

Source: [KBBiologyMasterIndex](#)

## 1 | Overview of Human Diseases

A lecture by the Legendary Dr. Paul Hauser. Slides are here  
#flo #disorganized

### 1.0.1 | Viral Genetic Shift + Viral Genetic Drift

**Shift** => whole segments of genome exchange abruptly as two flu viruses infect the same cell to create a new strand.

**Drift** => single/groups of nucleotides flip slowly over time.

The former is an environment-dependent process, where the latter is able to be modeled as it is due to transcription mistake.

### 1.0.2 | Retroviruses + How to Stop Them

**Viruses that have the ability to intergrate into the chromosomes of the host cell**

#### Early Events

- Viruses is uncoated, and uses an enzyme called reverse transcriptase to turn ssRNA to cDNA, and finally into dsDNA
- Then, the enzyme integrase threads the viral dsDNA into the cell's nucleus
- HIV protease cuts HIV polyproteins into individual parts ready for budding

#### Late Events

- Proviral region is transcribed slowly whenever ribosome comes across it by the host DNA polymerase II to make viral proteins + replicate the viral genome
- Components are later exported, assembled, and slowly released through budding

To make this happen, the virus needs...

- **Reverse Transcriptase**
  - Transcript RNA to double-stranded RNA
  - Take double-stranded RNA to turn into DNA
- **Integrase**
  - Force insert the DNA into the genome of the host cell

And because of the fact that viral DNA is now in cellular DNA, these viruses' DNAs are hard to get rid of.

And this is why we can't cure HIV.

Virus, in this case, spread through cell duplication

- Proviral region on the DNA, every time the ribosome comes across it, makes a new viron
- These components are then assembled, sent, etc. as usual

- Because of the fact that the ribosome needs to, well, come across the bit of DNA for this to work, the virions are made slowly by "trickling out."

