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HUMAN HEALTH
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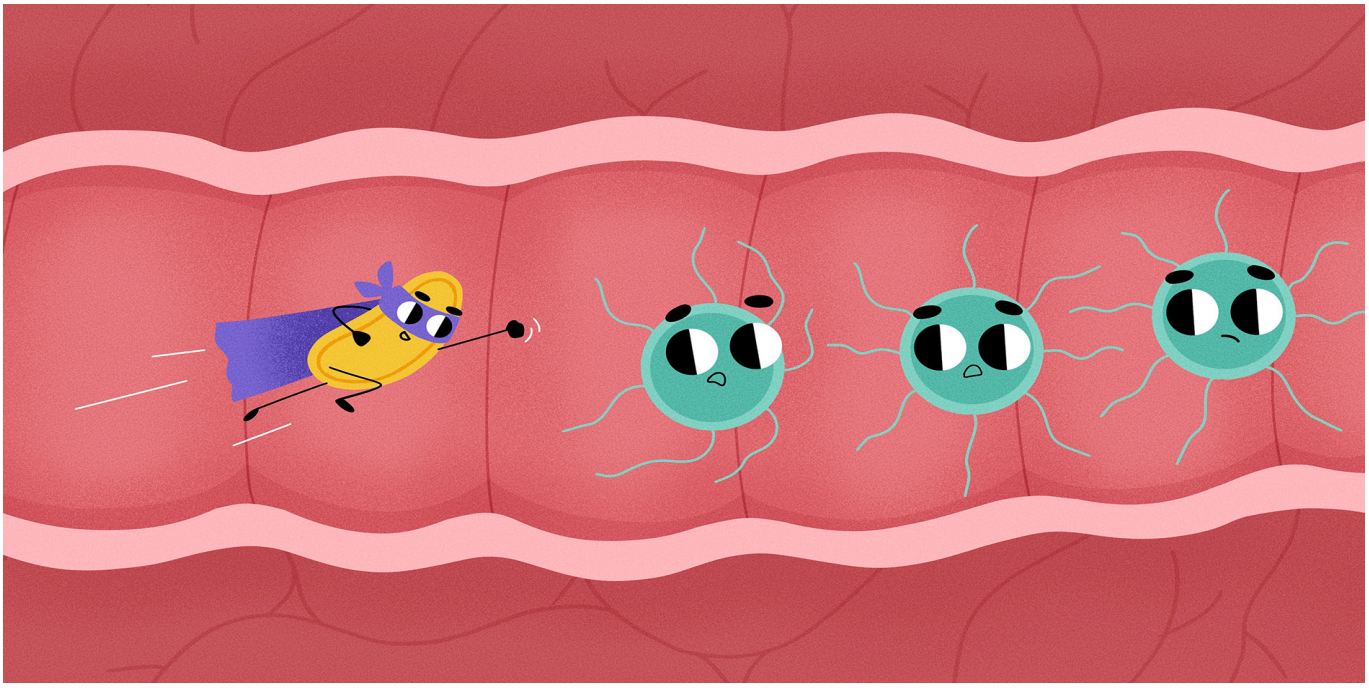

CAN TINY HELPFUL BACTERIA HELP US FIGHT DANGEROUS BACTERIA?

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YOUNG REVIEWERS:

BROOKLYN
AGE: 12

JACK
AGE: 15

WILLIAM
AGE: 8

Antibiotics were a huge advance for the field of medicine because they decreased the risk of people getting sick due to harmful bacteria. However, bacteria quickly learned to "fight back" against these powerful medicines. Antibiotic-resistant bacteria, increasingly frequent nowadays, cannot be killed by antibiotics, making infections with these organisms very dangerous. Some common infections have become extremely difficult or even impossible to cure, leading to an alarming public health problem. In this article, we will discuss how helpful "predator bacteria" might be useful in fighting antibiotic-resistant infections. The bacterium we chose to study is called *Bdellovibrio bacteriovorus,* it lives in the healthy human gut and is capable of preying on other bacteria. In the future, might this bacterium be an effective treatment for dangerous bacterial infections? We think so!

FIGHTING BACTERIA... AND HOW BACTERIA FOUGHT BACK!

