Source: KBBiologyMasterIndex

1 | Overview of Human Diseases

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

#flo #disorganized

1.0.1 | 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 nucleaus
- 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 virons are made slowly by "trickling out.

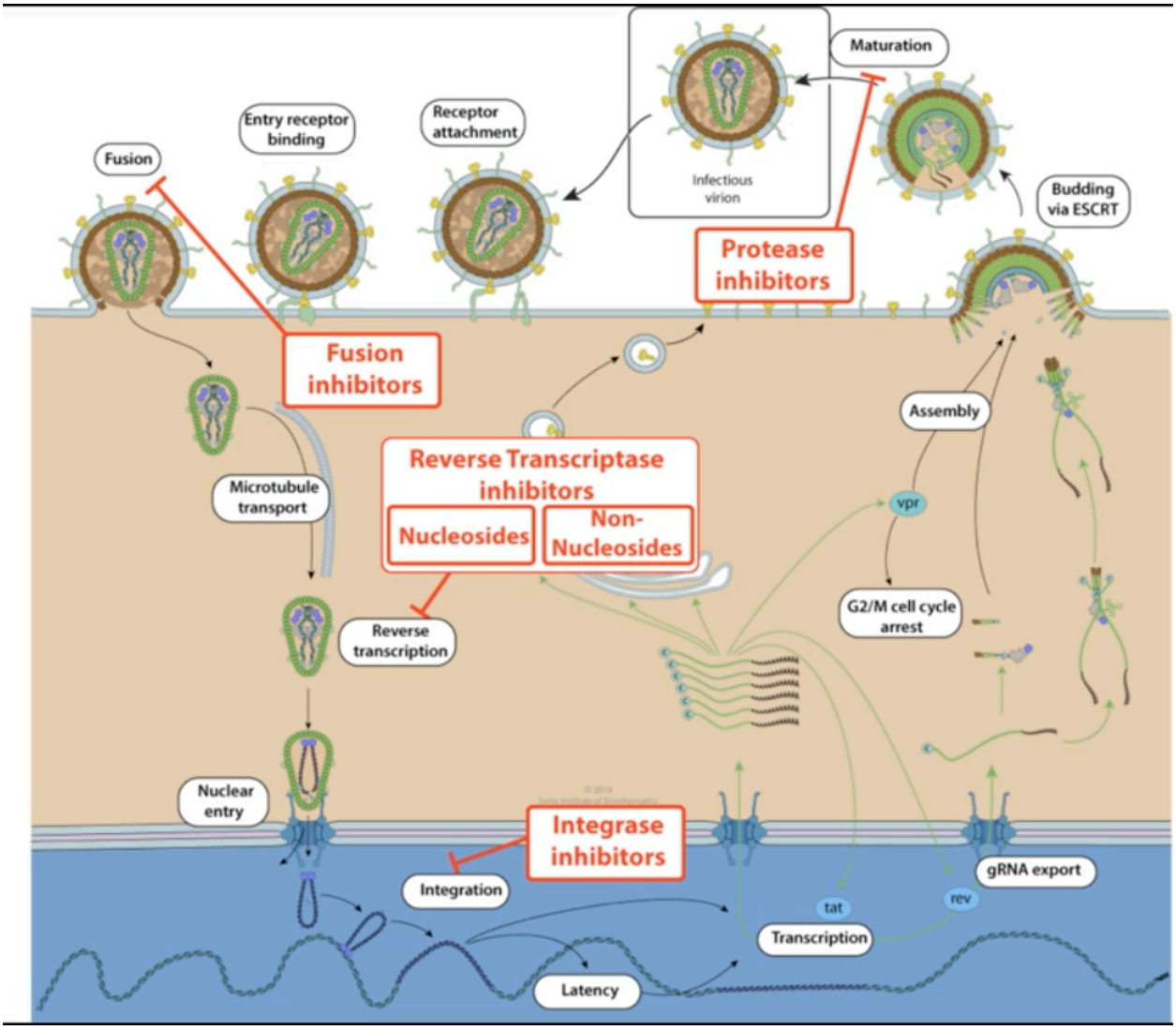

Figure 1: Screen Shot 2020-10-12 at 11.22.35 PM.png