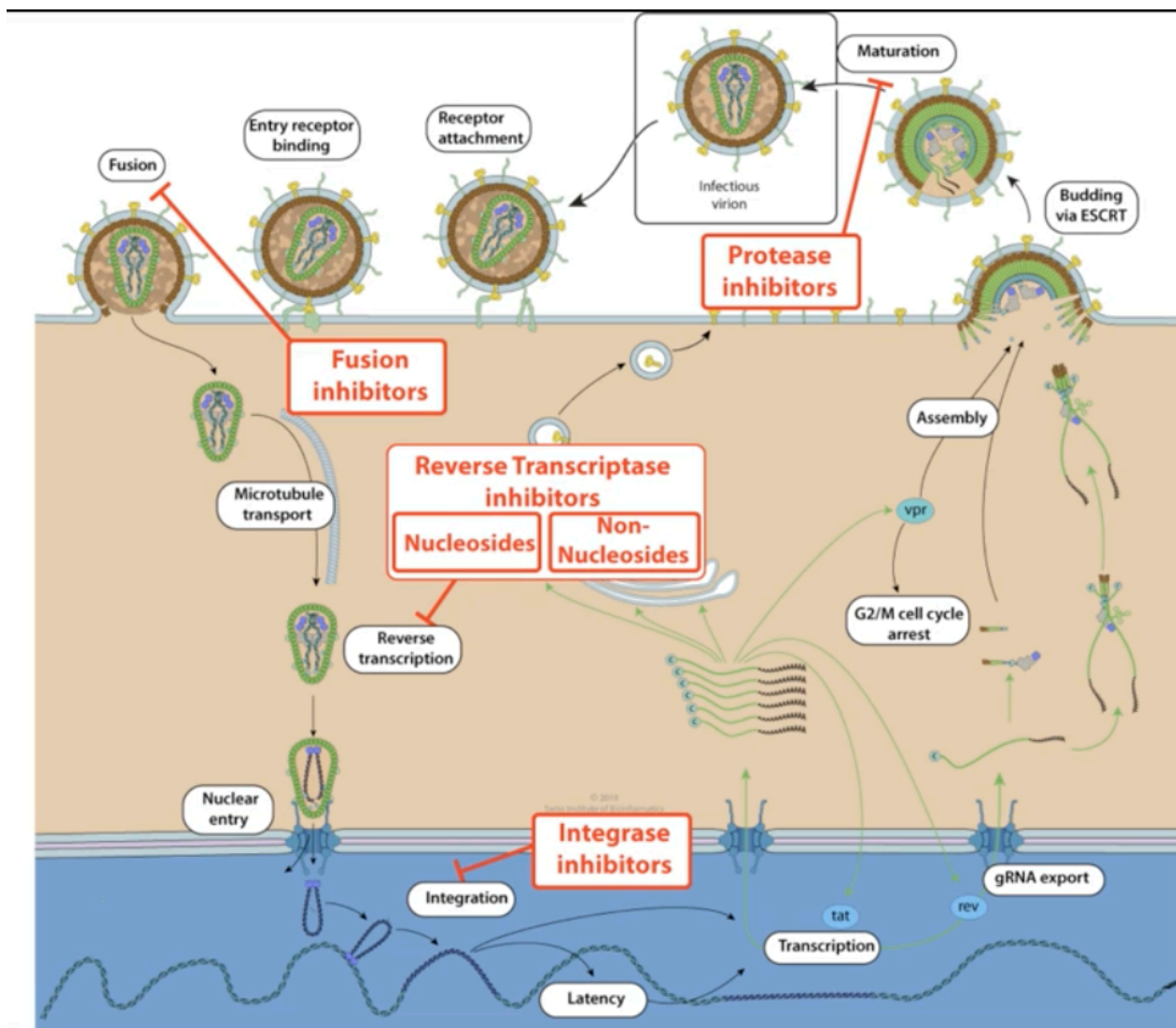


Figure 1: Screen Shot 2020-10-12 at 11.22.35 PM.png

## Preventing Retroviruses

- Prevent Fusion gp120, gp41, CCR5
- Prevent reverse transcription RT
- Prevent intergration via intergrease IN
- Prevent viron maturation PR

