Phages inject their genetic information into a bacterium, so that it will produce more phages—before it dies

RETURN OF THE BACTERIA EATERS

How can harmful bacteria be combated when antibiotics are powerless? The bacteria-eating viruses known as phages have the potential to save countless human lives. This therapy has actually been well known for a long time, but the knowledge was lost in the West after World War II. It could become very important for a healthy future

TEXT **BJÖRN THEIS**

The Red Army found itself confronting two enemies in 1942. One of them was the German Wehrmacht, which during its retreat from Stalingrad was ravaging the Red Army; the other was an invisible enemy that was causing a growing number of casualties. Cholera was spreading among the Russian soldiers and the civilian population. In order to get the situation under control, the leadership in Moscow sent Zinaida Vissarionovna Yermolyeva, one of the USSR's leading microbiologists, to Stalingrad. Because the city was cut off from medical supply lines, Yermolyeva devised a plan to make use of the natural predators of the cholera bacterium. She set up a production facility for bacteriophages and thus created enough anti-cholera suspension to treat 50,000 people a day. After just a few days, the epidemic in the city had been stopped.

In the decades since then, the fact that phages can be extremely effective in the struggle against bacteria has been forgotten in many places. However, in recent years researchers have once again been focusing more intensely on phage-based therapy. Bacteriophages—or phages for short—are viruses that select highly specific bacteria as hosts for their own multiplication process. For example, a phage that attacks cholera bacteria can infect only these bacteria, not human or animal cells. As a result, phages can be handled safely. Like all viruses, they dock onto their target bacterium, inject their genetic information, and reprogram it to produce additional phages after the infection—until no host bacteria are left.

TWO RESEARCHERS, ONE DISCOVERY

Phages received their name in 1917 from the French microbiologist Félix Hubert d'Hérelle, who had discovered them simultaneously with the English microbiologist Frederick Twort. Both of them observed the formation of holes in films of bacteria, within which the bacteria died off and stopped spreading. D'Hérelle suspected that special microbes were responsible for this phenomenon, and he named them phages, deriving this term from the Greek word "phagein" (to eat). He could not see these microbes. That only became possible when the transmission electron microscope was invented in 1931. Nonetheless, d'Hérelle immediately began to develop phage-based therapies against bubonic plague and cholera. His efforts were successful. The following two decades saw the rapid spread of commercially available phage-based products in France, the UK, Germany, Italy, and the USA—until the 1940s, when antibiotics entered the market. By contrast to the selective phages, antibiotics destroyed all bacteria with a high degree of effectiveness. As a result, research involving phages stopped almost completely in the West. Only in the USSR did it continue to develop.

THE WEST IS RACING TO CATCH UP

In Russia, Georgia, and Poland, phage-based products have been used and freely available for decades, but in most Western countries their use is not permitted. However, there are signs that a reevaluation is taking place. An important reason for this is the rapid spread of bacteria that are resistant to antibiotics. Approximately 1.2 million people have died from infections caused by antibiotic-resistant bacteria since 2019. According to some estimates, this figure could increase to ten million by 2050. In order to tackle these resistant bacteria with phage-based therapies, research is urgently needed. The cornerstones have been laid: The first National Forum on Phages convened in Germany in 2017, and the Leibniz Institute's German Collection of Microorganisms and Cell Cultures (DSMZ) has started to create a collection of potentially therapeutic phages. In the USA, some phage-based products have already been approved for use in the food production industry, for example in order to prevent *listeria* infections. In the West, the race to catch up with other countries' production of functional phages has begun.

That's a good reason for the Foresight team at Creavis to evaluate this topic in depth in the new Foresight focus project "GameChanger 2040." That's because phages could be suitable for some areas of application as sustainable and cost-effective alternatives to antibiotics.

Björn Theis heads the Foresight department at Evonik's innovation unit Creavis