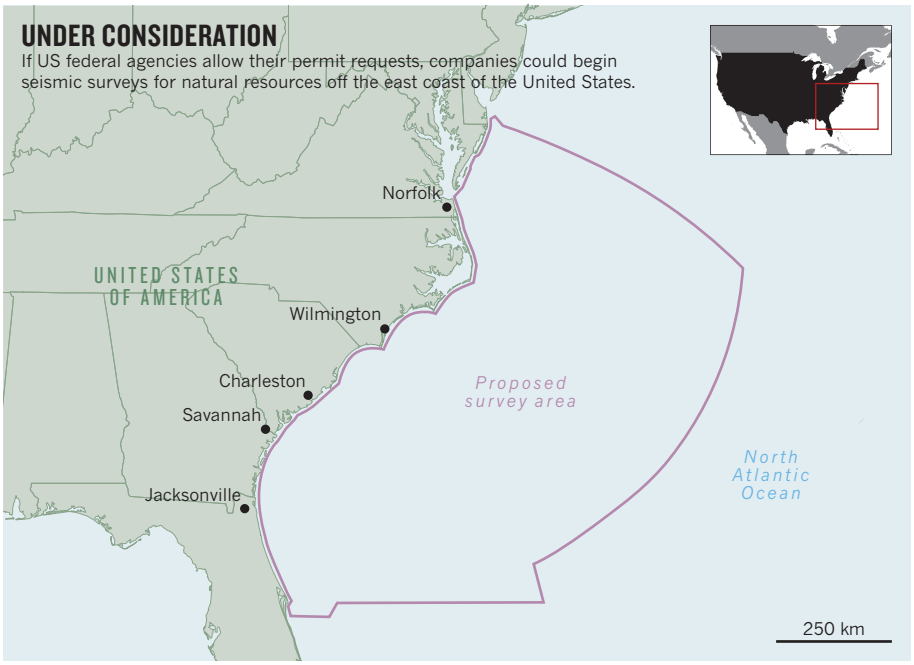
larvae and tiny crustaceans called copepods, before and after firing a series of air-gun shots. The team found that zooplankton abundance dropped by 64% within one hour of the blasts. And the proportion of dead zooplankton increased by 200–300% as far away as 1.2 kilometres — the maximum distance the researchers sampled. This suggests that the impact of the blasts could extend well beyond such distances, Semmens says.

"Dead bodies in net tows don't lie," says Doug Nowacek, a marine ecologist at Duke University Marine Laboratory in Beaufort, North Carolina, who was not involved in the study. He suggests the next question for researchers is figuring out what this means for the ocean ecosystem. "If you start impacting the zooplankton population, that can cause a serious cascade through the food web."



SOURCE: NOAA

THE FORGOTTEN ONES

The results come as US President Donald Trump proposes opening up large swathes of the Atlantic coast of the United States to seismic surveys (see 'Under consideration'). The US Bureau of Ocean Energy Management is considering permit requests from six companies to conduct seismic surveys that were denied under former President Barack Obama. As part of that process, the US National Oceanic and Atmospheric Administration (NOAA) must also evaluate permit requests from those companies because their proposed activities could affect marine mammals. The NOAA permit requests are open for public comment until 6 July.

Although it's unclear if the companies will be able to start seismic surveys, initiating the permit process is part of a larger effort — laid out in an executive order that Trump issued in April — to expand US offshore energy development.

The Tasmania study didn't pin down precisely how air-gun blasts kill zooplankton, Semmens says, but the noise they produce probably damages the highly sensitive hair-like receptors that the animals use to navigate. The blast might not kill them all directly, but it could disorient them and make it harder for them to survive.

Semmens is planning a follow-on study with a full seismic air-gun set-up similar to that used in industrial activities to determine how far the effects of the noise extend. He and his team also want to look at what these blasts do to zooplankton physically. Although most research has focused on the impact of air-gun blasts on marine mammals, Semmens notes, perhaps it's the invertebrates that are most at risk. "It could be that our focus has kind of been blinkered because it's been on whales," he says. "Invertebrates are the forgotten ones." ■

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DRUG RESISTANCE

Modified viruses deliver death to antibiotic-resistant bacteria

Engineered microbes use CRISPR to turn a bacterium's immune response against itself.