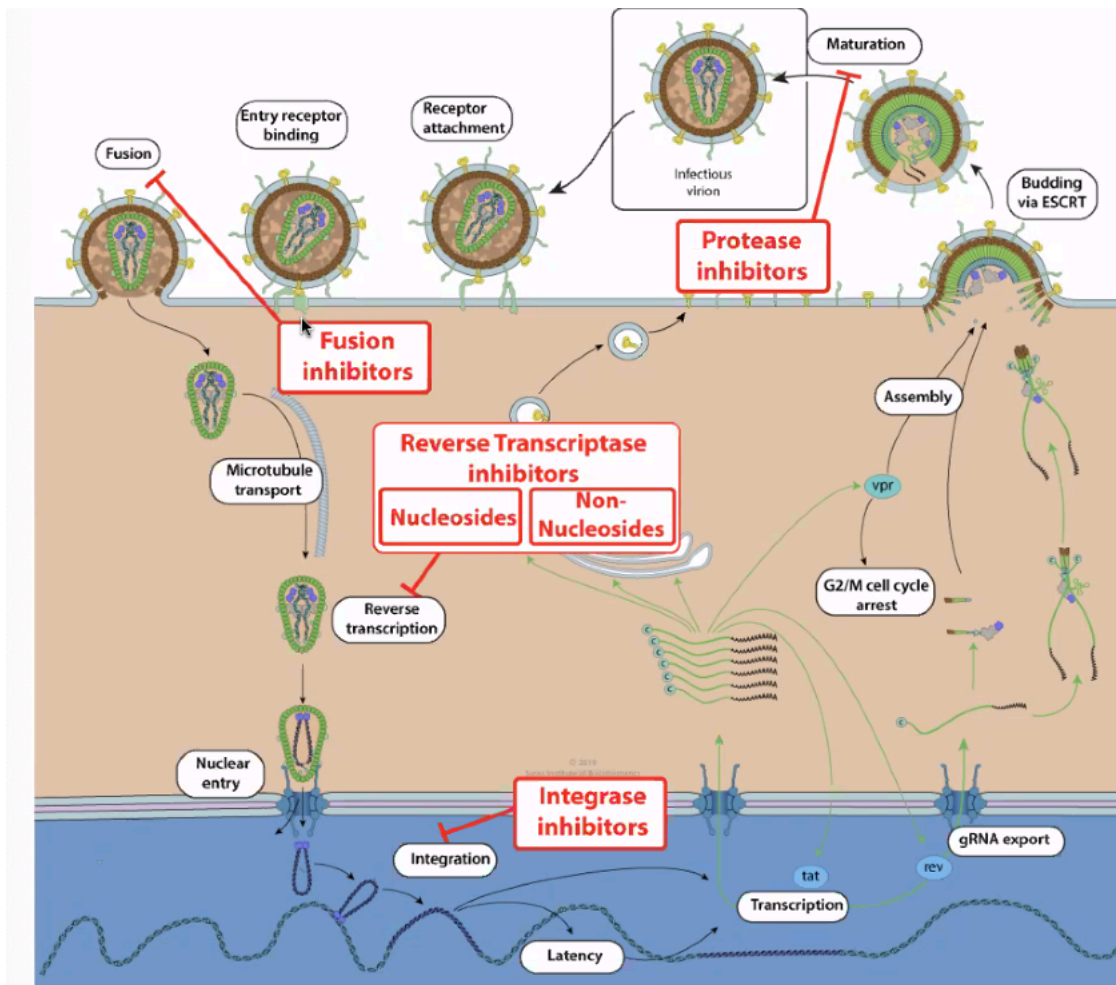


Figure 2: stophiv.png

- Most advanced: HAART (Highly-Active Anti-Retroviral Therapy)
  - Cocktail drug works together for inhibition
  - Two drugs to stop intergration, one to stop protease (viron maturation)
  - Could develop resistance

### 1.0.3 | Viral Genome vs Mutation Rate

## Viral genome size vs. mutation rate

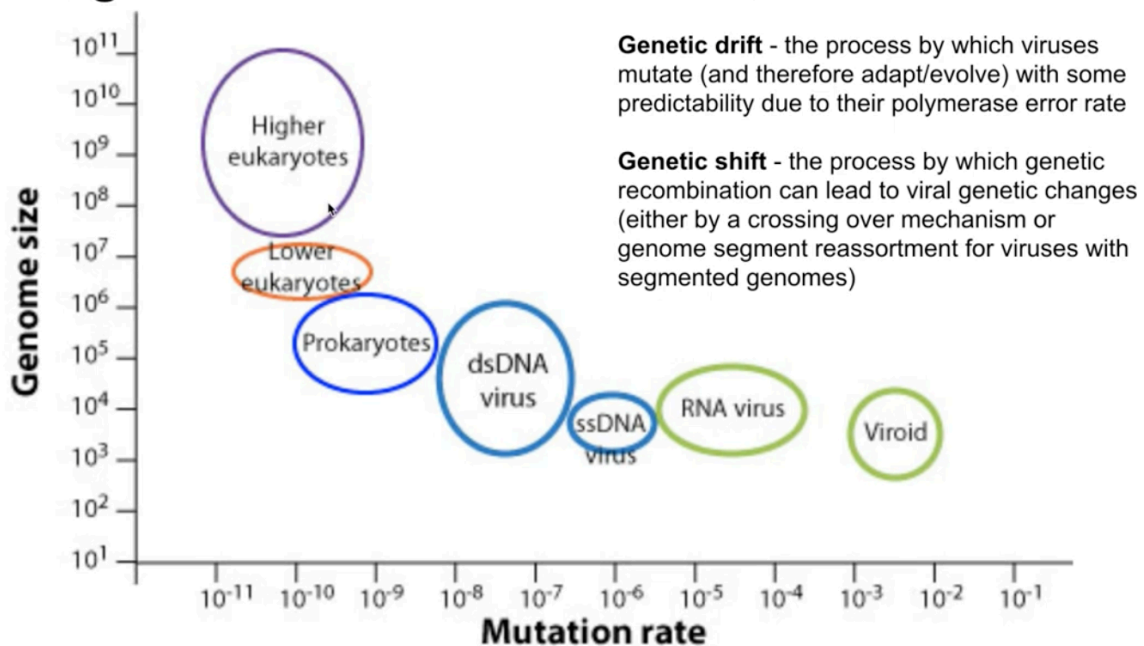


Figure 3: Screen Shot 2020-10-12 at 11.24.39 PM.png

- RNA viruses could mutate more because it does not have checks
- More complex+largest viruses harder to mutate

**Genetic drift** — viruses mutate due to polymerase error

**Genetic shift** — viruses recombine without mutating by crossing-over mechanism or genome segment reassortment. Think! the flu

### 1.1 | Why are viruses bad

Damage host cells/tissues by...

