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Can armadillos show us how to regrow a liver?

Authors:
Anura Rambukkana and others
Associate Editor:
Mary Bates and Rachel Watson

Abstract

What if we could make our body's old or sick cells act young again? Surprisingly, the bacteria that cause leprosy may show us how. Previously, we discovered that infecting cells with leprosy bacteria in a laboratory dish "reprogrammed" the cells back to an immature state. The cells may then be able to produce many different types of cells in the body – and maybe even regenerate an organ.

To test this in an actual animal, we infected nine-banded armadillos with leprosy bacteria. We compared their livers to the livers of uninfected armadillos. The livers of armadillos infected with leprosy were larger than those of uninfected armadillos. Importantly, these larger livers were healthy, with no signs of damage. We performed genetic analyses on the liver cells to determine which genes were active. Our results show that leprosy infection "reprograms" adult liver cells to make them resemble immature liver cells. Maybe someday we can adapt this natural process to regrow aging and damaged livers in humans.

Introduction

Sometimes people need a new organ because disease or injury has damaged one of theirs. Unfortunately, waiting for a transplant organ from an appropriate donor can take a really long time. Imagine needing a new heart but having to wait for years! What if they could just grow a new organ instead?

Scientists are interested in learning how to **regenerate** organs for people. They have tried different techniques in the laboratory to encourage organs to grow back. However, there are major safety concerns. These approaches often cause scars or **tumor** growth.

Previously, we made a surprising discovery. We infected nerve cells from adult mice with the **bacteria** that causes **leprosy** (Fig. 1). Leprosy is a contagious disease that affects the nerves, skin, eyes, and nose. The bacteria caused the cells to return to a more immature state – instead of looking like adult nerve cells, they looked more like **stem cells**. Stem cells are immature cells that don't have a specific role in the body yet. When an organism is forming, these cells can become any type of cell needed for a given organ. Some stem cells are also present in adult organs. Usually, they are inactive. When they sense damage to tissues, they activate to repair it. But as we get older, our stem cells have a harder time repairing our organs.

Figure 1:
Leprosy bacteria (*Mycobacterium leprae*), the microscopic rod-shaped bacteria that cause the disease leprosy.
Image: Kateryna Kon / Science Photo Library

Turning adult cells into stem cells could be a way to build a new, functioning organ or make an older organ young again. That's exciting! But those previous experiments with leprosy bacteria were on mouse cells in a laboratory dish. We wondered if the same process would occur in an actual living animal.

Methods

We chose to look at leprosy infection in nine-banded armadillos. Armadillos are mammals native to the southwest U.S.

We focused on potential regeneration of the **liver**. This organ has many functions, including removing toxins from the body's blood supply and maintaining healthy blood sugar levels. Unfortunately, the liver is also a target for bacterial growth. The liver has an astonishing ability to regenerate on its own in healthy people. However, we do not know how to trigger liver renewal in patients who need it most – those with liver disease or injury.

We infected armadillos with the leprosy bacteria. After 10–30 months of infection, we removed their livers and compared them to livers from uninfected armadillos. We looked at the liver cells under high-powered microscopes. We also performed analyses on the cells' **DNA** to identify which **genes** were active. We wanted to see if the pattern of gene activity in the cells looked more like adult liver cells or immature stem cells.

Results

We calculated the **ratio** of each armadillo's liver to its total body weight. We found that the livers of armadillos infected with leprosy bacteria were about 50% larger than those of uninfected armadillos (Fig. 2).

Even though the infected livers had grown, they were otherwise normal. Infected livers had the same anatomy as uninfected livers. Importantly, the enlarged livers were healthy and functional! They showed no signs of scarring or tumor growth.

Next, we measured gene activity in infected and uninfected livers. We found several signs that the liver cells of infected armadillos were "reprogrammed" to act like stem cells. The gene activity patterns of infected liver cells were similar to those of younger animals' livers and developing human livers. In infected armadillos, genes associated with growth and development became active. Some of these genes are usually active when the liver is forming in a developing organism. At the same time, genes associated with aging were **suppressed**.