BY SARA REARDON

Genetically modified viruses that cause bacteria to kill themselves could be the next step in combating antibiotic-resistant infections.

Several companies have engineered such viruses, called bacteriophages, to use the CRISPR gene-editing system to kill specific bacteria, according to a presentation at the CRISPR 2017 conference in Big Sky, Montana, this month. These companies could begin clinical trials of therapies as soon as next year.

Initial tests have saved mice from antibiotic-resistant infections that would otherwise have killed them, said Rodolphe Barrangou, chief scientific officer of Locus Biosciences in Research Triangle Park, North Carolina, at the conference.

Bacteriophages isolated and purified from the wild have long been used to treat infections in people, particularly in Eastern Europe. These viruses infect only specific species or strains of bacteria, so they have less of an impact on the human body's natural microbial community, or microbiome, than antibiotics do. They are also generally thought to be very safe for use in people.

But the development of phage therapy has been slow, in part because these viruses are naturally occurring and so cannot be patented. Bacteria can also quickly evolve resistance to natural phages, meaning researchers would constantly have to isolate new ones capable of defeating the same bacterial ▶

strain or species. And it would be difficult for regulatory agencies to keep approving each new treatment.

CRISPR-FUELLED DEATH

To avoid these issues, Locus and several other companies are developing phages that turn the bacterial immune system known as CRISPR against itself. Locus's phages hijack the normal CRISPR defence system of antibiotic-resistant bacteria. DNA inserted by the phages produce modified guide RNAs that home in on part of an antibiotic-resistance gene.

Once the guide RNA latches on to the resistance gene, it prompts an enzyme called Cas3 — which the bacterium normally produces to kill phages — to destroy that genetic sequence instead. Cas3 eventually destroys all the DNA, killing the bacterium.

Another company, Eligo Bioscience in Paris, uses a similar approach. It has removed all the genetic instructions that allow phages to replicate, and inserted DNA that encodes guide RNAs and the bacterial enzyme Cas9. Cas9 cuts the bacterium's DNA at a designated spot, and the break triggers the bacterium to self-destruct. The system will target human gut pathogens, says Eligo chief executive Xavier Duportet, although he declined to specify which ones.

The two companies hope to start clinical trials in 18–24 months. Their first goal is to treat bacterial infections that cause severe disease. But eventually, they want to develop phages that will let them precisely engineer the human microbiome by removing naturally occurring bacteria associated with conditions such as obesity, autism and some cancers. "We think we will be able to reach into the human body in any single location and eliminate any single bacteria we choose," says Barrangou.

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Both Barrangou and Duportet acknowledge that for now, causal links between the human microbiome and these conditions are tenuous at best. But they hope that by the time their therapies have been proved safe and effective in humans, the links will be better understood. Phages could also allow researchers to manipulate the microbiomes of experimental animals, which could help them to untangle how certain bacteria influence conditions such as autism, says Timothy Lu, a synthetic biologist at the Massachusetts Institute of Technology in Cambridge and a co-founder of Eligo.

Other companies are working to get phages to perform different tasks. 'Supercharged' phages, created by a group at Synthetic Genomics in La Jolla, California, could contain dozens of special features, including enzymes that break down biofilms or proteins that help to hide the phages from the human immune system.

But engineered phages still have to overcome some hurdles. Treating an infection might require a large volume of phages, says Elizabeth Kutter, a microbiologist at Evergreen State College in Olympia, Washington, and it's unclear whether this would trigger immune reactions, some of which could interfere with the treatment. Phages could also potentially transfer antibiotic-resistance genes to non-resistant bacteria, she says.

Lu adds that bacteria may still develop resistance, even to the engineered phages. So researchers might have to modify their phages frequently to keep up with bacterial mutations.

But as antibiotic resistance spreads, Kutter says, there will be plenty of space for both engineered phages and natural phage therapies, which are also growing in popularity. "I think they'll complement the things that can be done by natural phages that have been engineered for hundreds of thousands of years," she says. ■