Researchers assassinate disease-causing bacteria with virus cocktail

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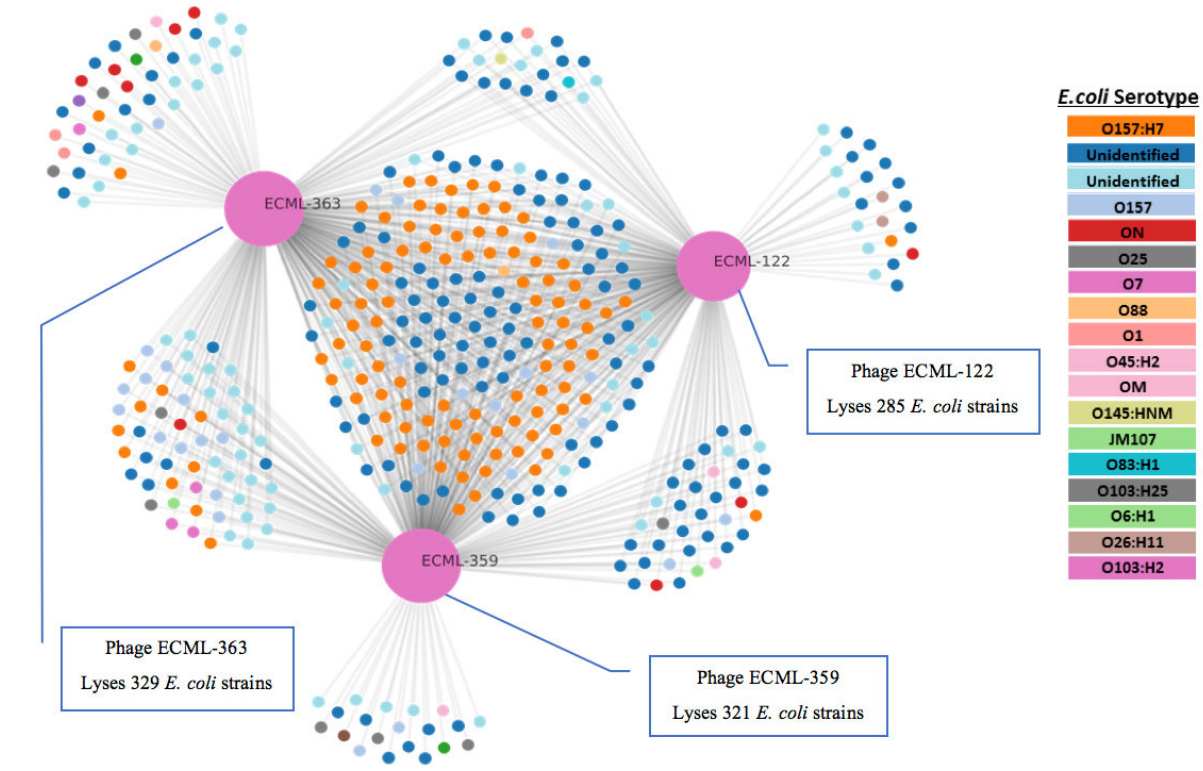
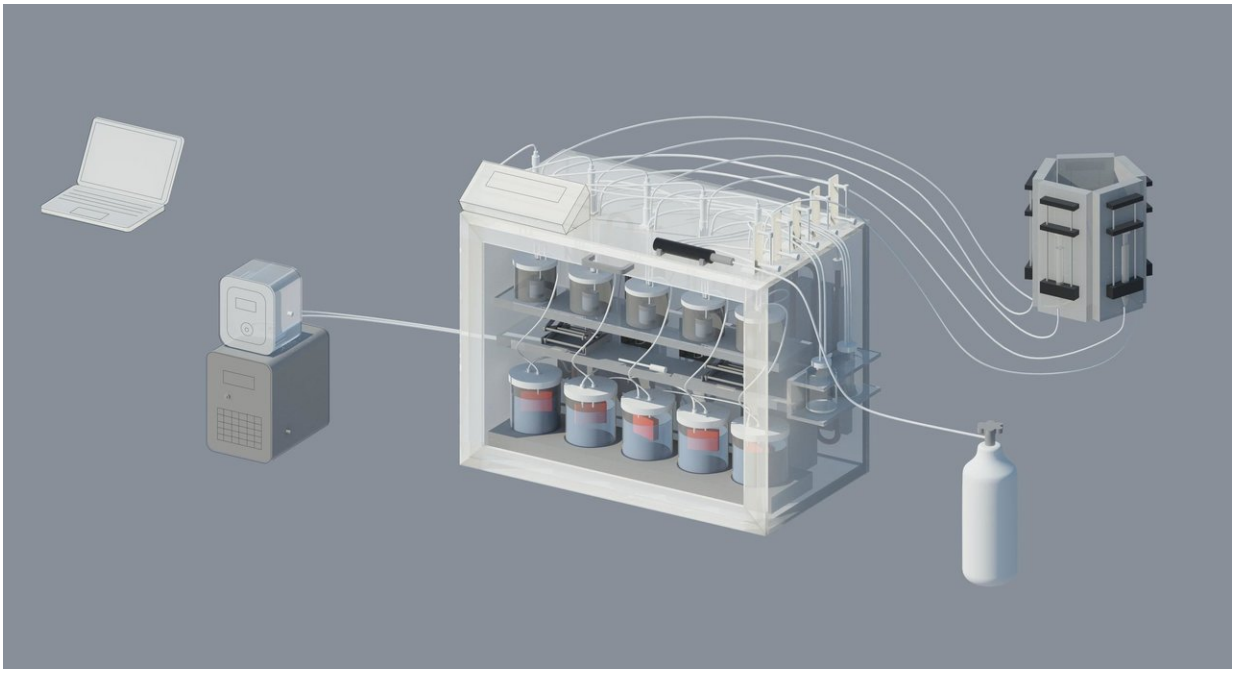


