A Coronavirus Explainer

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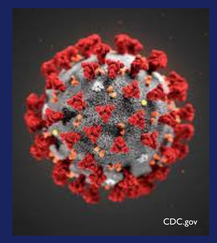

Introduction

As a professor or Microbiology, Biotechnology and Immunology here at Salem State, I've been following COVID-19 quite closely, and communicating the details to my students. Here is a brief coronavirus explainer during the time of the pandemic.

Biology of the Virus

A virus, from the Latin for 'poison', is an obligate intracellular pathogen of all types of cells.

- Obligate: an absolute requirement
- Intracellular: inside cells
- Pathogen: something that gets inside another organism and causes damage

A virus can only reproduce when it is inside a cell. All living organisms are made up of cells, and therefore all may fall victim to a virus.

All populations are subject to the limitations of their environment. Viral Ecologists study the roles viruses have in interacting with their hosts and in controlling population size. In marine ecosystems, when there is a cyanobacterial or algal bloom due to nutrient rich run off, viruses are critical in bringing the population back to normal levels. A keen observer of viral ecology may note that this pandemic is controlling an over large human population. Agent Smith in 'The Matrix' couldn't understand why humans in his fictional dystopia could not live in a balance with their environment.

Figure 1: Hugo Weaving as Agent Smith in 'The Matrix' 1999.

COVID-19 (Coronavirus Disease-2019) is caused by a virus called SARS-CoV-2

To be a virus you need these things…

- GENOME: the code or instructions for copying yourself.
- CAPSID: Holder for the genome as protection while travelling between host cells.

The genome of all viruses is made up of nucleic acids. Human nucleic acid is called DNA (deoxyribonucleic acid) and is about 3 billion (3×10^9) base pairs in linear segments. All cells on earth have genomes made up of DNA. Viruses have evolved some diversity in the types of their genomic material, and coronavirus has an *RNA genome*.

All viruses need their host cell resources and machinery to make copies of themselves. The *central dogma of biology* states that all *cells* reproduce and build cellular components in the same way: they have a genome of DNA that is the blueprint for the building of the cell, and translate the code into the biological molecules (proteins) through an intermediate signal called RNA (ribonucleic acid).

DNA → mRNA → protein

– *The DNA genome must also copy itself before a cell can divide. That process is called replication.*

Since viruses are made up of a genome and a capsid they use host cell processes to make copies of their genome and their capsid proteins. Their nucleic acid genome codes for the capsid proteins and any control proteins they use to take over the cell's biosynthetic machinery.

Before they can start making copies, they have to get into their host cell. There is a lock-and-key relationship between a virus and it's host cell. If a given cell does not have the receptor (lock) that fits the virus (key), entry into the cell will not occur.

All viruses have this basic 'life cycle'. 'Life' is in quotes, because we defined life as being made up of cells. A virus is 'sub-cellular' because although it has a genome, and sometimes a membrane, it lacks ribosomes. That's why it has to get in to a cell to reproduce. Perhaps 'replication' would be a better term!

The Viral Replication Cycle

A mnemonic for remembering the generic replication cycle is: APBAR.

- Attachment or Adsorption (specific recognition of host cell)
- Penetration (of the genome into the host cell)
- Biosynthesis (using the host cell machinery to copy the genome and synthesize viral proteins)
- Assembly (of the nucleocapsid - the genome surrounded by the viral proteins)
- Release (the virus leaves the cell by killing the cell - *lysis* - or by draping itself with the host cell membrane - *budding*)

Some viral genomes can integrate into the host cell genome and 'hang out', or not direct the synthesis of viral proteins. In bacteria, this is called LYSOGENY, in eukaryotic cells it is called LATENCY, and herpes and HIV are examples of latent viral infections.

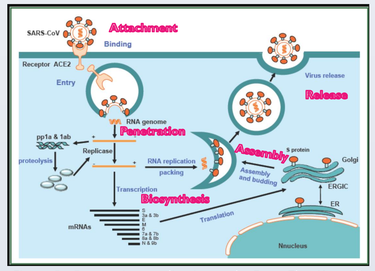

Figure 2: Coronavirus replication cycle. From Zhu, X., etal[5].

Epidemiology of the Virus

Epidemiology is the study of how a pathogen moves through a population.

In order to control a pathogen, you must know:

- **Reservoir** (where it came from or where it hangs out between hosts)
- Portal of Entry and Portal of Exit (how it gets in and out of the host)
- **Transmission** (how it gets between hosts)

SARS-CoV2 is called a **zoonosis**, because it came into the human population through animals. No, the conspiracy theory that it is from a lab in China is most likely false. A genetically modified virus leaves traces that are absent from SARS-CoV-2.

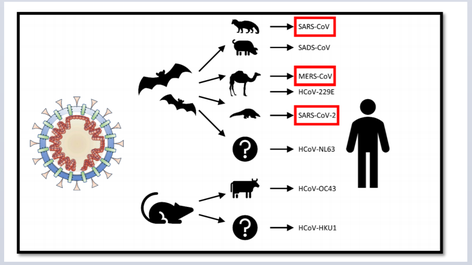

Figure 3: Origin of SARS-CoV-2, from Rabi, et. al. 2020

Transmission of SARS-CoV-2 is through respiratory droplets

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Immune Response to the Virus

The human immune system is exquisitely complicated, and science and medicine are still learning a lot about how it works. Coronavirus is called a NOVEL virus because of its zoonotic nature, and since it is new to circulating in the human population, there is no immunologic memory and no herd immunity.

