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How do viruses trick their hosts into feeding them?

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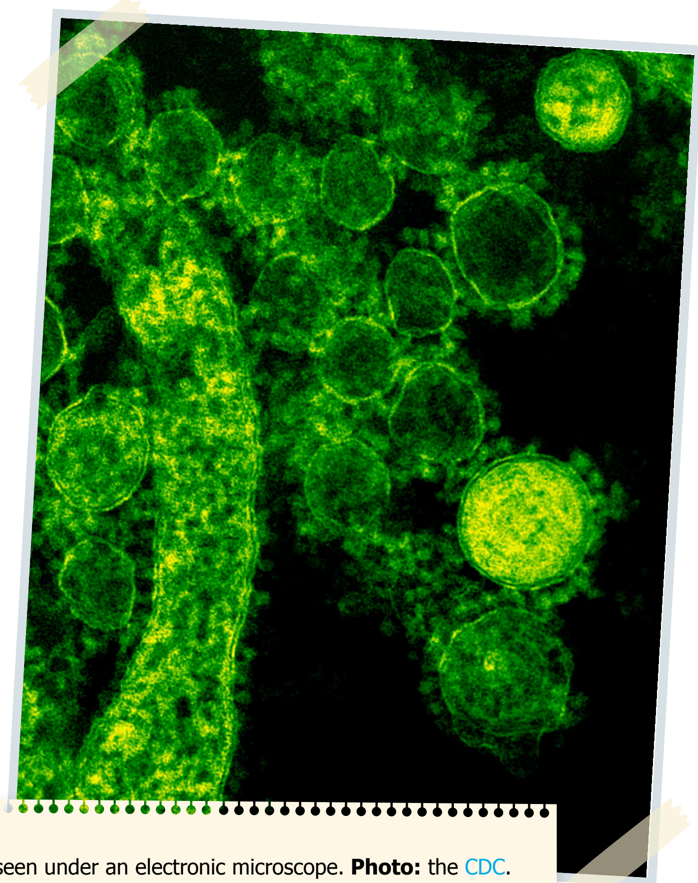
Abstract

Scientists estimate that mammals can be infected with more than 300 thousand virus species! All organisms need energy, but simple microorganisms like viruses cannot produce their own energy. Instead, viruses survive by redirecting energy from a host organism to their own benefit. Normally, viruses survive by infecting cells and forcing them to produce more viruses.

However, we have discovered a new class of viruses that redirect energy in a unique and fascinating way! These viruses are able to trick their host organism by producing their own version of insulin, called “viral insulin”. This viral insulin is like a wolf in sheep’s clothing because the host organism cannot tell the difference between its own insulin and the viral insulin.



A virus seen under an electronic microscope. **Photo:** the CDC.

Introduction

A molecule called **glucose** acts as the power source for our bodies, similar to how gasoline fuels a car. Eating food gives us energy because many foods contain glucose! After you eat a meal, the glucose from your food travels through the bloodstream to reach your cells.

Glucose needs the help of a protein called **insulin**, which unlocks our cells and lets the glucose inside. Once the glucose makes it into our cells, it is broken down to release the energy that we use to move, grow, and survive.

Just like our cells, viruses need glucose to survive. Normally, viruses infect one cell at a time and slowly steal energy and other resources. We wondered if there were any viruses out there that got their energy differently.

Methods

To find out, we used a database with information about viral proteins. We ran a computer simulation to identify any viral proteins that appear similar to human insulin. Once we found some, we needed to test them and see how they acted compared to human insulin.

1. We used chemistry techniques to make the viral insulin proteins in our laboratory.

2. We prepared three groups of laboratory mice to perform the tests.

- First group → we injected them with viral insulin. This was our **intervention group**.
- Second group → we injected them with regular insulin. This was our **positive control group**.
- Third group → we injected them with saline (a saltwater solution). This was our **negative control group**.

3. Over the next 2 hours, we measured how much glucose the mice had in their blood. The more glucose the cells had absorbed, the less glucose remained in the blood. This showed how strong the insulin was.

Results

Our computer simulation showed that half of the viral insulin structure was almost the same as human insulin.

Our lab experiment showed that human insulin was stronger than viral insulin (Fig. 1). The amount of glucose in the mice's blood decreased much more with human insulin over the first 90 minutes.

During testing, we also noticed viral insulin blocking an important marker of cancer. (A marker of cancer is any molecule found in very high amounts in people with cancer.)

Which injection caused the largest decrease in blood glucose after 30 minutes? Why do you think all three of the groups showed a decrease, even though saline doesn't help glucose enter cells?