Up until about 80 years ago, around the time when your grandparents

were kids, **antibiotics** were not available to treat bacterial infections. This meant that if a child got even a small wound while playing outdoors, for example, bacteria could get into the wound and cause a dangerous infection that could potentially lead to the child's death. Lucky for us, in 1928, a famous scientist discovered the first powerful antibiotic—penicillin—which could kill bacteria and cure infections. Penicillin virtually eliminated the risk of getting sick from bacterial infections for a little while. But unfortunately, in just a few years, bacteria managed to develop strategies to "fight back" against penicillin, so that this antibiotic was no longer as effective. Scientists responded by creating *new* types of antibiotics, but the bacteria fought back against those, too. This is the worrying phenomenon known as **antibiotic resistance**. Today, many antibiotics no longer work on certain types of bacteria, and infections with these antibiotic-resistant bacteria have become scary again! (to learn more about antibiotic resistance, see this Frontiers for Young Minds article).

KEEPING BALANCE IN ECOSYSTEMS: THE PREDATION PHENOMENON

How can this serious problem of antibiotic resistance be solved? Scientists are studying various strategies, and one involves something called **natural predation**. In any **ecosystem**, a group of living things coexist in harmony, interacting with each other within a specific environment. For example, in a forest ecosystem, wolves, foxes, deer, rabbits, birds, insects, oak trees, beech trees, bushes, and grass all form the living parts of the ecosystem. Imagine what would happen if, for example, all the **predators** (wolves and foxes) disappeared. The prey (deer and rabbits) would increase in number and would soon eat all the grass, bushes, and tree leaves until they eventually destroyed their own ecosystem—ultimately endangering their own existence.

Predators are not "bad guys"—they are actually nature's superheroes—, due to their important job of keeping ecosystems in balance. By keeping the populations of prey organisms in check, predators make sure prey animals do not destroy the ecosystem due to their out-of-control growth, so that all the plants and animals can continue to live together in a balanced and healthy way. So, predators are ecological balancers, keeping all the species in the correct proportions and preventing some species from overpopulating and destroying the harmony needed to keep an ecosystem functioning.

But ecosystems do not only exist in forests—there are ecosystems in and on our bodies, too!— One example is the **gut microbiota**. The gut microbiota is a team of billions and billions of microorganisms living in harmony inside our guts. These little guys help us to digest our food and they make important vitamins, strengthen the natural defenses of our bodies, prevent us from getting sick, and generally help us to feel good.

ANTIBIOTICS

Drugs capable of killing dangerous disease-causing bacteria.

ANTIBIOTIC RESISTANCE

The very widespread phenomenon nowadays, through which many bacteria have managed to develop various strategies to resist the antibiotic drugs.

NATURAL PREDATION

When a predator hunts and eats other animals overgrowing in the same environment, it helps keep this ecosystem naturally balanced and healthy.

ECOSYSTEM

the set of all living organisms, their relationships and the environment in which they live all together.

PREDATOR

An animal that hunts and kills other animals for food.

GUT MICROBIOTA

A community of various species of microorganisms living in harmony inside our gut playing a big role in helping us digest food and stay healthy.

We have therefore seen that ecological balance occurs when different species coexist in the right proportions in order to maintain a healthy and functional environment and that predators play a very important role in all of this. Everything works well when all the various members of the gut ecosystem get along and live together peacefully. However, if the balance among them gets messed up, like when one type of bacteria becomes too bossy and tries to take over, it creates disharmony or, in other words, an imbalance that can harm our health. But here is the cool part: just like there are helpful predators in a forest, there are also predator bacteria in our intestines that make sure that ecosystem stays balanced and healthy. Among these bacterial superheroes present in our intestines, the most famous is called *Bdellovibrio bacteriovorus*.

BDELLO: HELPFUL PREDATOR BACTERIA

Bdellovibrio bacteriovorus (called *Bdello* for short) was identified by two scientists during the late 1960s, at Indiana University (USA). Their work laid the foundation for understanding *Bdello*'s unique predatory behavior and how they might be used to control harmful bacteria.

Bdello is much smaller than other types of bacteria, but it is a very fast moving bacterium, capable of destroying bigger bacteria—including those harmful to our health—[1]. *Bdello* lives in both terrestrial (land-based) and aquatic (water-based) environments [2]. *Bdello* attack other bacteria (their prey) by invading them and replicating (reproducing) once they are inside. *Bdello* then returns to the environment by destroying their prey [2]. The main prey hunted by *Bdello* are certain bacterial species (belonging to the group of Gram-negative bacteria) that are frequently associated with human infections [3]. The ability of *Bdello* to prey upon dangerous types of bacteria (Figure 1) led scientists to wonder whether they could be used to treat infections caused by antibiotic-resistant bacteria [4].

