Hidden in Plain Sight: Immune Evasion by Herpes Simplex-1 Virus

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Part I — Immune Evasion by HSV-1

Herpes simplex virus-1 (HSV-1) has an interesting set of immune evasion genes that enhance its ability to replicate in the epithelial cells in your mouth. We will analyze three of these gene products in class: ICP47, gE/gI, and gC-1/2. All groups will research the viral gene product ICP47 before class and answer the questions below. Each group will also be assigned a research article concerning either gE/gI or gC-1/2. Read the article to prepare answers to the questions below before coming to class.

These are fairly complex mechanisms of immune evasion so work together and don’t wait until the last minute!

Each group is to answer the following questions before class:

1. What do these viral gene products do inside the host cell? Why does this benefit the virus?
2. Diagram the gene product’s effect on the immune response. Your diagram will be critiqued by at least one other group during the beginning of class on discussion day.
3. What effect does this have on the ability of the immune system to respond to HSV? What backup systems are available to overcome this issue?

These articles will help you in your search for the information:

Part II – The Gift That Keeps on Giving

It’s the middle of the semester and you are very stressed about the upcoming exam and paper you have due. You begin to feel that pesky cold sore developing on your lower lip. It has been happening for years, mainly when you get run down. You realize you are not alone in your dilemma and that over 50% of adults have cold sores (oral herpes). Though you have spent many waking hours wondering where you got the virus from, you have never figured it out. What bothers you most about the situation is how your body allows for the virus to keep causing the symptoms. You know the virus remains latent in nerves, but why would your immune system allow the virus to reactivate and cause you so much discomfort, over and over and over again?

Herpes viruses have the somewhat unique ability to remain latent (dormant) and stay with an individual for the rest of his or her life (i.e., no one is ever cured of a herpes virus). Herpes Simplex Virus-1 (HSV-1) is the virus that causes cold sores and remains latent in the nerve ganglia. While in the latent phase, the virus is not producing active viral particles. Therefore, the only time the host sees HSV-1 antigens is after reactivation and active replication of the virus in epithelial cells. Since the immune system has already seen HSV-1 during previous cold sores, HSV-1 has a very small window of opportunity to replicate and spread prior to memory immune response recognition. To expand this window of opportunity, herpes viruses have developed a set of evasion genes that “down modulate” the immune response.

Questions

1. As described above, HSV-1 has two infectious stages within the body: active replication and latent infection. Immune evasion genes are critical during active replication. What is the process by which HSV-1 replicates in epithelial cells?
2. Reactivation of the virus often occurs during times of stress. Why might this be the case?
3. How does HSV-1 evade the immune system to allow itself time to replicate? Critique your ICP47 diagram from the homework assignment, and explain the function of your other assigned gene to your assigned peer group.
Part III – What Do I Do Now?

You have an important event coming up and need to look your best. You decide to take an antiviral medication to reduce your cold sore symptoms. You have two choices: an antiviral prescribed by your doctor (Acyclovir) or an over-the-counter treatment (Abreva™). Even though you know Acyclovir works well, you would have to go to the doctor to get the prescription and you don’t have much time between all your classes and homework. You’ve seen commercials for Abreva™, and it’s a quick trip to the store to get it. However, you have no idea if it will work.

Questions

1. How do these drugs work to reduce the length of time of HSV-1 infection and/or symptoms?
2. Which medication would you choose and why?
3. Some viruses become resistant to antiviral drugs. Would this be an issue with these drugs? Why or why not?
4. Would you expect a virus that is resistant to Acyclovir to also be resistant to Abreva™? Why or why not?
5. You find a research study that shows that the initial HSV-1 strain that a person is infected with stays with them and doesn’t change for their lifetime. However, active viral replication can lead to mutations that can be passed along to other people. Does this change your mind about using antivirals for HSV-1? Why or why not?