Preventing Retroviruses

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

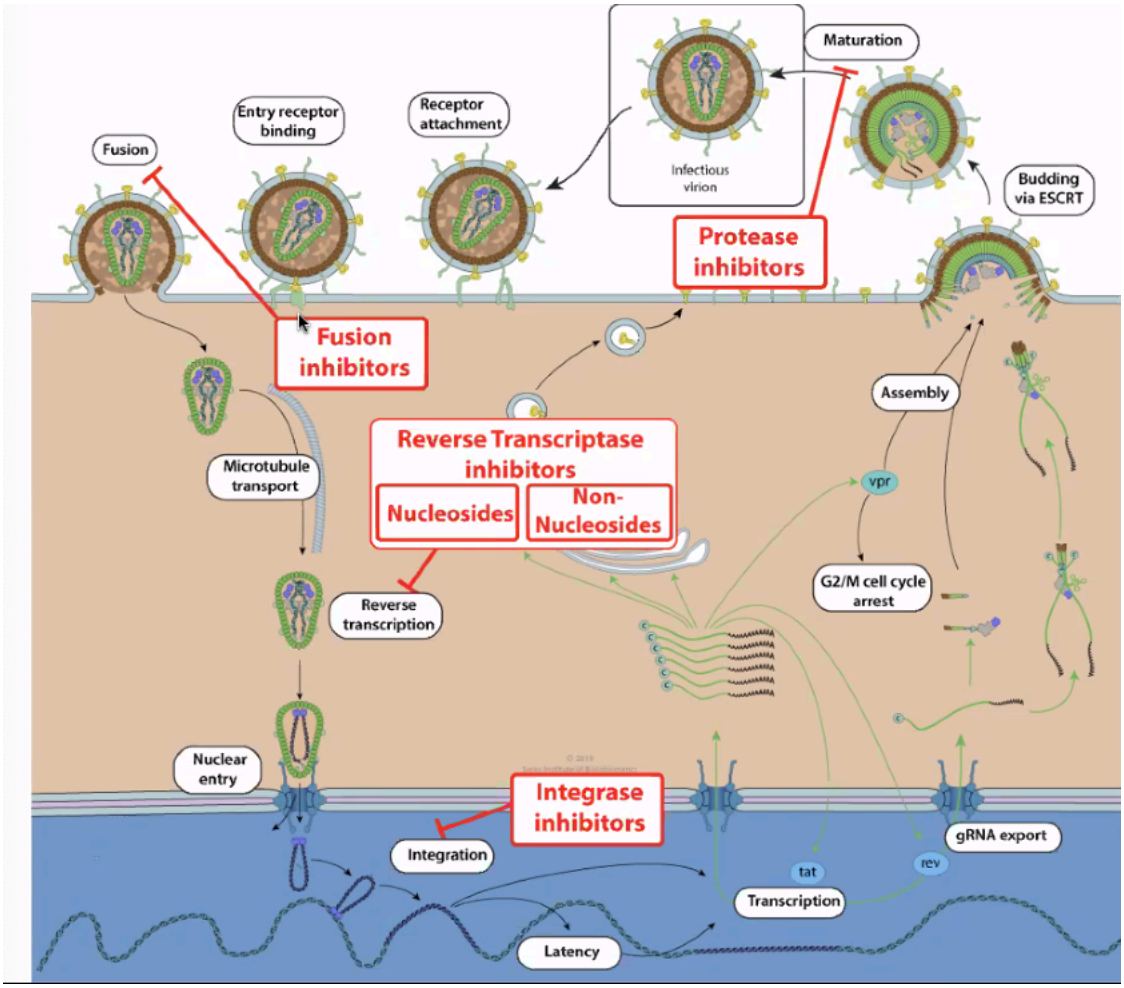

Figure 2: stophiv.png

- 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

1.0.2 | **Viral Genome vs Mutation Rate**

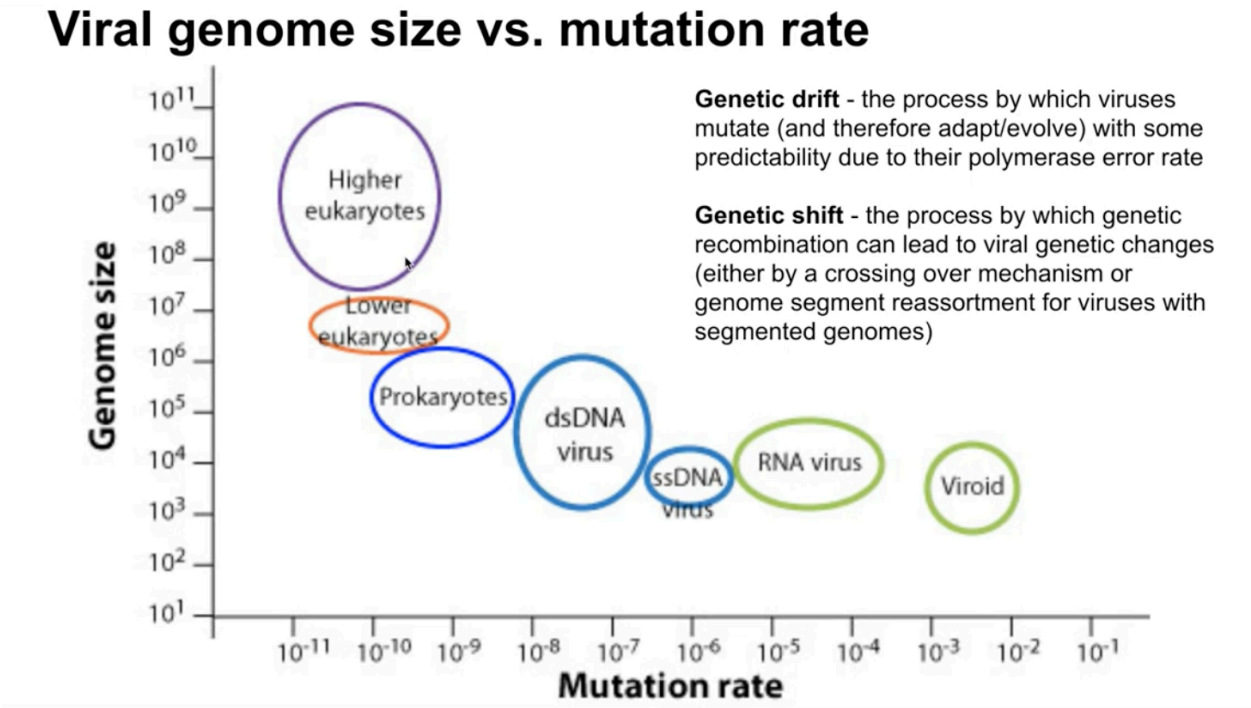

Figure 3: Screen Shot 2020-10-12 at 11.24.39 PM.png

