed in trophoblasts (layers of tissue that later form the placenta).



Chuong et al., “The placenta goes viral: Retroviruses control gene expression in pregnancy” (PLOS Biology, 2018)

Viruses aren't just invaders.
They can be open-source genetic repositories.

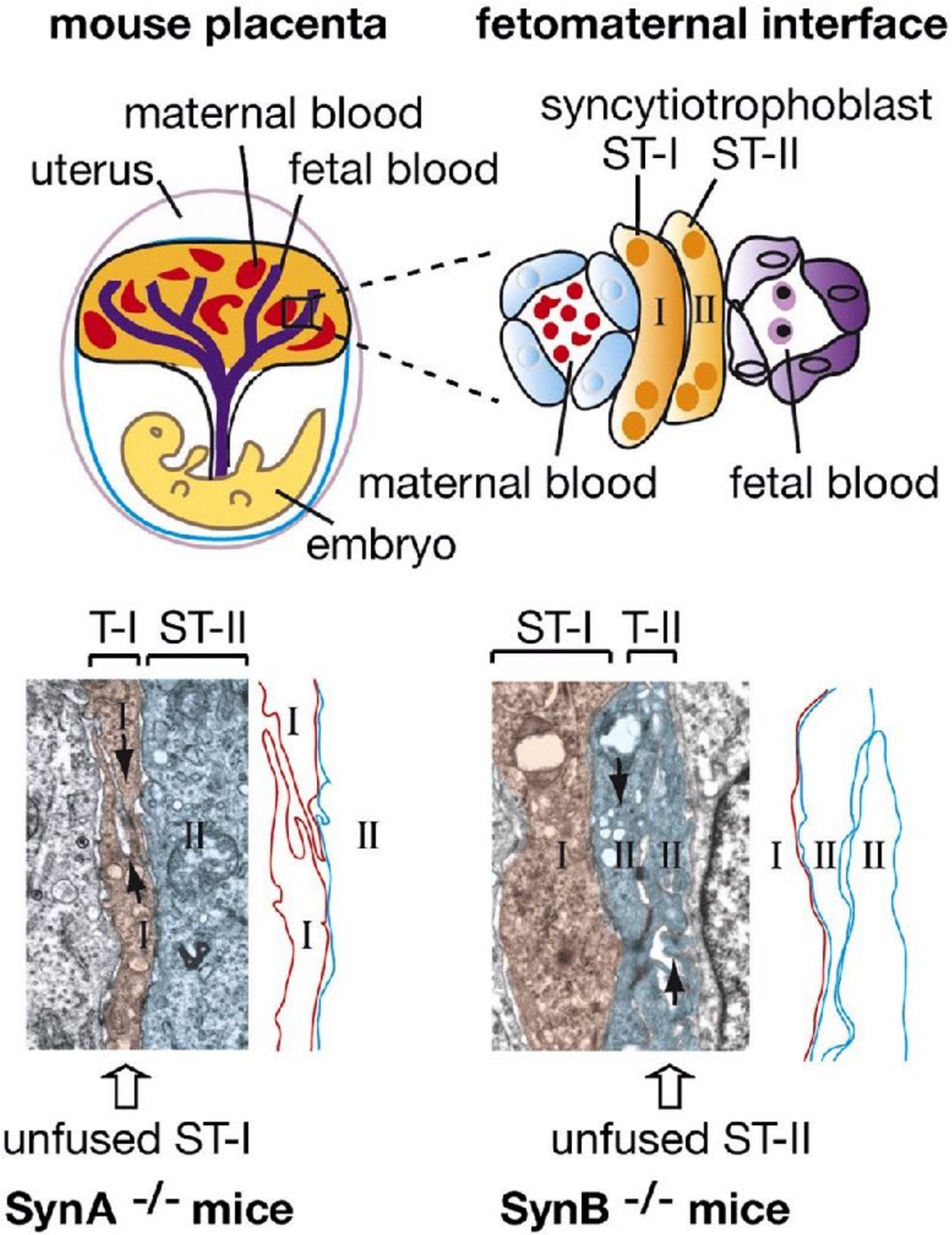
- The placenta needs a special layer called the "syncytiotrophoblast." Individual cells fuse together to create one large, multi-nucleated cell.
- This cell fusion is critical for the placenta to work properly, allowing nutrients and oxygen to pass from the mother to the fetus, and waste goes the other way.
- The Syncytin protein came from that ancient virus. It is the molecular "glue" or "key" that makes this cell fusion happen.