Your immune system is an army of evolutionarily captured amoebas that surveil your body for what is you, and what is not you. They travel through the entire body, in the blood and lymph circulation and in the tissue spaces, looking for things that don't belong. When they do find something that doesn't belong, they mount an attack to remove it.

The immune system is often described as having redundant lines of defense to invading pathogens: anatomical and chemical **barriers**, the **innate**, non-specific immune system, and the specific and **adaptive** immune system.

The innate system includes familiar responses that make us suffer the consequences of an infection like *inflammation* and *fever.* The innate system responds the same way to a virus or other cellular microbes.

The adaptive system is specific to the invading microbe, and has a ***memory*** response, responding faster and better the second time the microbe is encountered.

Immunologic Memory: The thing that we do not have because we haven't seen this virus before, and the basis for why immunization works. The adaptive immune system has two arms known as cell-mediated immunity(CMI) and humoral immunity. CMI is designed to kill virus-infected cells before they can make more virus. Humoral immunity is all about proteins made by B cells called antibodies. Antibodies are proteins that have a range of functions in the body, not the least of which is to **neutralize** virus particles, or stick on them and prevent their entry into a cell.

Creation of antibodies takes TIME, and the development of a vaccine must be tested for both ***safety*** and ***efficacy*** before being scaled up to the millions of doses that will be needed to protect everyone. Since SARS-CoV-2 is in a group of viruses that has been circulating as an agent of the common cold, the testing for it has to be ***validated*** as being specific to SARS-CoV-2, and not one of its more innocuous relatives. Clinical trials and manufacturing are being done simultaneously with several candidates in the hopes of shortening the typical timeline, in which vaccine development can take years. The goal of a good vaccine is to elicit ***neutralizing antibodies***.

Testing for the Virus

Viral Genome: The first testing that was done was for the viral RNA genome. The testing uses primers that are unique to SARS-CoV-2, and early stumbles in validating the specificity of the probes lead to a slow roll-out. The detection process, RT-qPCR, requires handling, expensive equipment, and reagents beyond standard PCR (polymerase chain reaction), and takes 24-48 hours to turn around.

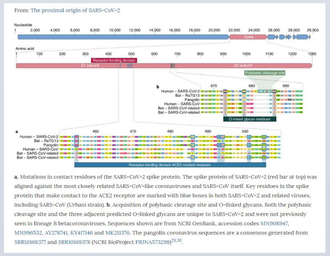

Figure 4: Sequence of the SARS-CoV-2 Spike Protein. From Andersen et. al. 2020.

WBUR.org

Neutralizing antibodies: This cassette looks for both IgG and IgM. Neutralizing antibodies are IgG, and demonstrate previous exposure to and recovery from the infection. Roll out of these tests has also been plagued with specificity problems.

Therapies for Active Infection

A therapeutic is an intervention in an ongoing infection. Antiviral therapies can only hope to shorten the duration of the suffering, and most must be administered by a qualified healthcare professional. The WHO is carrying out a program of clinical trials called SOLIDARITY to test the safety and efficacy of these possible therapies. The various possibilities and where they interrupt viral replication are in the accompanying figure.

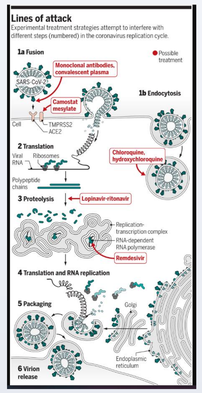

Figure 5: *Science* Apr. 2, 2020[8].

Staying Safe: Follow CDC Guidelines

Everyone Should:

- Wash your hands often with soap and water for at least 20 seconds especially after you have been in a public place, or after blowing your nose, coughing, or sneezing.
  - If soap and water are not readily available, **use a hand sanitizer that contains at least 60% alcohol**. Cover all surfaces of your hands and rub them together until they feel dry.
  - **Avoid touching your eyes, nose, and mouth** with unwashed hands.
- **Avoid close contact** with people who are sick
  - Put **distance between yourself and other people**.
    - Remember that some people without symptoms may be able to spread virus.
    - Keeping distance from others is especially important for people who are at higher risk of getting very sick.
- Cover your mouth and nose with a cloth face cover when around others
  - You could spread COVID-19 to others even if you do not feel sick.
  - Everyone should wear a cloth face cover when they have to go out in public, for example to the grocery store or to pick up other necessities.
  - The cloth face cover is meant to protect other people in case you are infected.
  - Do NOT use a facemask meant for a healthcare worker.
  - Continue to keep about 6 feet between yourself and others. The cloth face cover is not a substitute for social distancing.
- Cover coughs and sneezes
  - **If you are in a private setting and do not have on your cloth face covering, remember to always cover your mouth and nose** with a tissue when you cough or sneeze or use the inside of your elbow.
  - **Throw used tissues** in the trash.
  - Immediately **wash your hands** with soap and water for at least 20 seconds. If soap and water are not readily available, clean your hands with a hand sanitizer that contains at least 60% alcohol.
- **Clean AND disinfect frequently touched surfaces daily**. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks.

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