Yale SCHOOL OF MEDICINE

As of June, 2022

Teacher Guide 6: The Virus

Connections to NGSS:

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues
- HS LS1-6 Formation of Carbon-based Molecules
- HS LS4-2 Biological Evolution: Unity & Diversity
- HS PS3-4 Conservation of Energy & Energy Transfer

Scientific & Engineering Practices:

- Engaging in Argument from Evidence
- Constructing Explanations
- Asking Questions

Crosscutting Concepts:

- Structure & Function

Key Terminology:

- Virus
- Capsid
- Envelope
- Receptor
- Host Cell
- DNA/RNA
- Protein
- Mutation
- Natural Selection
- Ventilator
- Inflammation

Professional Opportunities:

- Virologist
- Immunologist
- Structural Biologist
- Biology Teacher

- Biomedical Engineer

Challenge 1: Connections to NGSS:

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues
- HS LS1-6 Formation of Carbon-based Molecules

Scientific & Engineering practices:

- Engaging in Argument from Evidence
- Constructing Explanations

Crosscutting Concepts:

- Structure & Function

Connections to NGSS: Challenge 2

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues
- HS LS1-6 Formation of Carbon-based Molecules

Scientific & Engineering practices:

- Constructing Explanations
- Asking questions

Crosscutting Concepts:

- Structure & Function

Connections to NGSS: Challenge 3

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues
- HS LS1-6 Formation of Carbon-based Molecules

Scientific & Engineering practices:

- Constructing Explanations

Crosscutting Concepts:

- Structure & Function

Connections to NGSS: - Challenge 4

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues
- HS LS1-6 Formation of Carbon-based Molecules
- HS LS4-2 Biological Evolution: Unity & Diversity

Scientific & Engineering practices:

- Engaging in Argument from Evidence
- Constructing Explanations

Crosscutting Concepts:

- Structure & Function

Connections to NGSS: Challenge 5

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues
- HS PS3-4 Conservation of Energy & Energy States

Scientific & Engineering practices:

- Asking questions
- Constructing Explanations

Crosscutting Concepts:

- Structure & Function

In This Lesson (NGSS): -Challenge 6

Disciplinary Core Ideas:

- HS LS1-1 Genes, Proteins, Tissues

Scientific & Engineering practices:

- Asking Questions
- Constructing Explanations

Crosscutting Concepts:

- Structure & Function

Module 6: The Virus

(Image of Students)

As Tash continues his quarantine following his testing positive for COVID-19, he receives a follow-up phone call from the Department of Public Health, a contact tracer, and his primary care physician. Though his symptoms remain relatively mild, he understands that not everyone his age has such a mild case. June, one of his best friends from school told him a story about a family friend she knows who contracted the virus at a nursing home. What happens to your body when you contract the coronavirus? Why is there such a variation in severity between cases?

Performance Expectations:

- *Find evidence to support a claim that a virus is either "alive" or "not alive."*
- *Construct an explanation of how the SARS-CoV-2 virus enters a host cell and how specificity plays a role in host cell recognition.*
- *Apply scientific ideas and evidence for the role of the Central Dogma in viral replication.*
- *Explain the specifics of how the SARS-CoV-2 virus takes over a host cell in order to replicate and make many copies of itself.*
- *Connect how mutation plays a role in viral evolution and how this plays affects the ability of a virus to infect its host.*
- *Distinguish between the symptoms of COVID-19 and the potential complications that accompany a severe case.*
- *Investigate lung function and how ventilators help people breathe if they have Acute Respiratory Distress Syndrome associated with COVID-19.*
- *Relate how inflammation is associated with COVID-19 and case severity.*
- *Differentiate case severity associated with preexisting conditions and demographics.*

CHALLENGES:

1. Is a virus alive?
2. How does a virus enter a host?
3. Molecular Hijacking: How does a virus take over?
4. How do mutations cause viral evolution?
5. How does COVID-19 affect the respiratory system?
6. Why does COVID-19 affect people differently?

Challenge 1: Is a virus alive?

