

## HOW CAN BACTERIA HELP US FIGHT BACK AGAINST BACTERIA?

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Microbes live everywhere and have an intense social life, interacting with many different species. Like each of us, they must be able to survive in a certain location, and they develop strategies to get what they need. Bacteria, a type of microbe, produce small compounds called bacteriocins that can kill other microbes that they compete with for resources. Bacteriocins can help us solve problems, such as antibiotic resistance or food spoilage. We are already taking advantage of some bacteriocins, like nisin, but many more are to come for health and food applications.

### WE LIVE ON A VERY POPULATED PLANET

Microbes are extremely small organisms that can be found almost everywhere in nature, including in and on our bodies. Microbes are so small that we cannot see them with the naked eye, but with sophisticated magnifying glasses called microscopes. All living things on Earth are classified, based on their characteristics, into big

## SPECIES

A group of similar individuals that can reproduce among themselves.

## ECOLOGICAL NICHE

The environment associated with a species, including the resources and relationships with other species.

## ANTAGONISTIC STRATEGY

A type of interaction between species in which one benefits by harming the other.

## ANTIMICROBIAL

A substance that kills microbes or stops their growth.

biological groups: Bacteria, Archaea, and Eukarya. Microbes can be found in all three groups. There are many **species** in each group—so many that we still do not know how many species there are in total, and scientists keep discovering new ones. To give you an idea, all humans are only one species (and see how many we are!). There are 60,065 species of trees in the world, one million species of insects, and there could be one trillion species of microbes [1]! That is 1,000,000,000,000 different types of microbes! How do we manage to live all together?

Luckily, each species has different needs, and eats and lives in a different place. Like humans, microbes also have complicated social lives and they interact with each other to survive. The specific conditions that an organism needs to live are called the **ecological niche** of that species. For example, you know your neighborhood very well. You know your home, the park where you hang out with your friends, and where to go for groceries. Sometimes your niche overlaps with the niches of other species: you have plants in the garden, you walk your dog every evening, and mosquitos bite you during the summer. Microbes do not go to the supermarket or water their plants, but they do develop smart strategies to survive and get what they need. They are very well-adapted to their ecological niches. Let us see how the Bacteria adapt so well and how we can take advantage of it.

## BACTERIAL WARS

The Bacteria domain includes more than 30,000 species. Bacteria can be divided into two big groups: Gram-positive and Gram-negative bacteria, depending on what type of defense-wall they have. Imagine a medieval town surrounded by a wall. This wall is very thick in Gram-positive bacteria, but much thinner in the Gram-negative ones. Bacteria live everywhere, even under very harsh conditions. Some of them feed on sulfur compounds near the deep-ocean hydrothermal vents, some use sunlight to obtain their energy, while still others help to break down food in the guts of animals (and humans). Often, many bacteria live together and fight for a living space, for food, and for other resources. This competition for resources can occur between members of the same species or between members of different species.

The strategies used by bacteria for this competition for space and resources are called **antagonistic strategies**. The antagonistic strategies used by bacteria are quite varied. They include getting rid of important compounds required by their competitors, or modifying the micro-environmental conditions and making it very tough for other bacteria to live. Other bacteria produce compounds called **antimicrobials** to kill or slow down the growth of their neighbors.

### PATHOGENIC

A microbe that can cause disease.

### ANTIBIOTIC RESISTANCE

The ability of a microbe to survive the effect of an antimicrobial that previously would kill it.

### BACTERIOCINS

Small antimicrobial proteins produced by bacteria to kill other bacteria.