Physical structure built by cell fusion: Syncytin drives this.

Mouse placenta cross-section showing maternal/fetal blood and two trophoblast layers (T-I, ST-II) that merge via fusion.

Knockout mice lacking the ST-I and ST-II genes do not survive.

Source: Dupressoir et al. (PNAS, 2009), co-opted syncytin genes in mice

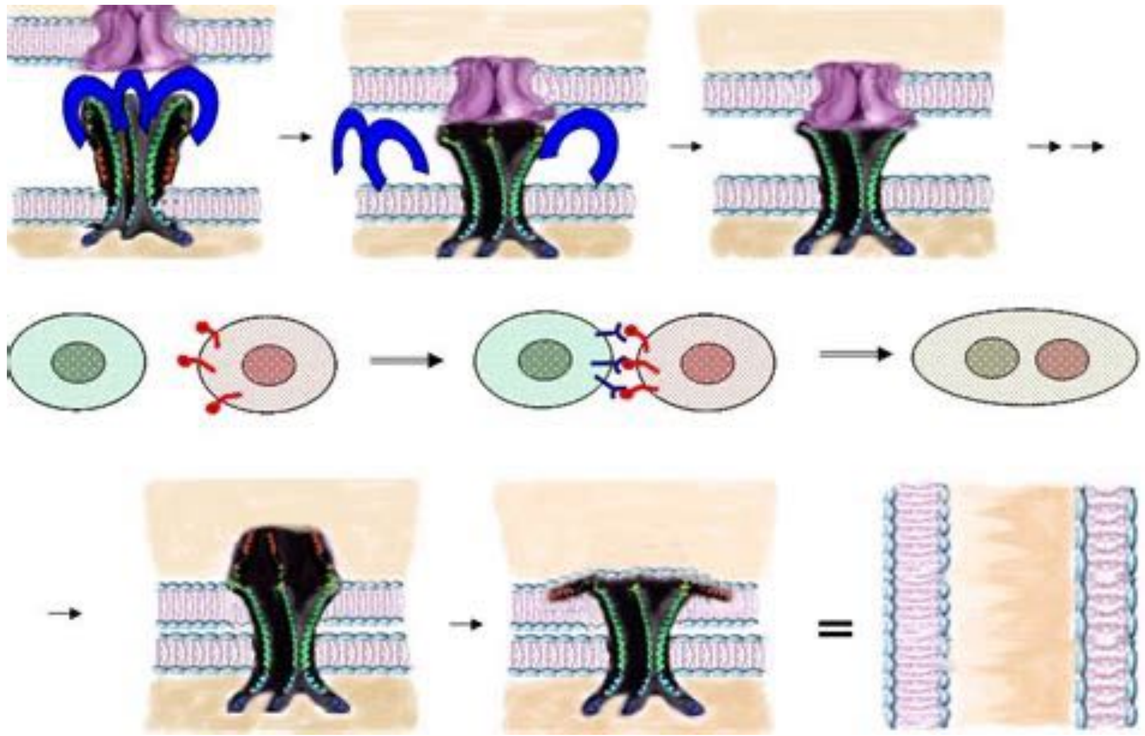


Mechanism: Membrane Fusion by Syncytin-1

Multi-step schematic of Syncytin-1 functional mechanism—SU binding to **receptor**, **cleavage**, **conformational change**, **membrane apposition**, **fusion**.

How the viral fusion protein works: Direct functional reuse inside human cells.

Drewlo et al., “Molecular mechanisms of cell-cell fusion”