Learning Targets:

- *I can use the criteria for living things to classify an entity as "alive."*
- *I can use scientific evidence to argue whether a virus is alive or not*

Estimated Time: 30 minutes

1.1 READ: The story continues… (Kids image)

Unable to meet in person these days, June, Tash, and Ray communicate daily over text. In their group text one evening, they start a debate.

Ray: Yo, it says we need to steer clear of live virus.

Tash: Wait, viruses are tiny little particles, they aren't alive!

Ray: Of course they are alive, they can infect people tho.

June: I remember the teacher of my freshmen biology class saying that there are certain criteria in order to classify something as alive, but I don't remember exactly what those were.

Ray: No, I'm telling you viruses are ALIVE!

Tash: skeptical face emoji

1.2 Make a Claim: Do you side with Ray or Tash and June?

1.3 READ: The Forbes article -- "A Biologist Explains: What is Life?" Look for evidence that supports your claim.
https://www.forbes.com/sites/jvchamary/2019/03/27/what-is-life/#3db01d1c1c77

1.4 Discuss & Reflect:

a. What processes do cells (of either single-celled or multicellular organisms) complete when they are alive?
b. What evidence exists to support that viruses are alive?
c. What evidence exists to support that viruses are not alive (HINT: what do they lack that living cells have?)

1.4 RESEARCH & DEBATE:

As a group: Either divide students into two groups, one supporting the idea that viruses are alive and the other that they are not. Have the students conduct a debate providing evidence to support each side of the argument. Each group should find at least three credible sources with supporting evidence.

Individual: Choose one of the statements below and write an argument to support your choice providing scientific evidence:

a. Viruses are alive.
b. Viruses are not alive.

Find at least three credible sources with supporting evidence.

Professional Opportunities:

Info about a Career as a Biology Teacher:

- CareerOneStop.org - Biology Teacher https://www.careeronestop.org/Toolkit/Careers/Occupations/occupation-profile.aspx?keyword=Biological%20Science%20Teachers,%20Postsecondary&onetcode=25104200&location=UNITED%20STATES

Challenge 2: How does a virus enter a host?

Learning Targets:

- *I can explain how the SARS-CoV-2 virus enters a host cell and how specificity plays a role in host cell recognition.*

Estimated Time: 30 minutes

2.1 WATCH: 2 Videos

a. "COVID-19: An illustrated scientific summary" [8:17]
https://www.youtube.com/watch?v=AaXZflLkB80 and

b. "Why is the New Coronavirus So Good at Infecting Human Cells?" [2:35]
https://www.youtube.com/watch?v=v0lXtzfSPbw

2.2 READ: What is the ACE2 Receptor? The Conversation
https://theconversation.com/what-is-the-ace2-receptor-how-is-it-connected-to-coronavirus-and-why-might-it-be-key-to-treating-covid-19-the-experts-explain-136928

2.3 READ & DESCRIBE:

SARS-CoV-2 Tracker - Follow a single viral particle

Imagine you have a teeny tiny camera like a GoPro attached to the surface of a single SARS-CoV-2 particle, the coronavirus that causes COVID-19. This particle, also called virion, is on the smaller side of SARS-CoV-2 particles and is only 70 nanometers in diameter (a nanometer is a million times smaller than a millimeter!).

a. In the periphery of the viewing window captured by the camera, it is possible to see the surface of the viral particle. Describe what is on the surface?

(Kids Picture)
The story continues...

The virion is currently in the air within the lungs of a classmate of our friends Tash, Ray, and June. This teen doesn't know he is infected yet. Up until now he's been asymptomatic, so he's not wearing a mask while he rides the school bus at the end of a long school day. He's starting to feel a tickle in his lungs and has the sudden urge to sneeze. Our virion is now in a droplet that is about 5 microns in diameter (a micron is 1000 times smaller than a millimeter!) that contains 100 more particles that look almost identical to the one we are following but vary in size.

"Aaaaa aaaaa aaaaa choo!" The student sneezes. At a speed of 100 miles per hour, the droplet is expelled from the lungs, travels up the trachea and through the mouth and enters the air of the bus where Tash is sitting several rows away.