- Reducing gene expression capacity
- Depleting cellular resources
- Causing cell lysis (to explode)
- Promoting tumorigenesis — cancer
- Creating damaging immunological response

### 1.2 | Preventing Viruses

Let's talk about **Remdesivir**! A drug developed by Pfizer that's used to combat Ebola + influenza viral replication.

Modified nucleotide triphosphate which adds onto the RNA strand copied by the RNA-Dependent RNA Polymerase carried by viruses

- Pretends + gets inserted as a nucleotide
- Once added onto the RNA chain, jams further actual nucleotides from being inserted

*Could* but usually does not jam up normal RNA polymerase which does normal transcription

- Inhibiting transcription in the short term won't kill you immediately
- So, we hurt normal cell transcription a little in order to rid of the virus
- Need hospital treatment for regular and safe dosing for this exact reason
- Viral proteins are usually easy to assemble

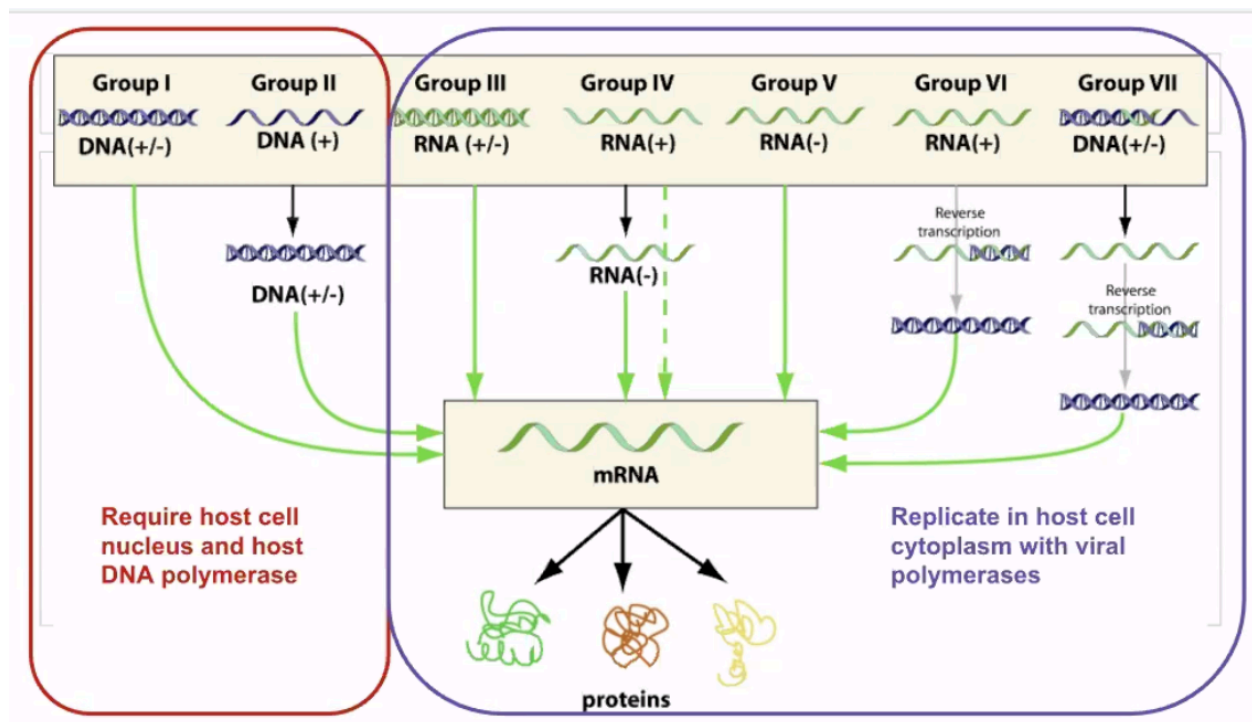


Figure 4: Screen Shot 2020-11-02 at 2.48.22 PM.png

#### Question: how are proteins made in the viral genome

- No viruses produce ribosomes
- Ribosomes become centrally important for the virus
- What serves as the template to make new virus copies

Viruses attempt to overwhelm the enzyme to entry.

**DNA** viruses are "less complex", in that as long as they are able to get into the nucleus, the rest would just be the body's work automatically.