



CELL CULTURES: A LABORATORY TOOL FOR STUDYING VIRUSES

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YOUNG REVIEWERS:



ARYAN
AGE: 12



PABLO
AGE: 15



PRANJAL
AGE: 11



SANAYA
AGE: 14

When you hear the word virus, you might think of diseases like rabies, influenza, or COVID-19. Viruses are organisms that must infect living cells to reproduce. Studies done on cells grown in the lab, called cell cultures, have contributed significantly to our understanding of viral diseases and to the development of treatments and vaccines. In the laboratory, cells can be grown in layers or in three-dimensional systems. By infecting cell cultures with viruses, scientists can study various aspects of the infection, such as how the virus gets into the cells or how the cells respond to infection. Knowledge gained from infecting cell cultures with viruses has helped scientists to vastly improve human health!

INTRODUCTION

Do you remember being sick with the flu, or maybe having a blister on your lip? You probably know that the flu is caused by the influenza

HOST

Any organisms infected with a virus.

CELL CULTURE

Group of cells grown up into a culture dish in a laboratory.

TROPISM

Ability of a virus to choose the right cell to multiply. A virus can infect several types of cells.

RECEPTOR

Molecule produced by cell able to stick to viruses allowing them to enter the cell.

virus, but did you know that lip blisters, often called cold sores or fever blisters, are also caused by a virus called herpes virus? Viruses are also responsible for diseases like measles, smallpox, COVID-19, and hepatitis. People are likely to become ill if they come into close contact with infected individuals or, in rare situations, animals.

The organism that is infected by a virus is called the **host**. Viruses infect the cells of various organs in the host's body, such as the skin, lungs, or liver. Viral infection can cause our bodies to stop working properly, which makes us feel sick. Some viruses can be prevented by vaccines, and for certain viruses, doctors can give us medicines that help us to feel better. Have you ever wondered how scientists develop treatments and vaccines against viral diseases? To study viruses, scientists frequently grow cells from the human body in the laboratory, a process known as **Cell culture** [1]. Cell cultures can be infected with the virus scientists want to study, which can help them to learn a lot about a virus, including how to prevent or treat it.

WHAT ARE VIRUSES AND WHY DO THEY INFECT US?

Viruses are smaller and less complex than cells. They are primarily made up of a protein "shell" surrounding their genetic material (RNA or DNA). All the information required to make more viruses is encoded in their genetic material. Proteins perform several functions, including protecting the genetic material from the environment. Cells, on the other hand, have sophisticated machinery that allows them to make copies of their genetic material and to build proteins from it. Because viruses lack this machinery, they must infect cells before they can produce more viruses from their genetic material.