Within minutes, Tash inhales and SWOOSH the droplet enters Tash's nose and is whisked down the trachea and into his lungs. Once there, the droplet breaks open and the virion is released into the lung cavity. After floating for a matter of minutes, it bumps into a cell on the epithelium of the lung.

b. There are epithelial cells in the lungs as mentioned above, but also in other organs like the skin, digestive tract, etc. If "epi" is Greek for "on" or "upon," where specifically in an organ do you think you would find epithelial cells?

After the initial bump, the virus particle bounces around a bit, but at once, seems to lock into place.

c. Draw a picture of what is happening upon host cell recognition. Provide the names of the proteins that interact on the virus and on the host cell.

The process of how the virus physically enters the cells is not completely clear. Structural biologists and virologists are working to elucidate the exact mechanism, but for now they know that the process involves the viral envelope fusing with the membrane of the host cell (fusion is the process by which two membranes join to form one contiguous membrane). This allows the virus to "infect" the host cell.

d. When the virus "infects" the host cell, what viral contents are required to enter the host cell?

2.4 Reflect & Discuss:

a. Can the SARS-CoV-2 virus enter any cell of the body? Explain why or why not.

b. The common symptoms of COVID-19 are the following: coughing, sneezing, congestion, loss of taste and smell, shortness of breath, vomiting, and diarrhea. Given this list, what types of cells can SARS-CoV-2 infect?

c. Some patients with COVID-19 also have complications involving damage of organs such as the heart, kidneys, and even the brain. What does this mean about the cells in these organs? HINT: Think surface of the cell.

2.5 HYPOTHESIZE and Write:

Data indicate that children and young adults are more likely to have asymptomatic or mild cases of COVID-19 and some preliminary data indicates they may have to do with the number of ACE2 receptors. Write a hypothesis statement about the relationship between age and ACE2 receptors. How would you test your hypothesis?

Professional Opportunities: Info about a Career as a Virologist or Structural Biologist:

- CareerOneStop.org - Biologist https://www.careeronestop.org/Toolkit/Careers/Occupations/occupation-profile.aspx?keyword=Biologists&onetcode=19102001&location=UNITED%20STATES

Yale SCHOOL OF MEDICINE

As of June, 2022

Challenge 3: Molecular Hijacking: How does a virus take over?

Learning Targets:

- *I can discuss the role of the Central Dogma in viral replication.*
- *I can describe the specifics of how the SARS-CoV-2 virus takes over a host cell in order to replicate and make many copies of itself.*

Estimated Time: 30 minutes

3.1 WATCH: "COVID 19: An illustrated scientific summary" [8:17]

https://www.youtube.com/watch?v=AaXZflLkB80

3.2 READ: "How Corona Virus Hijacks your Cells" -- an article from the New York Times

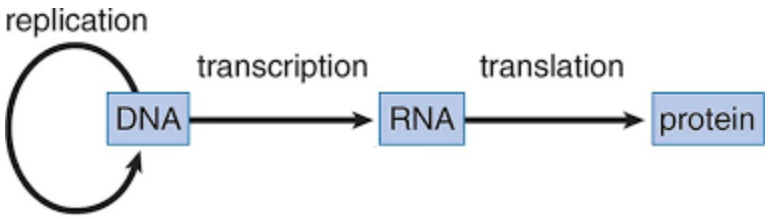
https://www.nytimes.com/interactive/2020/03/11/science/how-coronavirus-hijacks-your-cells.html

3.3 READ and DECIDE: "Bring, Build, Borrow, or Steal"

To complete this activity, you will read the information provided and then use the following verbs: **bring**, **build**, **borrow** or **steal** to fill in the words missing from the paragraph below. For each blank you must choose one of those four words. First, read the important information below.

Background: Viruses are clever entities and they are minimalists. Most viruses carry very little within their capsid (and envelope if they have one) and the majority of their insides is genetic material made of either strand(s) of deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). The viral genome (genetic material) has the instructions, aka genes, to take over the host cell and to build new copies of itself. This process of host cell takeover is known as "molecular hijacking." When a virus replicates it has to build entire viral particles and it has to not only make the proteins that comprise the viral capsid (and enclose it with an envelope), but it must also replicate its genetic material.