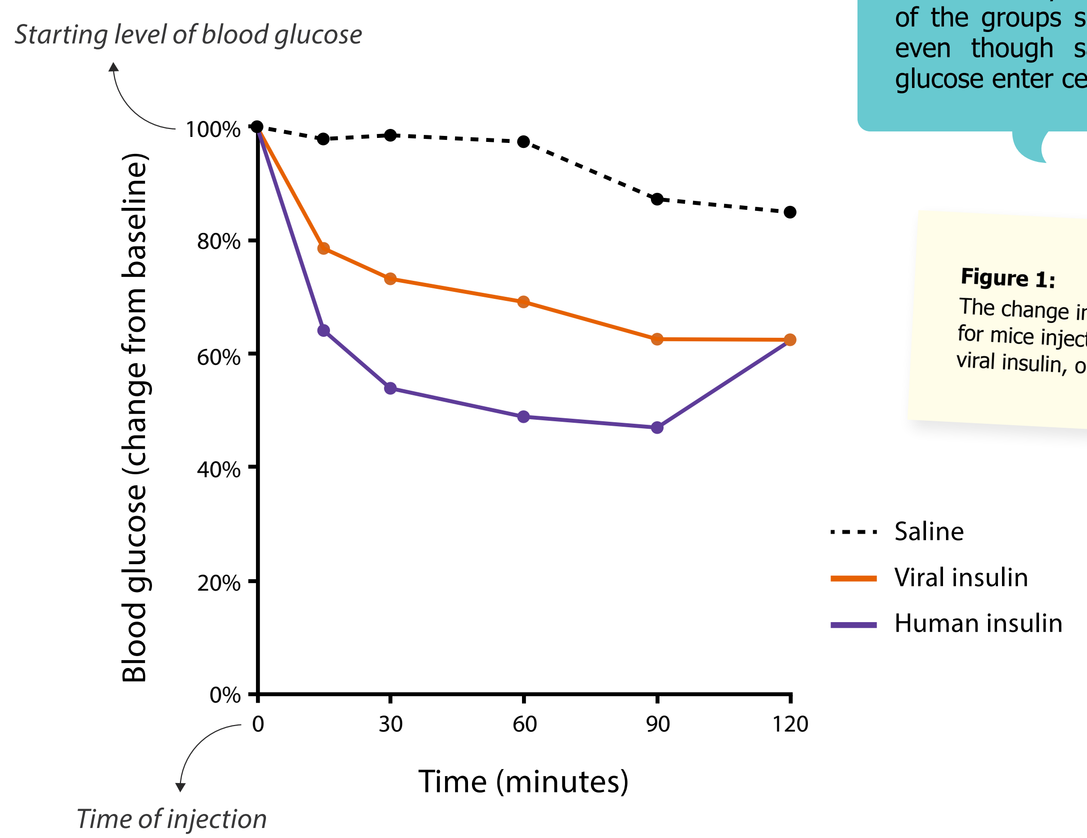


Figure 1:
The change in blood glucose over time for mice injected with human insulin, viral insulin, or saline.

Discussion

Because the viral insulin shares 30–50% of its structure with human insulin, it is able to force the host's cells to absorb glucose. In biology, structure determines function! It makes sense that human insulin is stronger than viral insulin because human cells have evolved to recognize human insulin. The similarity of viral insulin is enough to make cells absorb some glucose, but not as much as human insulin.

This means that the host will deliver glucose directly to the viruses! When viruses have access to all of this glucose energy, they can reproduce more quickly. This means that infections might begin to make the host organism very sick. Scientists are still trying to understand the function of viral insulins during the disease. Luckily for you and me, this particular class of virus can only infect fish, reptiles, and bugs – not humans!

We were excited to find that viral insulin blocks a marker of cancer. This marker is called **insulin-like growth factor 1 receptor (IGF1R)**. In cancer, IGF1R causes dangerously fast cell growth. This rapid growth is one of the several factors that cause tumors in cancer patients. Our discovery that viral insulin blocks IGF1R means that viral insulin might one day be used as a medicine for treating cancer in humans!

Conclusion

We discovered a new strategy that viruses use to trick their hosts. It is useful to understand the microorganisms that surround us, especially the ones that cause disease. If we can learn how viruses work, we can learn how to treat the illnesses that they cause. Think about the COVID-19 pandemic. How important was it for scientists to understand the SARS-CoV-2 virus? That was a huge help in developing vaccines against it!

Getting vaccinated is an important way you can protect yourself against diseases caused by viruses and other germs. Do you have all of your shots? Some vaccines, like the flu shot, work best only when most of the people around you had them.

Glossary of Key Terms

Glucose - a molecule in food that is the major energy source for human cells.

Insulin - a protein that unlocks cells and allows glucose to enter.

Insulin-like growth factor 1 receptor (IGF1R) - a protein found in high concentration in cancer cells. It can be blocked by viral insulin.

Intervention group - in an experiment, the group that receives the new treatment. The results of the intervention group will tell how effective the new treatment is compared to the positive and negative controls.

Negative control group - in an experiment, the group that receives no treatment. The negative control should not affect the result being measured. In our experiment, we used saline, which doesn't affect blood sugar and is a safe inert addition overall. The results from this group are compared to the intervention results.

Positive control group - in an experiment, the group that receives a treatment already known to affect the result being measured. The results are used to compare to the intervention group.

Check your understanding

1. Will a healthy person produce more or less insulin after eating a meal high in glucose?

2. How could viral insulin make a host organism sick?

3. What would happen if a person could not produce insulin, as is the case in people with diabetes (Type 1)?

4. How does viral insulin affect cancer cells?

5. Our findings show that viral proteins are a potential source of new medicine, even though we normally think of viruses as bad for our health. Can you think of another example of something that is usually harmful to health but can be used as medicine?

REFERENCES

Francois Moreau, Nicholas S. Kirk, Fa Zhang, Vasily Gelfanov, Edward O. List, Martina Chrudinová, Hari Venugopal, Michael C. Lawrence, Veronica Jimenez, Fatima Bosch, John J. Kopchick, Richard D. DiMarchi, Emrah Altindis, and C. Ronald Kahn (2022) *Interaction of a viral insulin-like peptide with the IGF-1 receptor produces a natural antagonist.* Nature Communications
https://www.nature.com/articles/s41467-022-34391-6

Emrah Altindis, Weikang Cai, Masaji Sakaguchi, Fa Zhang, Wang GuoXiao, Fa Liu, Pierre De Meyts, Vasily Gelfanov, Hui Pan, Richard DiMarchi, and C. Ronald Kahn (2018) *Viral insulin-like peptides activate human insulin and IGF-1 receptor signaling: A paradigm shift for host–microbe interactions.* PNAS.
https://www.pnas.org/doi/10.1073/pnas.1721117115

MicrobeTV: Science shows by scientists
https://www.microbe.tv/science-shows-by-scientists/

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