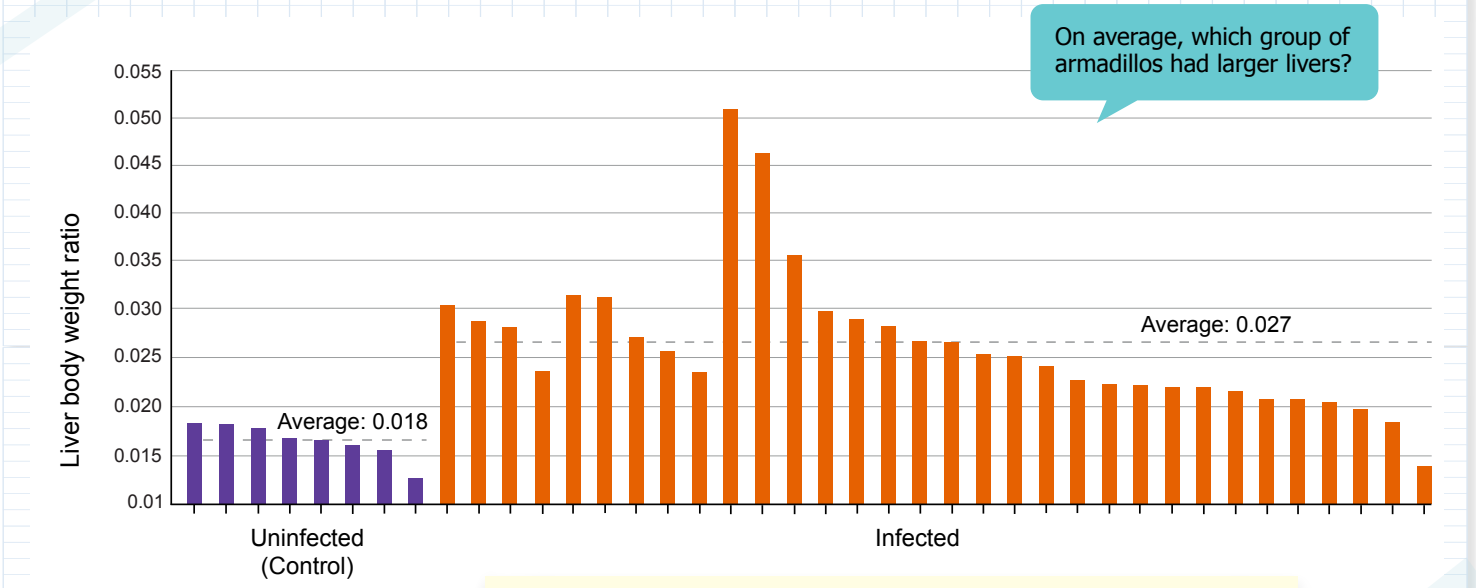

Figure 2:
The weight of the liver compared to the total body weight of armadillos uninfected or infected with leprosy. Each bar represents an individual armadillo.

Discussion

Our results suggest that leprosy bacteria "reprogram" liver cells and return them to a stem cell–like or more "youthful" state. Once in this state, the cells can encourage new liver cells to mature and grow new liver tissue. This leads to liver growth.

We think that the bacteria take advantage of the natural regenerative ability of the liver to increase the organ's size. This gives the bacteria more cells to infect.

We cannot say for sure if these findings would work in human livers. And we are not about to infect any people with leprosy bacteria! But figuring out how armadillos' livers keep growing under the influence of leprosy bacteria – without forming scars or tumors – might help scientists better understand the mechanisms of regeneration in the human liver. If we could harness this ability, we might someday be able to help people with liver disease regenerate healthy livers.

Conclusion

Leprosy has affected people since ancient times. Today, the disease is rare in many places, including the United States. However, it still occurs in more than 120 countries. Currently, about 208,000 people worldwide are infected with leprosy every year, most of them in Brazil, Africa and Asia.

Fortunately, you don't have to worry too much about catching it. Leprosy is not very contagious – social distancing is enough to stop its spread from person to person. Plus, most people have natural immunity to it.

If leprosy is treated early, it is curable. Still, you shouldn't handle any wild armadillos! Wild animals of any kind may carry diseases that can spread to humans.

Glossary of Key Terms

Bacteria – microscopic, single-celled organisms. There are millions of different bacteria and only some infect humans.

DNA – the microscopic material inside cells that contains the genetic information responsible for the development and function of an organism. Instructions in your DNA tell your cells how to grow, develop, and work properly.

Gene – a sequence of DNA that carries information determining one's traits that is passed from parent to offspring. For example, you might inherit the gene for brown eyes from your mother.

Leprosy – a disease caused by a bacterial infection that affects the skin, eyes, nose, and nerves. With early diagnosis and treatment, leprosy in humans can be cured.

Liver – an organ that is part of the digestive system and carries out many tasks in the body. Some of the liver's major roles are cleansing the blood of toxins and helping with digestion.

Ratio – the relationship between two numbers, or one number divided by another. We found that the liver to body weight ratio of infected armadillos was higher than that of uninfected armadillos, showing that infected livers were larger.

Regenerate – regrow or replace lost or damaged tissue.

Stem cells – immature, non-specialized cells that have the ability to develop into any kind of cell in the body. Therapies using stem cells may be able to replace lost or damaged cells that our bodies cannot replace naturally.

Suppress – to cause a gene not to be expressed.

Tumor - an unusual growth of cells that may become cancerous if the growth is uncontrolled.

Check your understanding

1. How does infection with the leprosy bacteria affect armadillo liver cells?

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2. Why would reprogramming an adult cell to a stem cell–like state be helpful in regenerating organs?

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3. Why might regenerating organs be a better alternative to transplanting organs from donors? What are the potential benefits of regenerating organs?

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4. We have studied how leprosy bacteria impact mouse nerve cells in a laboratory dish as well as liver cells in living armadillos. What experiments would you suggest running next?

REFERENCES

Samuel Hess, Timothy J. Kendall, Maria Pena, Keitaro Yamane, Daniel Soong, Linda Adams, Richard Truman, and Anura Rambukkana (2022) *In vivo partial reprogramming by bacteria promotes adult liver organ growth without fibrosis and tumorigenesis.* Cell Reports Medicine.
https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(22)00379-2

The Conversation: Why can some organs regenerate while others can't?
https://theconversation.com/curious-kids-why-can-some-organs-regenerate-while-others-cant-128217

Science News Explores: What is a stem cell?
https://www.snexplores.org/article/explainer-what-stem-cell

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