Antimicrobials can be non-specific or specific. They are non-specific when they attack any other bacterial competitor. One non-specific antimicrobial is hydrogen peroxide ( $H_2O_2$ )—yes, the antiseptic for wounds. We say that  $H_2O_2$  has a wide spectrum of activity, meaning that it can kill many different types of bacteria. Other examples of non-specific antimicrobials are chemical compounds, such as lactic acid, formic acid, acetic acid, ethanol, carbon dioxide, ammonia, or phenolic compounds. Specific antimicrobials, on the other hand, are those that kill or prevent the growth of a specific type of bacteria. This means that the competing bacteria know each other's weaknesses well and produce tailor-made weapons to fight against each other. We say that specific antimicrobials have a narrow spectrum of activity. This makes specific antimicrobials very effective against some **pathogenic** (disease-causing) bacteria and they can help us fight the superbugs that cause **antibiotic resistance** [2]. Antibiotic resistance happens when bacteria change such that the antibiotics that previously killed them or controlled their growth during an infection no longer work. Pathogenic bacteria that are resistant to antibiotics can then spread and kill many people. The specific antimicrobials, designed by nature to kill only the targeted pathogenic bacteria, can help us to fight the problem of antibiotic resistance that threatens humankind.

## SOPHISTICATED WEAPONS: THE BACTERIOCINS

**Bacteriocins** are specific antimicrobial compounds produced by bacteria to fight other bacteria. Bacteriocins are made of small proteins called peptides that are produced inside bacteria. Some bacteriocins can stay attached to the surface of the bacteria, while others are fully released into the surrounding environment. A total of 816 bacteriocins have been described so far [3].

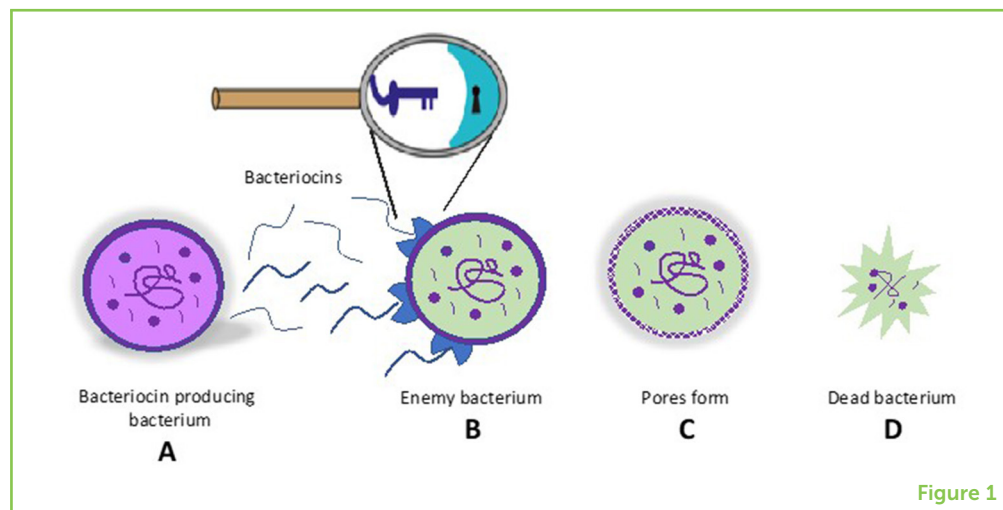
Bacteriocins are grouped into three classes, depending on their size: class I bacteriocins are the smallest and class III are the largest. Bacteriocins have special shapes, which they need to be active and attack enemy bacteria. Although the way bacteriocins work to kill other bacteria is not fully understood, it seems that bacteriocins contact other bacteria through structures on the surface of enemy bacteria called **receptors**. This process works like a key in a lock. When bacteriocins bind to the receptors and contact the enemy surface, the attacked bacterium develops little holes, called pores, in its surface. The contents of the bacterial cell leak out through these pores, which kills the enemy bacterium (Figure 1).

## HOW CAN WE USE THESE BACTERIOCIN WEAPONS?

Bacteriocins can be obtained from the bacteria that produce them by purifying these substances in the lab. This means that large amounts of the bacteria are grown so that they release bacteriocins to their

### Figure 1

Bacteriocins in action. Bacteriocins produced by bacteria (A) can kill "enemy" bacteria. The bacteriocins bind to molecules called receptors on the enemy bacterium (B), similar to the way a key fits into a lock. This causes tiny holes called pores to develop in the membrane of the enemy bacterium (C). The bacterial contents leak out through these pores, which kills the enemy bacterium (D).



surrounding environment. The bacteriocins are then recovered by sophisticated strainers and magnets. We can even manipulate the bacteria so they can produce more bacteriocins.