The Central Dogma is a concept coined by Francis Crick in the 1950s. Crick received a Nobel Prize along with his colleague James Watson for elucidating the structure of DNA. The Central Dogma (pictured below) describes the transfer of genetic information (blueprints) into function in a cell. DNA, which is the makeup of the genome of most organisms, can be replicated, but also transcribed into RNA molecules, which are then translated into proteins. Proteins go on to perform functions, such as the capsid of a virus is made of proteins that provide a structure to encapsulate the viral genome.



Facts: Host cells and viruses have many, many differences with respect to the proteins and molecules within each. Because the virus is a minimalist and carries only a few things with it, it has to either borrow or steal the machinery of the host cell it infects or it must bring the blueprints to build what it needs.

The host cell has the following:

- DNA polymerase – the enzyme needed to replicate DNA (DNA --> DNA)
- RNA polymerase - the enzyme required to transcribe DNA into RNA (DNA --> RNA)
- Ribosomes – the entities responsible for translating RNA into proteins (RNA --> Proteins)
- Phospholipids that make up membranes

Now decide which word (**bring**, **build**, **borrow**, or **steal**) correctly fills in the blanks in the paragraph below. Remember that borrowing is distinct from stealing; assume borrowing involves the return of the goods to the host, but stealing does not.

SARS-CoV-2, the virus that causes COVID-19, has a protein capsid that is surrounded by a phospholipid envelope. Inside its capsid is a genome of RNA. Spike proteins called, S proteins, recognize the ACE2 receptors of host cells allowing the virus to enter the host cell. Upon entry

into the host cell, the virus hijacks the host and turns it into a factory producing many, many copies of SARS-CoV-2. First, the virus _____ its own genome of RNA, which then needs to be coded into proteins. Thus, the virus _____ the genes coding for viral structure, such as capsid and spike proteins. Then the virus must code these genes into proteins and _____ ribosomes for translation, a process that also requires the virus to _____ amino acids, which are the building blocks of proteins. In doing this, the virus _____ many capsid and spike proteins to make many viral particles. SARS-CoV-2 also _____ a gene that codes for a protein enzyme that is capable of copying RNA into more RNA molecules. This way the virus can then _____ many, many copies of its own genetic material to be carried within each viral particle produced. This protein enzyme, called an RNA-dependent RNA polymerase, will then copy the virus's RNA genome which requires it to _____ ribonucleotides, which are the building blocks of RNA molecules. Once the capsid, spike proteins, and RNA genomes are produced, they are assembled and get ready to leave the host cell. Upon exit, each virus obtains its envelope and when doing so, the virus particles _____ phospholipids from the host cell's membrane. One the new viral particles exit the cell, they go on to find new cells to infect.

3.4 MODEL:

SARS-CoV-2 is an RNA virus, meaning its RNA genome can be directly translated into proteins, but it needs to make copies of its RNA genome when the virus replicates, a process that cannot naturally occur in animal cells. If a virus has a genome composed of DNA, such as the viruses that cause herpes, HPV, and chicken pox to name a few, then the virus needs a very different strategy to hijack its host cell. Think about what enzymes these viruses can borrow from the host cell in order to replicate entirely. Draw and model a viable strategy a DNA virus uses to hijack its host cell.

3.5 REFLECT and Discuss::

The human immunodeficiency virus (HIV), which is the virus that causes AIDS, also has an RNA genome, but this virus does not use the same strategy for molecular hijacking as SARS-CoV-2. HIV can remain latent in host cells, meaning it is not actively replicating and making many copies, but rather it hides out and replicates only once along with the host cell when it divides. In order to do this, HIV integrates its genome into that of the host cell. Considering this, what must HIV bring into the host cell and what process must occur in order to integrate the viral genome into the host cell's genome?

Challenge 4: How do mutations cause viral evolution?

Learning Targets:

- *I can describe relationships between mutations and viral evolution.*
- *I can provide evidence for how viral evolution affects the ability of a virus to infect its host.*

Estimated Time: 30 minutes

4.1 WATCH: "What is a Coronavirus?" [5:15] https://www.youtube.com/watch?v=D9tTi-CDjDU

4.2 READ: "The pandemic virus is slowly mutating. But is it getting more dangerous?: AAAS - Science
https://www.sciencemag.org/news/2020/07/pandemic-virus-slowly-mutating-it-getting-more-dangerous

4.3 READ & EVALUATE

To complete this activity, read the following information and then evaluate the statements below.