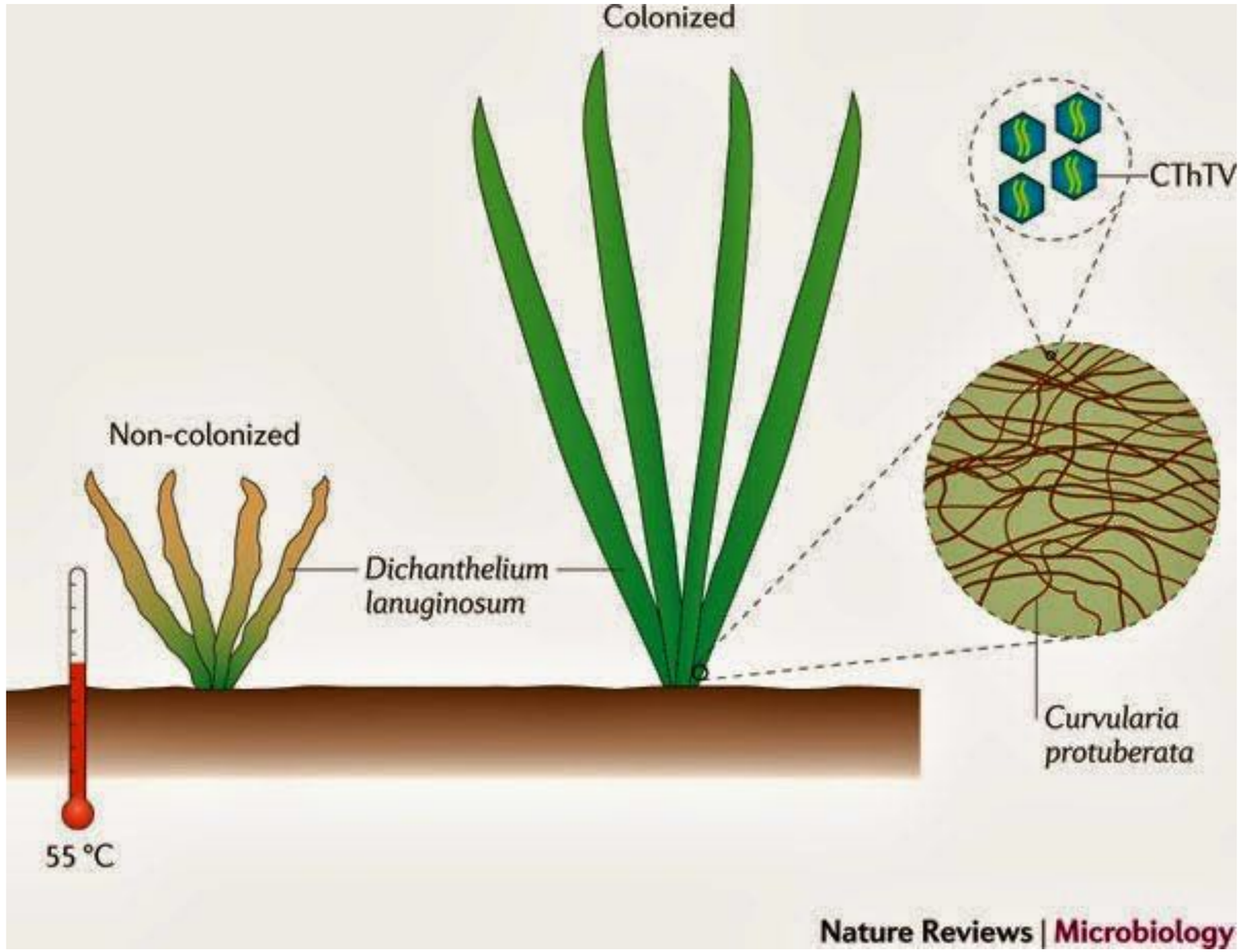
Yellowstone Panicgrass Symbiosis: Virus Enables Survival in Extreme Heat

3-way symbiosis between **panicgrass** (Dichanthelium lanuginosum), the **endophytic fungus** Curvularia protuberata, and its **virus** (Curvularia Thermal Tolerance Virus, CThTV).

Grass thrives in geothermal soils (~65 °C) only when the virus is present in the fungus.

Without the virus **or** the fungus—the plants perish under extreme heat.

A virus in a fungus in a plant: three-way symbiosis required for thermal tolerance, Luis M Márquez



Virus–Host Co-Evolution

Viruses are not isolated agents driven by random mutation.

- Hosts actively shape viral genomes via Gene editing (e.g. ADAR/APOBEC), Recombination, Integration into host genomes

Viruses function as:

- Gene vehicles across species and ecosystems
- Accelerators of evolution, spreading adaptive solutions

“Open Source” biology

- Genes = modular code
- Hosts = developers and testers
- Viral platforms = distribution channels

From Enemies to Engineers

Viruses, **alive or not**, are **liminal lifeforms** capable of co-engineering with host cells.