As we mentioned, bacteriocins are particularly interesting weapons in the fight against antibiotic-resistant bacteria. Bacteriocins could be used as an alternative or complement to traditional antibiotics to treat infections. Moreover, scientists are realizing that bacteriocins and the bacteria that produce them may play a role in the natural balance between the different types of bacteria in our bodies. This means that bacteriocins help to keep the bad bacteria in low numbers. Some studies show that bacteriocins can even fight viruses and cancers [4, 5]. Bacteriocins are harmless to healthy human cells. Currently, bacteriocins are used by veterinarians, but we cannot get them from the pharmacy for human use yet.

Bacteriocins can also be used as food preservatives, to keep our food safer by preventing its spoilage by harmful bacteria. **Nisin**, a bacteriocin produced by a species of bacteria called *Lactococcus lactis*, is one of the best-known bacteriocins. Nisin is widely used for the preservation of dairy products, such as milk, yogurt, and cheeses, and it is also used in meat and seafood preservation. Bacteriocins produced by what are called lactic acid bacteria, a group of Gram-positive bacteria, have attracted a lot of interest because they have a long and safe history of use by humans [6]. These substances include pediocins (produced by the bacterial group *Pediococcus*) and enterocins (produced by the bacterial group *Enterococcus*) both of which are showing promising results in the lab.

Scientists think that most bacteria can produce bacteriocins, but that many of them have not been discovered yet. Since bacteriocins may be extremely useful to humans and may help to fight antibiotic resistance, research in this field is extremely important. Bacteriocin researchers are studying new ecological niches, discovering new bacteriocins,

### NISIN

A type of bacteriocin that is commonly used.

figuring out how bacteriocins work, and finding new ways to produce them. Hopefully, new bacteriocins will soon be ready to use for more applications in the fields of human health and food preservation.

## AUTHOR CONTRIBUTIONS

EG-G and SA designed and wrote the manuscript. Both authors have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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## REFERENCES

1. Locey, K. J., and Lennon, J. T. 2016. Scaling laws predict global microbial diversity. *Proc. Natl. Acad. Sci. U.S.A.* 113:5970–5. doi: 10.1073/pnas.1521291113
2. Bonatelli, M., Oliveira, L., and Pinto, T. 2020. Superbugs among us: who they are and what can you do to help win the fight? *Front. Young Minds* 8:5. doi: 10.3389/frym.2020.00005
3. van Heel, A. J., de Jong, A., Song, C., Viel, J. H., Kok, J., and Kuipers, O. P. 2018. BAGEL4: a user-friendly web server to thoroughly mine RiPPs and bacteriocins. *Nucleic Acids Res.* 46:W278–81. doi: 10.1093/nar/gky383
4. Chikindas, M. L., Weeks, R., Drider, D., Chistyakov, V. A., and Dicks, L. M. 2018. Functions and emerging applications of bacteriocins. *Curr. Opin. Biotechnol.* 49:23–8. doi: 10.1016/j.copbio.2017.07.011
5. Yang, S. C., Lin, C. H., Sung, C. T., and Fang, J. Y. 2014. Antibacterial activities of bacteriocins: application in foods and pharmaceuticals. *Front. Microbiol.* 5:241. doi: 10.3389/fmicb.2014.00241
6. Acedo, J. Z., Chiorean, S., Vederas, J. C., and van Belkum, M. J. 2018. The expanding structural variety among bacteriocins from Gram-positive bacteria. *FEMS Microbiol. Rev.* 42:805–28. doi: 10.1093/femsre/fuy033

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## YOUNG REVIEWER



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I am a curious and fun gentleman who is fascinated by how the world works. I enjoy reading about a number of things from aviation science to medical science. I also enjoy helping my grandmother with cooking in the kitchen and also doing my school work.

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Enriqueta is a biologist whose work is focused on investigating the discovery and use of bacteriocins as alternatives to traditional antibiotics. She earned her Ph.D. looking for new bacteriocins produced by bacteria isolated from human feces and fermented foods, such as yogurt or kefir, and studying how these bacteriocins affected the bacteria in the human gut. Currently, Enriqueta works as post-doctoral researcher at Teagasc Food Research Centre in Ireland.



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