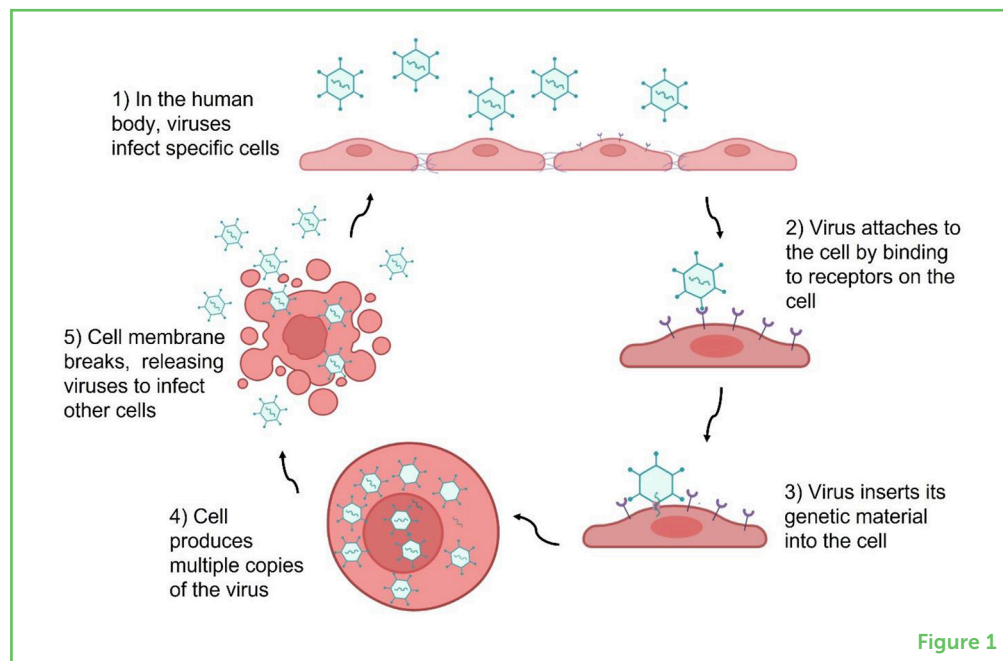
The ability of a certain virus to infect only specific cells, tissues, or animals is known as **tropism**. For example, the flu virus mostly affects the respiratory tract and only rarely attacks other organs. Certain features of the host's cells or tissues, including the presence of proteins called **receptors** on the surface of cells, affect tropism. Viruses recognize and stick to certain receptors, like a lock and a key—this helps the viruses to get inside of certain cells. It is important to note that a key cannot open all locks, just like a virus cannot infect all cells—only the ones with the right receptor.

The genetic material of the virus can be read by the machinery of host cells, resulting in massive production of viral proteins and genetic material, which is used to assemble more viruses. In this way, an infected cell becomes a virus factory. The cell membrane eventually bursts, releasing new viruses to infect new cells. As a result, the virus spreads throughout the body (Figure 1).

Upon infection, host cells release specialized proteins that warn other cells, including those of the body's defense system, that a virus

Figure 1

Viruses multiply within host cells. **(1)** Viruses enter the body and **(2)** infect specific cells by sticking to receptors on those cells. **(3, 4)** Once the virus's genetic material is inside the cell, the cell makes many copies of the virus. **(5)** Eventually, the cell breaks open and viruses are released and can infect other cells.



is present. These protein signals prepare the body's cells to fight infection. Infected people can spread viruses to others, for example, through saliva or blood. Some viruses can also persist for a short time on non-living surfaces like clothes or door handles.

HUMAN CELLS CAN BE GROWN IN THE LABORATORY

Researchers can grow and study almost any type of cell in the laboratory, to understand its functions and behavior outside of the human body [2]. To accomplish this, a tissue sample must first be taken from a person and chopped up into smaller pieces. The tissue fragments are then treated with chemicals that break down the substances that surround the cells and hold them together. The cells are then spread out in a culture dish, or a special bottle called a tissue culture flask (Figure 2). Many cells die during the isolation procedure, but the cells that survive and attach to the plastic of the culture flask get most of the substances they need to grow from a nutrient-rich liquid called **culture media**, which scientists add to the cells. Cultures are typically incubated at 37°C, which resembles human body temperature. Cells are examined under the microscope daily to ensure they are in good condition and free of common contaminants like bacteria or yeasts. Some types of cells can now be purchased along with instructions for growing them in the lab.

Cells cultured in the laboratory often grow by forming a thin sheet called a **monolayer** attached to the surface of the culture flask. However, to create an environment that is more like body tissues, three-dimensional (3D) cultures are often used. In a 3D culture, the cells grow inside a gel that can be made of various molecules (i.e.,