Mutations involve changes to the sequence of an organism's genetic code. As you have learned, viruses typically mutate more rapidly than human cells do. This is because human cells have mechanisms to proofread the genome and also mechanisms to repair a sequence if an error is detected. Mutations can vary in severity from having zero consequence to majorly altering a protein and its function. Mutations can involve the substitution of one DNA base to another, a G for an A for instance. Or mutations can involve the insertion of additional DNA bases or the deletion of existing DNA bases. Once a mutation occurs, if it changes the function of a resulting protein, a virus or organism is then changed. Because cells and viruses interact with the environment or surrounding cells, this change is either going to give the mutated cell or virus an advantage, allowing it to thrive more easily in its environment, or will make it disadvantaged, making it more difficult to survive. This is a process called natural selection. If the mutation confers an advantage, the mutated sequence then spreads within a population and if the

mutation confers a disadvantage, the mutated sequence dies out.

Consider the following scenarios (actual or hypothetical) and decide if the mutation in SARS-CoV-2 virus will be detected in an increasing portion of the population of viruses or will not be detected. Explain your answer choice.

a. A mutation in the gene coding for the SARS-CoV-2 capsid proteins. The mutated proteins prevent the capsid from forming.

b. A mutation in the gene coding for the spike protein responsible for recognizing the ACE2 receptor on the host cell. This mutation changes the spike proteins slightly so that they interact more loosely with the ACE2 receptors.

c. A second mutation in the gene coding for the spike protein responsible for recognizing the ACE2 receptor on the host cell. This mutation makes the spike proteins a different completely different shape.

d. A mutation in the gene that codes for the enzyme that copies the RNA genome of SARS-CoV-2. The mutation causes the enzyme to work at a faster rate.

e. A mutation in the SARS-CoV-2 RNA genome that changes the RNA molecule so that the ribosomes no longer recognize it.

4.4 REFLECT & DISCUSS:

a. Why are RNA viruses more likely to mutate than those that have genomes made of DNA?
b. What would happen if a virus that infects humans mutates and becomes more deadly to people? Would this virus continue to be a threat to the human population

Challenge 5: How does COVID-19 affect the respiratory system?

Learning Targets:

- *I can make and use a model demonstrating lung function.*
- *I can explain how ventilators help people breathe if they have Acute Respiratory Distress Syndrome associated with COVID-19.*

Estimated Time: 40 minutes

5.1 INVESTIGATE

Refer to the following resource summarizing the characteristics of COVID-19 to answer the questions below.

"Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)" -- CDC Publication

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

a. **Research:** Use the information provided to determine the factors that distinguish mild/moderate cases of COVID-19 from those that are severe. Write down those factors.

b. **Evaluate:** Are there any symptoms that are common to all types of cases mild to severe?
c. **Define:** What is asymptomatic transmission of COVID-19?
d. **Research:** Did you find any risk factors that seem to be associated with having a poorer outcome (more severe case)?

5.2 READ

The Centers for Disease Control and Prevention estimate that 3-17% of COVID-19 patients develop a complication known as Acute Respiratory Distress Syndrome (ARDS). With ARDS patients lose the ability to breathe normally and this is known as respiratory failure that results from severe inflammation in the lungs. Inflammation arises when there is damage to cells and in the case of COVID-19, which infects lung cells and damages them. Inflammation causes swelling, which is the result of increased fluid moving to the site of injury or damage. Unfortunately, when fluid moves into the lungs, the lungs cannot perform their normal function, taking in oxygen and releasing carbon dioxide. Watch the video below to learn more about lung function and then read the following article to learn how ventilators can help patients who are experiencing ARDS.

5.3 WATCH: "How do Lungs Work?" [3.22]
https://www.youtube.com/watch?v=8NUxvJS-_0k

5.4 READ:
"Ventilators and COVID-19: What You Need to Know?"
https://www.yalemedicine.org/stories/ventilators-covid-19/

5.5. MODEL Construct a drawing to explain how molecules in the air move in and out of lung tissue.

5.6 DISCUSS & REFLECT

a. What is the role of diffusion in the movement of oxygen and carbon dioxide in the lungs? In which direction does oxygen move? Carbon dioxide?

b. How does a ventilator work to help someone with ARDS breathe?

c. What is "proning" and why do doctors do this with patients who are on ventilators?

