

LESSON 8(b): POLIO-- AN RNA VIRUS

Polio is a “naked” (no envelope) positive sense (+) RNA virus, and is a member of the “Picorna” family, one of the Group 4 viral families in the Baltimore classification system. Other members of the Picorna family include rhinovirus (common cold) and Coxsackie B. (Coxsackie is always capitalized because it is named after Coxsackie, New York, where it was first isolated.) There are two stories about the name “Picorna.” One says that each letter stands for one of the original viruses put into this group. The other idea is that “pico” means “small” and “rna” stands for “RNA.” This would suggest that all the viruses in this group have small RNA genomes (less than 10,000 base pairs).

Polio can also be classified as an “enterovirus” because it enters the body through the digestive system and attaches to the cells that line the intestines. After they replicate and make billions more of themselves, the virions eventually get into the blood. In about 1% of people infected with polio, the virus will begin invading nerve cells called motor neurons. The bodies of these cells are located in the spinal cord. Whenever there is inflammation in the spinal cord, this is called myelitis (mi-eh-LIE-tis), so when polio gets into the spine we call the disease “poliomyelitis.”

Since polio has RNA(+) and reads the same as mRNA, it doesn’t go into the nucleus and it doesn’t bring any of its own tools. The genome is small and the capsid is small, too, only about 30 nanometers. Polio has been heavily researched for decades and its genome was completely mapped back in the early 1980s. That means they made a list of every A, U, C and G, and had a pretty good idea of which parts of the code made certain proteins. Of course, you remember from lesson 3 that Jonas Salk made a vaccine in 1955. A researcher named Albert Sabin perfected the vaccine in the 1960s, making it even more effective.

Here are the stages of polio virus infection of a cell:

- 1) Attachment to Poliovirus Receptor (PVR) also known as CD155.
- 2) Entry and uncoating--the RNA goes into the cytosol. (Some diagrams show this happening at the surface, other diagrams show the virion inside a small endosome.)
- 3) Ribosomes read the polio RNA like it is a cellular mRNA, and a very long protein chain is made. This “polyprotein” chain contains all the virus’s proteins in one long line.
- 4) Two of polio’s proteins are proteases (“scissors”) and will cut the polyprotein into its smaller units.
- 5) Host Shut Off: One of the scissors is the right shape for snipping an important cellular protein tool (“EIF4G”), which is the first protein to attach to a mRNA. A group of tiny proteins has to cooperate to make a big clump that is just the right shape to stick to a ribosome. If you get rid of the first protein, the rest won’t attach and no mRNA will be translated. This prevents the cell from making its own proteins.
- 5a) But wait-- if polio just got rid of all the starter proteins for using a ribosome, then how is polio going to use the ribosomes? Turns out that one section of the polio RNA will coil up into a 3D shape that will mimic the shape of that group of starter proteins, and the ribosome will be fooled into attaching to the polio RNA! (If you want to know more about this topic, you can search using the term IRES, which stands for Internal Ribosomal Entry Site).
- 6) Formation of “replication complexes”: As the cell becomes stressed its ER and Golgi bodies lose their shape and turn into small blobs (vesicles). The polio RNA polymerase (“RdRp”) copy machines will attach themselves to the edges of these vesicles and then start making gazillions of copies of the polio genome. The original genome is positive sense, so it takes two rounds of copying to produce a new genome. (POSITIVE copies to NEGATIVE, which copies back to POSITIVE)
- 7) Ribosomes start manufacturing polio capsids and new virions assemble themselves.
- 8) The cell ruptures (this is called “lysis”) and all the new virions exit.

Poliovirus is being used to treat a very difficult form of brain cancer. The brain tumor cells happen to express CD155 on their surface, whereas normal brain cell don’t. That gave some researchers the idea to use poliovirus to destroy those tumor cells. They cut and pasted a different IRES area into some polio viruses, using an IRES from another Picorna virus-- the rhinovirus (common cold). The adapted polio (with the rhino IRES) would be unable to cause an actual polio infection in the patient receiving the treatment, but the virus would attack the tumor cells. The immune system would then be alerted to the need to destroy those bad cells and they would start helping to destroy the tumor cells. This treatment has been successful in several patients.

