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Freunde zu Verbündeten gemacht

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Phagen statt Antibiotika: Das Spin-off Invitris der TUM entwickelte ein neues Herstellungsverfahren für Bakteriophagen. Das sind hochspezialisierte Viren, die sich gegen bakterielle Infektionen einsetzen lassen. Es ist deutlich schneller und kostengünstiger als bisherige Methoden. □

Turning **Enemies into Allies**

A team of students has developed a new production method for bacteriophages. These are highly specialized viruses that can be used to counter multidrug-resistant bacterial infections. This discovery at the TUM Chair of Biophysics has led to a spin-off called Invitris. The novel production method could soon be used in practice for the first time and there are plans to found a company to promote the concept.

Bacterial infections can occur anywhere in the body, from the lungs to the stomach to the intestines. While infections of this type are frequently treated with antibiotics, bacteria are swiftly becoming immune to these substances. Very specific groups of viruses could represent an alternative to antibiotics. Known as bacteriophages, these viruses infect and kill bacteria but are not harmful to human cells. As the natural enemies of bacteria, they are highly suitable as a treatment for bacterial infections. Although their existence has been known for almost a century, the use of phage therapy has been limited to date. This is due to the lack of safe and efficient production methods for therapeutic bacteriophages.

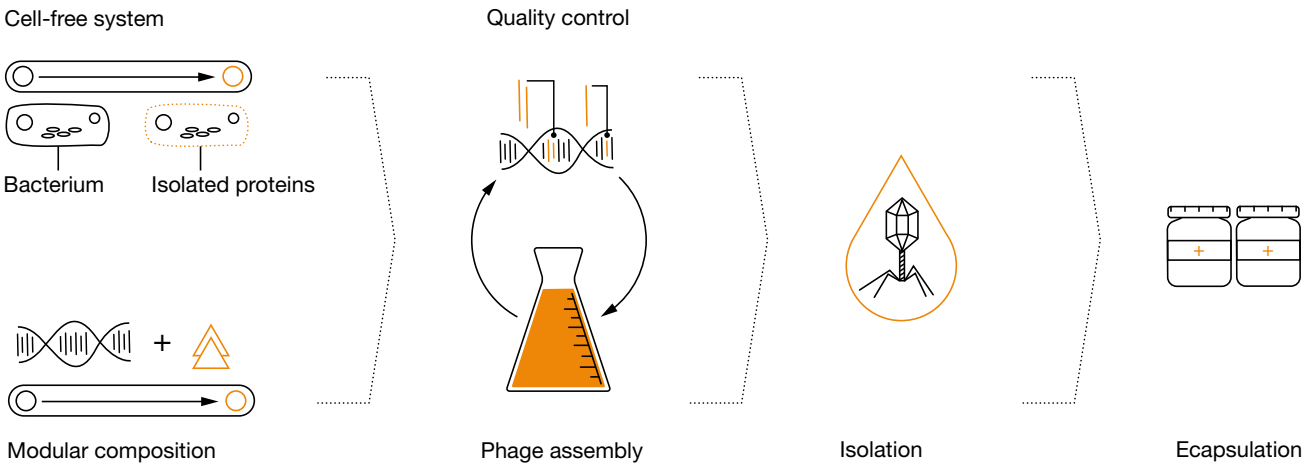
Back in 2018, a team of students from TUM and LMU Munich decided to take up the gauntlet and address this problem. Their work on the topic formed their entry to an international contest for students of synthetic biology called iGEM (International Genetically Engineered Machine Competition). TUM and LMU students have successfully collaborated on iGEM entries for years. In 2018, the 16-strong team brought together students from a range of disciplines, including molecular biology, biotechnology, bioinformatics and electrical engineering.

The cell-free production of phage is faster and requires less effort in the laboratory than conventional methods. Proteins are isolated from non-pathogenic bacteria. DNA of the desired phage is added. The quality or purity of the phage DNA is ensured before isolating and encapsuling the phage.

Cell-free production system proves promising

The team collaborated to develop the idea for a new phage production method. An important aspect to bear in mind is that, in order to multiply, phages require a host cell – a bacterium. Production systems developed to date involve removing all pathogenic endotoxins secreted from a bacterium before using it to produce phages. This method entails cost-intensive and time-consuming cleaning procedures and the use of high-grade cleanrooms. The iGEM team, on the other hand, have based their approach on a cell-free system. First, they isolate the proteins in non-pathogenic bacterial cells ordinarily responsible for the production of proteins and phages. They obtain an extract and add the DNA of the desired phage. The major benefit of this cell-free system is that it avoids the need for laborious cleaning procedures, thereby enabling phages to be produced significantly faster and more safely. At the iGEM final in Boston in October 2018, the joint TUM-LMU project won through against 350 other teams to claim second prize overall alongside other awards, such as the Best Entrepreneurship Project.

“According to current estimates, ten million people will die as a result of antibiotic resistance each year by 2050 [...].” Franziska Winzig



The spin-off Invitris was set up to continue developing the cell-free method after the competition. Three students and a supervisor from the iGEM team have been joined by a graduate bioinformaticist/business administration specialist as they strive to improve the technique further. In principle, it would be a suitable treatment for all bacterial infections. “As each bacteriophage only infects a specific species of bacteria, the Invitris method can compose any desired variety of phage, typically with an incubation period of just a few hours,” explains Invitris’ Franziska Winzig. Currently in the sixth semester of her biology studies, she plans to write her bachelor’s thesis on the method. “According to current estimates, ten million people will die as a result of antibiotic resistance each year by 2050 – more than the sum of deaths caused by all cancers. Hopefully, we will be able to counteract this trend,” says an optimistic Winzig.

Set for deployment

Plans to found a company to promote the method are also in the pipeline, reveals Winzig. To prepare for this step, the team has called on funding from TUM and also took part in the UnternehmerTUM Medtech Bootcamp 2019, which is geared to preparing entrepreneurs for the incubation and initial financing phase of their new company. Invitris aims to bring the method to market as soon as possible. “We will likely start in Belgium,” says Franziska Winzig. Thanks to the country’s adoption of magistral preparation (also known as compounding pharmacy), phages can now be applied as a therapy in Belgium without having to pass through clinical studies. Germany is examining this approach at present. The Invitris team is currently working to obtain certification to apply its phage medicines. In fact, they are already in contact with a Belgian military hospital where the cell-free production method for phage medicines to fight wound infections could be used for the first time.

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Link
www.invitris.com

Graphics: ediundsepp (source: Invitris)