CULTURE MEDIA

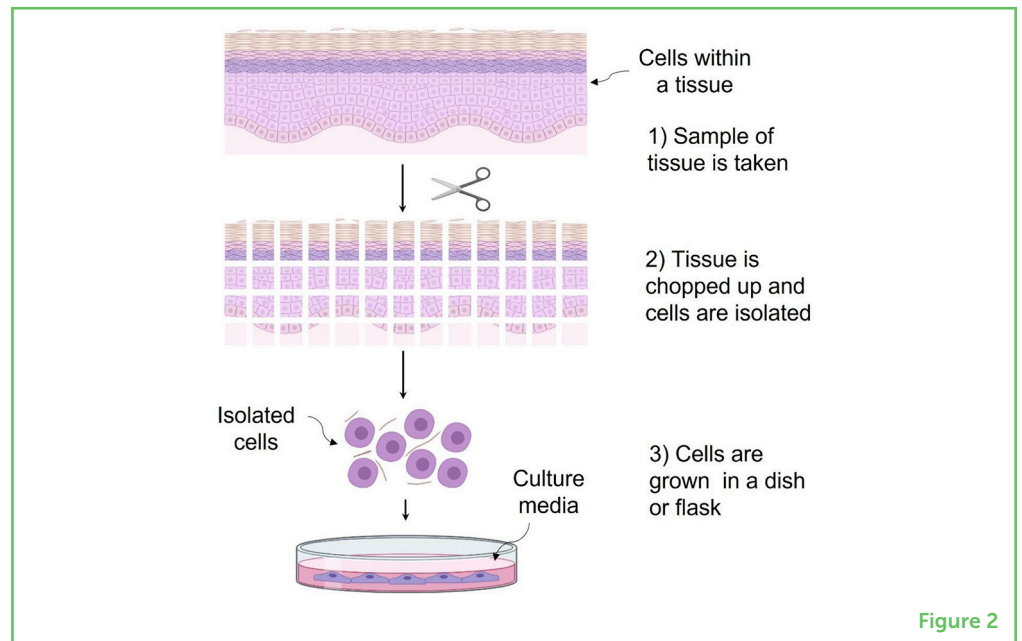
Mixture of nutrients, usually in liquid form, used to nourish cells.

MONOLAYER

Cells in a dish growing side by side to another filling all available surface in the dish.

Figure 2

(1) To create a cell culture, a tissue sample is taken from a person. **(2)** Scissors and a scalpel are used to chop up the tissue sample. Chemicals are also added to help separate cells. **(3)** Once the cells are released from the tissue, they are placed in a culture dish or flask with some nutrient-rich culture media, at 37°C.



HYDROGEL

Polymer chains arranged in a three-dimensional network that can hold a lot of water.

ORGANOIDS

Cells grown in a dish able to organize in a similar way as complex organ.

proteins) found in actual tissues [3]. These 3D cultures, known as **hydrogels**, behave more like actual tissues than monolayer cultures do, and they are also susceptible to viral infections.

Complicated 3D cultures called **organoids**, are generated from cells that can self-organize to mimic some characteristics of complex organs such as the liver, kidneys, lungs, or intestines. The organ-like structure of organoids improves viral tropism and increases the likelihood of viral infection.

In general, cell culture makes it possible to study multiple aspects of viral infection and to develop treatment strategies and vaccines.

HOW DO SCIENTISTS STUDY VIRUSES IN THE LABORATORY?

Animals can also be used to study viruses in the lab. The choice to use animals or cell cultures depends on the type of virus being studied and the purpose of the study. For example, cell cultures are good for studying the multiplication of viruses. For SARS-CoV-2, the virus that causes COVID-19, the cell cultures allow researchers to study the type of cells that the virus can infect and the kind of damage the virus can cause to those cells. Researchers can also observe what happens when multiple viruses infect cells at the same time, as can happen when people are infected with both SARS-CoV-2 and influenza or hepatitis viruses.

Furthermore, infecting monolayer cell cultures allows scientists to produce vast quantities of viruses, for use in vaccine development or

in the creation of treatments against viral diseases [4]. For example, poliovirus was one of the first viruses grown in cell culture and used to develop a vaccine. Poliovirus causes a dangerous disease called poliomyelitis, which, in severe cases, can result in paralysis of the legs, arms, and muscles that help control breathing. Thanks to cell culture, researchers can keep developing new vaccines, including some against SARS-CoV-2 [1].