BACTERIA FIGHTING BACTERIA TO KEEP US HEALTHY?

First, we wanted to see whether *Bdello* was healthy or harmful to the human body. We found that *Bdello* is always present in the intestines of healthy people [5]. Interestingly, in patients affected by several diseases (such as Celiac Disease and Inflammatory bowel disease) *Bdello* was heavily reduced. So, *Bdello* is not harmful to human health. Furthermore, we observed that *Bdello* is important because it controls the overgrowth of its bacterial prey, keeping harmony within the natural microbial populations living in our intestines. Therefore, this bacterium is very beneficial for the wellbeing of the human body.

Figure 1

Microscope image of the small predator *Bdello* attacking the bigger, harmful, and frequently antibiotic-resistant bacterium *Pseudomonas aeruginosa* (Image obtained in our university laboratories at Sapienza University of Rome-Italy).

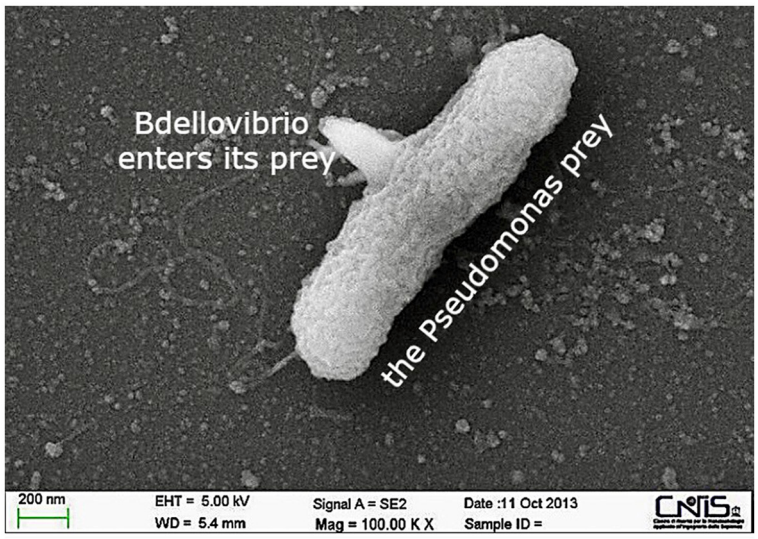

Figure 1

Next, we wanted to know whether *Bdello* could be used to fight infections caused by antibiotic-resistant bacteria (Figure 2). We evaluated the predatory activity of *Bdello* against some antibiotic-resistant bacteria that often cause human infections, such as *Pseudomonas aeruginosa* and a disease-causing strain of *Escherichia coli*—both difficult to cure with antibiotics [6, 7]. Our results, conducted **in vitro** (in test tubes) also confirmed **in vivo** (using a living grater moth larva) [7] indicate that Bdello may prey on both the harmful to humans bacteria *P. aeruginosa* and *Escherichia coli* reducing their growth. These encouraging experimental results, obtained in our laboratory, give rise to hope that one day the same good results can also be obtained directly on human patients suffering from infections with antibiotic-resistant bacteria, obviously, more experiments will be needed before we can get to this.

IN VITRO* AND *IN VIVO

Scientific expressions of Latin origin which refers respectively to experiments conducted in test tubes (*in vitro*) or on live animals (*in vivo*): what happens *in vitro* does not always also happen *in vivo*.

BDELLO VS. ANTIBIOTIC RESISTANCE: MOTHER NATURE GIVES US A HAND?

So far, our research has taught us that the tiny bacterium *Bdello* seem to be a natural part of the ecosystem of the healthy human intestines, and that this predatory bacterium is essential to maintain the healthy balance of the others bacteria within the intestinal ecosystem. Our work using simple *in vitro* and *in vivo* experimental models, so far indicates that *Bdello*'s natural predatory activity could be used to treat worrying infections with antibiotic-resistant bacteria that cannot be effectively treated with antibiotics. Who knows, maybe in the near future we will be using *Bdello* to treat infections, instead of using ineffective antibiotics! This would help to reduce the dangerous health problems all over the world caused by dangerous infections with

Figure 2

Bdello (green ovals) enters into the cell of the harmful bacteria (red ovals), replicates within it and comes out destroying the harmful bacterial prey.

