Microbial predators: an unlikely ally?

The Biochemical Society identifies and celebrates outstanding science communication talent in molecular biosciences with its annual Science Communication Prize. Iris Floria (University of Glasgow, UK) won 3rd Prize in the 2022 written category with her entry, 'Microbial predators: an unlikely ally'.

Iris Floria (University of Glasgow, UK)

It was in the air, he could feel it, smell it even. They were close. He started slithering towards them at speed, careful not to emit a sound that would alert them of his presence. Suddenly he could see them, right in front of him. Dinner. He lunged forward and sunk his teeth into the nearest one, piercing its skin. The prey struggled to get free, but to no avail. It was too late. A disgusting sucking sound could then be heard as the predator syphoned the prey's insides into its mouth. Satisfied with his appetiser, he moved on to his main course…

Are you horrified yet? What if I told you that this is the fate that awaits hundreds of bacterial prey every day? What if then I told you that these microscopic predators are exactly what we may be in desperate need of? But let me start from the beginning.

Unusual heroes

The predator in this story is none other than a microbial 'cannibal'. Yes, you read that right. The microbial world has 'cannibals' and they're known as predatory bacteria due to their predator-like behaviour. These pesky little bacterivores are actually quite sophisticated creatures that employ a variety of hunting strategies to be able to enjoy their meals. The ones described in the grim scene above are known as *Vampirococcus*, aptly named due to their vampire-like tendency to suck the 'blood' (well, insides but it's close enough as far as bacteria are concerned) in order to feed, and kill their prey. Other predatory bacteria, such as the *Bdellovibrio bacteriovorus* species, employ a different technique in which they burrow into their prey. In doing so, they then 'shimmy' themselves into the hole created to enter a space known as the periplasm, a midpoint area between the protective outer layer (exposed to the outside environment) and an inner layer (surrounding the internal organelles) of the prey bacteria. The much smaller predator then proceeds to effectively eat its prey from the inside out as it feeds on the nutrients it contains, forming a circular structure known as the bdelloplast. Inside this structure, the predator produces copies of itself, inflating the bdelloplast and thus the prey bacterium like a balloon. Once the victim's nutrients have been thoroughly consumed, the 'balloon' pops. The explosion of the swollen prey releases the hundreds of newly created prey progeny into the surrounding environment, thus leading to a brand-new predation cycle.

But why should we care about this vicious, albeit fascinating, mechanism that some bacteria evolved? Well, it turns out that these tiny cannibalistic predators might well be the solution we desperately need to combat the rising problem of AMR.

Antimicrobial resistance versus bacterivores

Microbes have been increasingly gaining the skills to evade antibiotics and drugs that were previously able to kill or inhibit them. AMR is a monster far more vicious and deadly than these tiny microbes could ever be. If things do not change immediately, if action is not taken now, resistance to antibiotics is set to cause 10 million deaths a year by 2050. But what big numbers and scary words often fail to underline is the loss of tangible things. Without functioning antibiotics, we lose our ability to conduct things such as routine surgeries, have caesarean births and treat common infections. Therefore, as several microbes 'level up', we are in dire need to do the same by using innovative weapons to fight them. Syphoning the power of these tiny predators to create treatments against infectious diseases caused by bacteria might aid us in this fight.

The previously mentioned *B. bacteriovorus* species, for instance, feeds only on specific prey species. Luckily for us, this prey range includes bacteria that are notoriously resistant to antibiotics such as *Helicobacter pylori* (cause stomach infections), *Escherichia coli* (cause diarrhoea) and *Salmonella* species bacteria (cause diarrheal infections). In addition, their vicious killing is conducted at impressive speed, taking less

than 30 minutes. These are only some of the many ways predatory bacteria have a 'one up' on antibiotics.

Bacteriovorus bacteria use another mechanism that makes them attractive as a therapeutic: they re-seal the pore created to gain entry into the prey once situated inside. This may feel like an insignificant action that only benefits the predator to allow it to grow, but it is far from that. Not only does sealing the entry pore prevent the insides of the prey bacterium from being released into the surrounding environment, but it also prevents the triggering of an immune response. A strong immune response, known as the inflammatory response, can be triggered by certain compounds released by dying microbes. By avoiding the inflammatory response from being activated, the predator can easily continue its feeding uninterrupted by agents of the immune system. Antibiotics, on the contrary, often work together with the immune system of the infected individual by causing the activation of the inflammatory response. In doing so, however, healthy tissues of the individual treated with antibiotics can become damaged in the cross-fire. Our tiny predator warriors may enable us to circumvent this issue by not creating an inflammatory response in the first place.

In short, *bacteriovorus* predators are highly efficient predators that avoid being spotted by a larger threat (the immune system) by not allowing the dying prey to sound an alarm (the release of inflammatory compounds). Figure 1.

Safety first

To recap, these extraordinary creatures kill pesky antibiotic-resistant bacteria at record-breaking speed without activating a strong inflammatory immune response in the surrounding areas. Sounds idyllic! Why then have we not replaced all current antibiotics and treatments for these infections with predatory bacteria-based therapies? Unfortunately, it's never quite that simple. Many points need to first be addressed to make sure the potential treatment is safe to be administered. Many different questions regarding safety, duration and feasibility of such treatments need to first be thoroughly explored and answered.

The desire to store a potential therapeutic containing live bacterial predators, for instance, presents an obstacle. As the predators' only food source is their prey, they are unable to survive for long periods of time in its absence. Antibiotics and other drugs that do not contain live bacteria, on the other hand, are not faced with this issue and therefore have longer shelf lives. From the standpoint of commercial production, this may be an important drawback as it would make it harder to store and distribute the product due to the time constraint imposed by their shelf life. While this obstacle may be considerable, it is insufficient to declare predatory bacteria unfeasible treatments against infections. After all, every treatment for infectious diseases, including antibiotics, has its advantages and disadvantages and shelf life may be the least of our concerns if the treatment is effective.

Another important point to address is the circumstance under which predatory bacteria can be used. Antibiotics can be broadly divided into two categories: broad spectrum and narrow spectrum. As the name suggests, broad-spectrum antibiotics work against a broad range of different bacterial species while

narrow-spectrum drugs only affect a limited and specific number of bacterial species. The use of broad-spectrum drugs allows us to treat infections of which the specific bacterial culprit is unknown. However, we would only be able to deploy predatory bacteria in cases in which the bacterial cause has been identified due to their specific tastes in prey. Predatory bacteria-based therapies would nevertheless still have a spot in our arsenal of therapeutic therapies, as they could be employed akin to how we use narrow-spectrum antibiotics, used only against a known target.

Looking ahead

If we want to have a fighting chance against the horrors that AMR is unleashing on our world, we need to think outside the box. Employing an army of bacterial cannibals to fight against bacteria may not be the first thing that comes to mind, but it might just be what we need. These vicious tiny predators and their intriguing lifestyles deserve our attention. The careful study of their physiology and the way they interact with surroundings and prey is necessary to create an army ready to serve on the front lines of our battle against AMR without harming us in the process.

Find out more about the Science Communication Prize, view winners from the other 2022 categories, and winners from previous years https://biochemistry.org/education/science-communication-prize/. ■

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Iris is a microbiology student entering her fourth year of studies at the University of Glasgow. Her passion for creative writing, combined with her love of microbiology, compels her to explore new ways to share the fascinating world of microbes with the public. She has a particular interest in the topic of antimicrobial resistance and the various methods to combat this rising threat.