While they can cause disease (e.g. COVID), their broader role includes:

- Driving adaptation
- Enabling innovation
- Supporting resilience in ecosystems

Reframes evolution as:

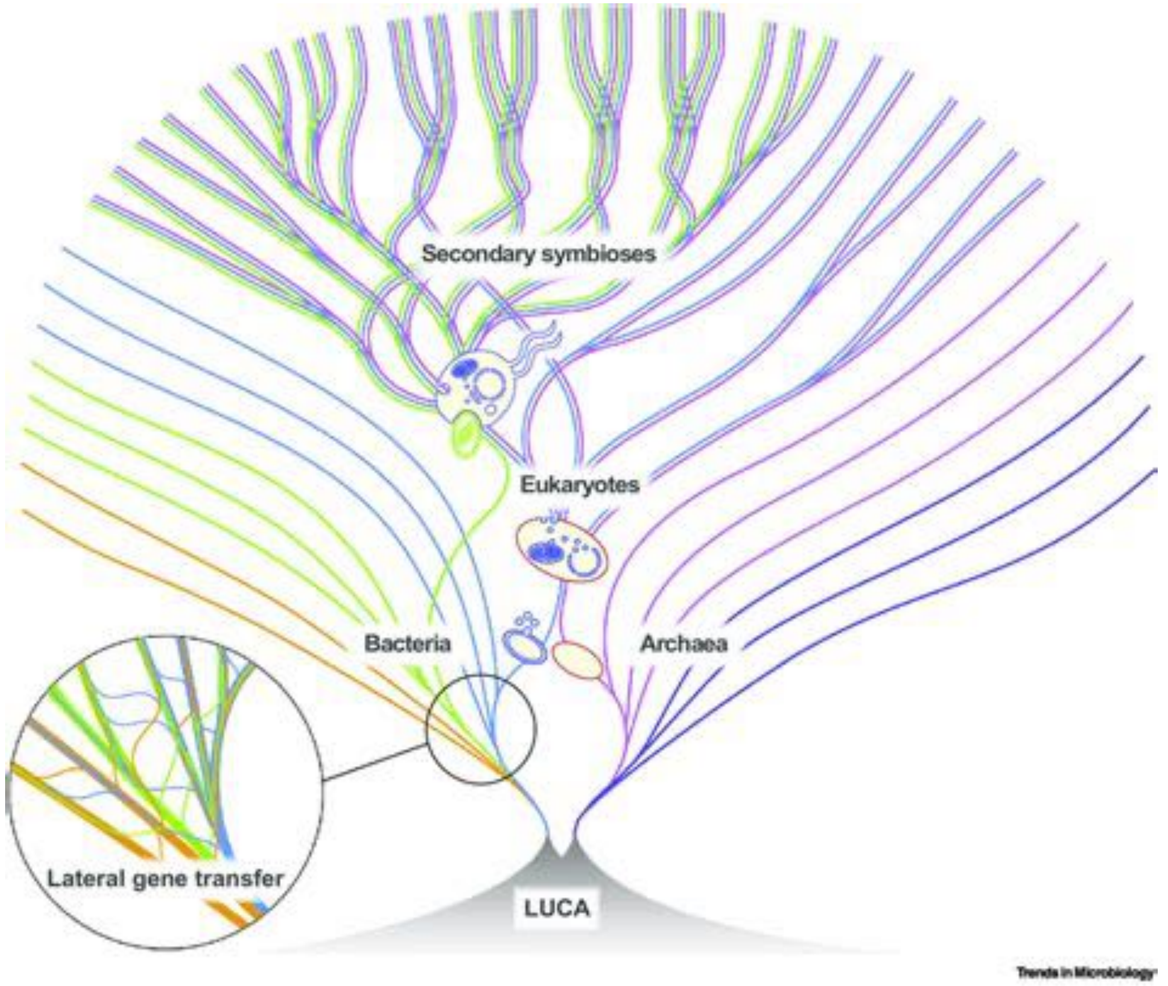
- Not just random mutation and selection, but cognition-based information exchange
- Intelligent cells and viruses solve survival problems collaboratively

Viral-Mediated Gene Exchange Across Life’s Domains

Horizontal gene flow enabled by viruses and symbiosis

Viruses are Cross-Domain Engineers

Brunk, C. & Martin, W. (2019). “Schematic Diagram of Symbiosis in the Tree of Life and the ‘Union’ of the Bacterial and Archaeal Domains to Form the Eukaryotic Domain, Taking Lateral Gene Transfer into Account.” Archaeal Histone Contributions to the Origin of Eukaryotes. (CC BY-NC-ND 4.0).