Three bacteriophages (pink dots) were tested against a huge collection of *Escherichia coli* strains representing different serotypes. In combination the three bacteriophages kill most of the tested strains. Credit: The graph was generated using proprietary PhageSelector™ program developed by Intralytix, Inc.

New research from the Department of Food Science (FOOD) at the University of Copenhagen suggests that in the not-too-distant future, it might be possible to drink a cocktail of selective viruses (bacteriophages) that travel directly into the gut and kill the disease-causing bacteria without the use of antibiotics, and without harming the beneficial commensal intestinal bacteria.

"The research shows that we have an opportunity to kill specific bacteria without collateral damage to otherwise healthy intestinal flora," says Professor Dennis Sandris Nielsen from Department of Food Science at the University of Copenhagen. He emphasizes that the result was created in a model of the small intestine, so the next step will be to test the study on mice and later on humans if such treatment is to be implemented.

Model of the small intestine



3-D representation of the TSI in vitro model. TSI consists of five elements: main

unit, water bath, syringe pump station, nitrogen tank and computer which controls the whole setup. In the main unit, there are multiple reactors capable to test up to five samples at the same time. Credit: Maja Czesnik

The model in which the research has been conducted, TSI, was developed at FOOD by postdoc Tomasz Cieplak, in connection with his Ph.D. project, with Professor Dennis Sandris Nielsen as his supervisor. "The novelty of the TSI model is that it simulates the presence of the small intestinal microbiota, which has largely been overlooked in other models of the small intestine. Other models existing on the market simulate only the purely biophysical processes, such as bile salts and digestive enzymes or pH, but here we included this important aspect of human gut physiology to mimic the small intestine more closely," says Cieplak.

The composition of the intestinal flora in the model is representative of how the intestinal flora could look in a healthy person. In the study, researchers have added E. coli bacteria to the intestinal flora, which they then attempted to kill by utilizing a targeted cocktail of viruses (bacteriophages) developed by the company Intralytix.

New research in an old method

"Using bacteriophages to kill pathogenic bacteria is not new, and has actually been used to treat food-borne illnesses and other diseases in Eastern Europe for almost a century, but it was not until relatively recently that this approach started to attract more widespread research interest," says Dennis Sandris Nielsen

The research into combating infectious diseases with viruses was not as interesting because you already had an effective treatment with

antibiotics. "It is different today, where resistance to antibiotics is an increasing problem in modern medicine. At the same time, we have become more aware of how important the commensal bacteria in the gut are for our health," says Nielsen.

Phages (bacteriophages) are viruses that attack bacteria—in this context, bacteria in our intestinal microbiome. The classic lytic phage attacks bacteria by attaching to the surface of the bacterium and injecting its genetic material into the bacterium. It takes over the bacterium's metabolism and redirects it to create new viruses. The bacterial cell, now taken over by the phage, will explode and send a lot of new phages into the surrounding area, which can then attack new bacteria.

More information: Tomasz Cieplak et al, A bacteriophage cocktail targeting Escherichia coli reduces E. coli in simulated gut conditions, while preserving a non-targeted representative commensal normal microbiota, *Gut Microbes* (2018). DOI: 10.1080/19490976.2018.1447291

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