3D cultures can be used to grow and study viruses to mimic infection in more realistic environment than in a monolayer. Organoid cultures grown from intestinal cells can be used to study the replication of rotavirus, a virus that causes severe diarrhea in infants. Also, brain organoids have been used to study Zika virus; this is important since Zika causes brain malformations in unborn babies when their mothers are infected with the virus. Virus such as papilloma, which cannot grow in monolayer cultures, have been successfully grown in 3D cultures. This virus is involved in the development of cervical cancer by infecting skin cells and even cells of the body's defense system. 3D cultures can also help researchers to understand some of the communication strategies cells use to defend themselves against infection [5].

CELL CULTURES COULD HELP SAVE LIVES

Controlling viral diseases is one of the most important public health challenges that humanity faces. In this fight against viruses, cell cultures are an important tool for understanding the mechanisms by which viruses infect cells and cause disease. Cell cultures can also help researchers to develop vaccines and other treatments for viral infections. The next time you get a vaccine or visit the doctor for treatment of a viral illness, remember that cell cultures may have played a key part in the development of that treatment or vaccine.

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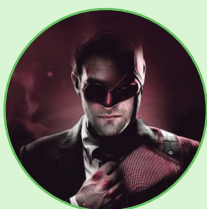
YOUNG REVIEWERS

ARYAN, AGE: 12

I am a sturdy youngster just entering the teens. I spend my time thinking about interesting things which are not exactly that interesting to other kids my age. I believe in the metaverse, not the “Marvel or Spiderman/ Doctor Strange” variety, but the real idea of existence of parallel universes with their own good and bad entities. I see myself in future traversing through these multiple realities experiencing mostly the good side of things each realm has to offer.

PABLO, AGE: 15

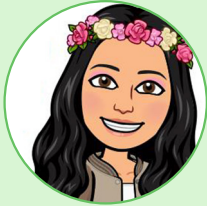
My Name is Pablo, I am half Mexican and half Spanish. I like to read and ask questions to improve my knowledge. I am very fond of science and technology and would like to become an engineer. My hobbies are to play the piano, videogames, football and padel. I also like animals and cars, especially competition cars. My favorite animal



is the eagle, and my favorite car is the Aston Martin Valkyrie. My idols are Adrian Newey and Fernando Alonso.

**PRANJAL, AGE: 11**

I am studying at a grammar school in seventh grade. My favorite subjects are Biology, History and Latin. I enjoy reading all kinds of story books in German and English and playing football with my friends. I am a Star Wars movie fan.

**SANAYA, AGE: 14**

I am currently at high school in year 10. My favorite subjects by far are history and computer science. I enjoy learning about historical events and how technology has advanced from the past to now. I spend the majority of the day doing my homework and like to talk to my friends when I have some free time. Currently, I am trying to get the best grades I can for my future. Thank you!!

AUTHORS

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I started work in the Laboratory of Virology at the Escuela Nacional de Ciencias Biológicas at the Instituto Politécnico Nacional in Mexico City, after obtaining my Ph.D. at Friedrich Loeffler Institute in Greifswald Germany. I am deeply interested in the study of viruses, especially in the development of antiviral drugs against dengue virus and other viruses. I also enjoy spending time with my children and listening to rock music.

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I received my Ph.D. from UNAM-México. Currently, I work in the Connective Tissue Laboratory of the Instituto Nacional de Rehabilitación, Luis Guillermo Ibarra Ibarra, México. My research interests are mainly focused on the study of wound-healing processes in the skin by the development of 3D skin wound models. I found interesting to analyze how cells interact with each other, and with the substances surrounding them; and how biomechanical properties of skin changes during its repair. I enjoy spending time with my family; my children teach me a new way of seeing the world. *chopin.mario@yahoo.com.mx