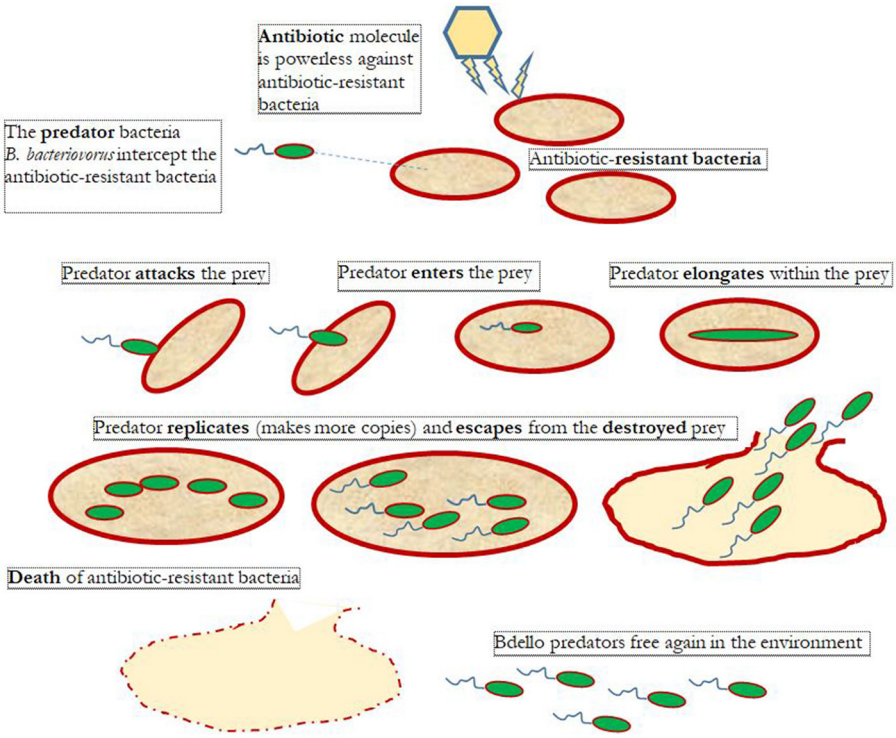

Figure 2

antibiotic-resistant bacteria. Who knows, maybe Mother Nature will give us a hand once again!

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YOUNG REVIEWERS

BROOKLYN, AGE: 12
Brooklyn likes to dance and hang out with her friends playing volleyball, ball hockey, and soccer.

JACK, AGE: 15
I am a high school student who enjoys computer science programming and finance. I like to use the scientific methods of inquiry and discovery to help me address challenges and problems in the world. When I am not working on a new project, I enjoy playing basketball and video games.

WILLIAM, AGE: 8
My name is William and I am in 3rd grade. I like to play baseball. My favorite animals are fish and whales. I like to play video games. I have 4 pets 2 dogs and 2 chickens.

AUTHORS

GIULIA RADOCCHIA

Giulia Radocchia is a young researcher at Sapienza University of Rome. Research is her passion and, together with her team, she faces new challenges every day. She loves studying bacteria; these tiny organisms are her best friends. Her goal in research is to understand how bacteria interact with each other inside the human body. She also tries to find new ways to fight antibiotic-resistant bacteria. She guides young researchers in the lab, trying to pass on her passion for science.

SERENA SCHIPPA

Serena Schippa is a microbiology professor at Sapienza University in Rome, Italy. She loves studying bacteria, especially how they interact with each other, like in the intestinal microbiota. Her research focuses on many scientific aspects, including methods to counteract antibiotic resistance bacteria. Serena is passionate about uncovering the secrets of these tiny creatures and how they affect our bodies. She loves sharing her research with her young students, contributing to making the complex world of microbes easier to understand for all of us.

FABRIZIO PANTANELLA

Fabrizio Pantanella is a microbiologist with a Natural Sciences degree. When he is not busy studying microbes in the lab, you will find him getting up close and personal with Mother Nature herself! He is a birdwatcher, a nature enthusiast and he is a mountain maven! Whether it is scaling peaks or observing birds in their natural habitat, Fabrizio is all about that outdoor adventure. In a nutshell, he is the Microbiologist with a passion for all things natural, especially when it involves a hearty dose of mountain air and feathered friends! *fabrizio.pantanella@uniroma1.it