- 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 recombinate 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 tumorigenisis — 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

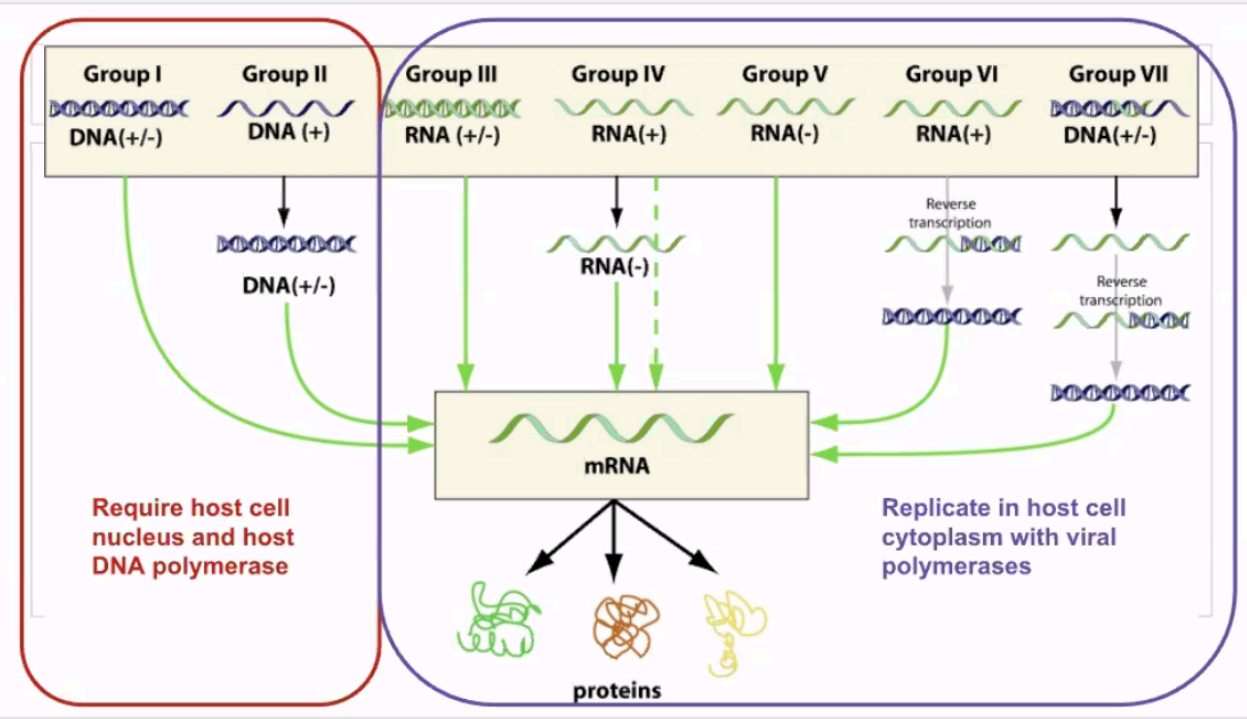

Figure 4: Screen Shot 2020-11-02 at 2.48.22 PM.png

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 nucleaus, the rest would just be the body's work automatically.