5.7 Research and Write:
Why is it important that we "flatten the curve" during this COVID-19 pandemic with respect to the availability of ventilators? Find a few credible sources that indicate if the hospitals in the US have an adequate supply of ventilators. What do the sources report?

Professional Opportunities:

Biomedical Engineer – design ventilators or medical equipment
https://www.careeronestop.org/Toolkit/Careers/Occupations/occupation-profile.aspx?keyword=Biomedical%20Engineers&onetcode=17203100&location=UNITED%20STATES

Intensivist
https://www.bioexplorer.net/how-to-become-intensivist.html/

Challenge 6: Why does COVID-19 affect people differently?

Learning Targets:

- *I can explain how inflammation is associated with COVID-19 and case severity.*
- *I can discern the differences in case severity that are associated with preexisting conditions and demographics.*

Estimated Time: 60 minutes

6.1 WATCH: "COVID-19" [7:09]
https://www.youtube.com/watch?v=gXJtL72VWrU&list=PL6uC-XGZC7X4a_gow8GoxGHdYmFOMSIp7&index=9

6.2 LISTEN "Radiolab: Invisible Allies" - first 23 minutes
https://www.wnycstudios.org/podcasts/radiolab/articles/invisible-allies

6.3 READ "Racial disparities persist in Connecticut's COVID-19 outbreak, prompting concern about effects of potential second wave**"**
https://www.courant.com/coronavirus/hc-news-coronavirus-covid-racial-disparities-20200713-y722eyl3erekvn7qlwvl6a6akm-story.html

6.4 READ and REFLECT
Generally speaking, inflammation is a good thing. This is a reaction that your body has to injury, invasion by foreign cells or agents like bacteria or viruses or even toxins. When your body or a part of your body is inflamed there are several common physiological responses including swelling, redness, heat, and pain. Think about the last time you got a bug bite, the area immediately surrounding the bite swelled a bit and turned red, right? That's inflammation! The reason this is a good thing is that inflammation increases blood flow.

- Why do you think that increasing blood flow is helpful for a site of injury or invasion? What does the blood bring to the site?

6.5 READ and EVALUATE

However, there are times when inflammation is not a good thing. Periods of long-term (chronic) inflammation is associated with many serious conditions including heart disease, asthma, arthritis, autoimmune diseases like Crohn's or Celiac Disease, and diabetes, to name a few. Inflammation that occurs for long periods of time can also affect the body's ability to fight off infection. COVID-19 seems to be connected to inflammation in two ways. First, COVID-19 causes an inflammatory response in the body. Some individuals who contract COVID-19 have what is called a "cytokine storm," which is an aggressive immune response that leads to even higher levels of inflammation. Second, as the Radiolab podcast discussed, people who have chronic inflammation seem to be affected more severely by COVID-19. The podcast also points out that there may be an association between vitamin D levels and COVID-19. Vitamin D is a fat-soluble vitamin, made by the body or consumed, that is thought to bolster and temper the immune system.

a. What key observation played a role in the thought that vitamin D levels may be associated with COVID-19 outcome and lower vitamin D levels are associated with more severe cases of COVID-19?

b. If this association is true and vitamin D can help to prevent severe COVID-19, what is the hesitation to urging people to take vitamin D supplements? Why should we use caution with this line of thinking?

6.6 DESIGN

Design a study that you could do to further investigate vitamin D levels and COVID-19.

6.7 REFLECT and DISCUSS

Based on what you have listened to and read in this challenge, what groups of people seem to be more greatly affected by COVID-19?

6.8 HYPOTHESIZE & INVESTIGATE

Do you have a hypothesis or two as to why people of color are more likely to be affected by COVID-19? Think about social or health factors that may be playing a role. Search for a few credible sources for evidence to support your ideas and report your findings.

Professional Opportunities:

Immunologist
https://www.careeronestop.org/Toolkit/Careers/Occupations/occupation-profile.aspx?keyword=Allergists%20and%20Immunologists&onetcode=29106901&location=UNITED%20STATES