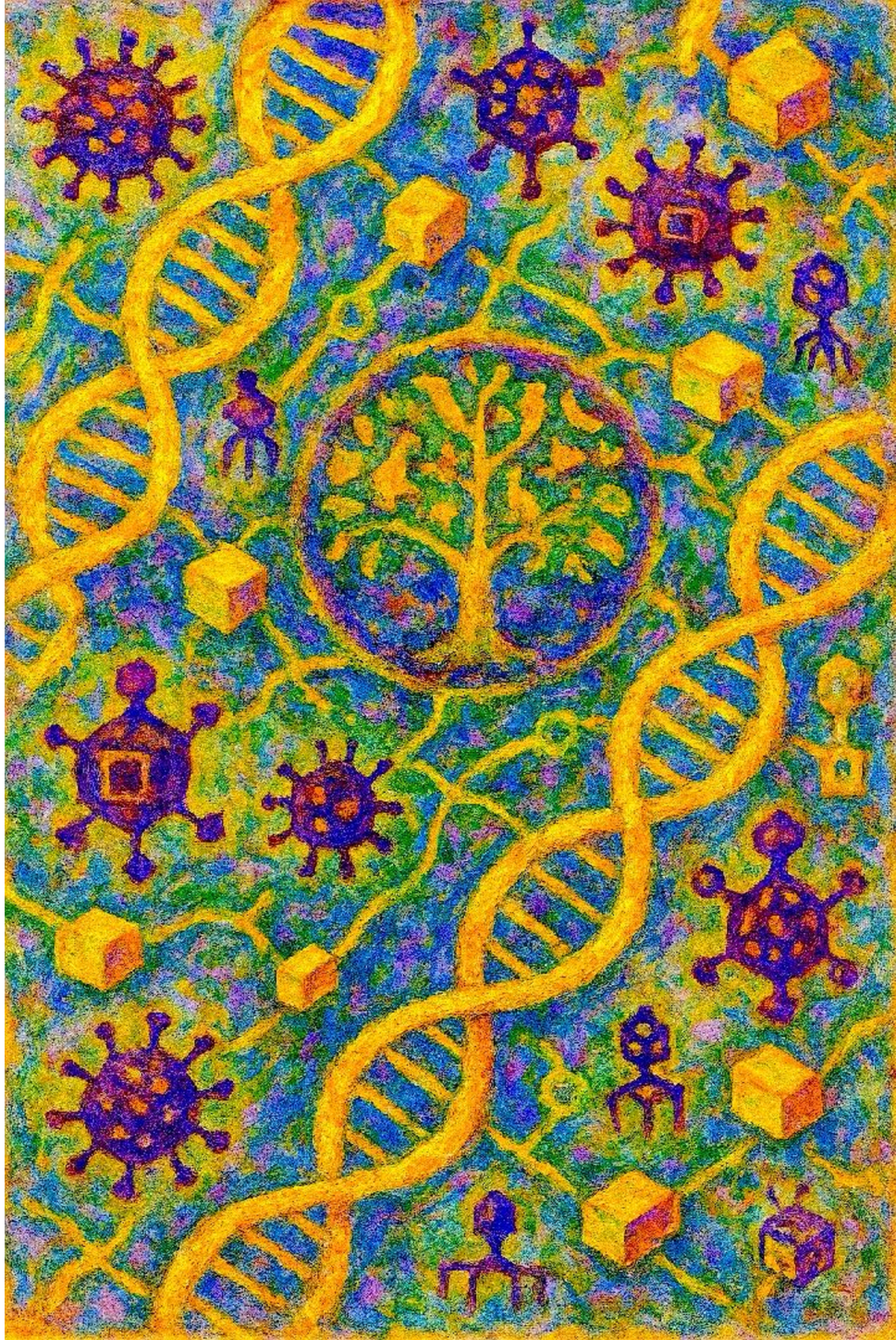
Natural Viral Engineering:

Viruses are not just pathogens that make us sick—they are also powerful tools that help life evolve.

Viruses don't act alone, or randomly. They work together with host cells, which rewrite and edit viral genes.

Just as people share and improve ideas in open-source software, cells and viruses share and improve genes across different forms of life.

Evolution is not driven by random changes, but teamwork, communication, and problem-solving between living things and the viruses they interact with.



Thanks to…

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