Scientists discover new phage therapy combination to combat antibiotic-resistance

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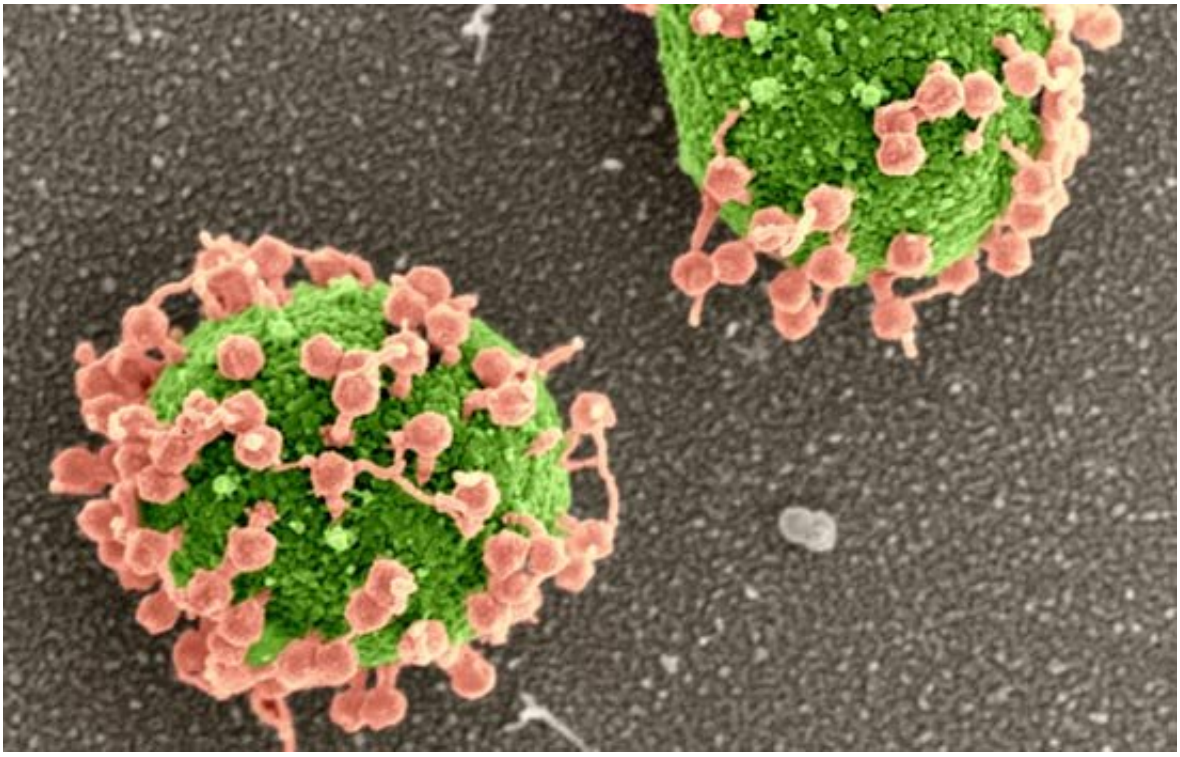

Colourised scanning electron microscopy image of phage FG02 (orange) infecting Acinetobacter baumannii bacteria (green). Credit: Denis Korneev

A preclinical study led by Monash University scientists has found that using a combination of phages and antibiotics may be far more effective against bacterial infections than using the agents individually.

The study, published today in *eBioMedicine*, has wide ranging

implications for antibiotic resistant bacterial infections—described by the World Health Organization (WHO), as one of the greatest threats to global health.

Phage therapy is the use of bacterial viruses to clear a bacterial infection.

In recent years there has been growing interest in the use of phage therapy as a potential treatment to combat antibiotic-resistant infections

"However, questions remain around the efficacy of phage therapy as a treatment option," said study author Dr. Jeremy Barr, from the Monash University's School of Biological Sciences, and the Centre to Impact AMR.

"This has been obfuscated by the fact that clinical phage therapy is almost always administered alongside antibiotics, making it difficult to determine the efficacy of phage therapy," he said.

In this study the researchers used a phage-antibiotic combination against the world's leading antibiotic-resistant superbug—Acinetobacter baumannii.

In previous work, the researchers showed that phages can kill antibiotic resistant A. baumannii, but in doing so they found that phage-resistant mutants emerged; similar to how antibiotic-resistance emerges with prolonged antibiotic use, phage-resistance also occurs.

"We found that while A. baumannii rapidly became phage-resistant, in doing so they were also resensitized to the same antibiotics they use to resist," said lead study author Fernando L. Gordillo Altamirano, also from the Monash School of Biological Sciences.

"Applying this knowledge, we conducted a pre-clinical trial using animal

models and found that the combined use of phages and antibiotics led to significantly improved treatment outcomes than either antibiotics or phage therapy alone," he said .

Dr. Barr said of particular note the findings explained the mechanism through which the combination of these two agents had resulted in a superior treatment effect.

"We have been able to confirm that, even in complex living systems, treatment with our characterized phages can reliably steer bacteria towards a phage-resistant variant that is re-sensitized to antibiotics."

The researchers had hypothesized that the success of the combination therapy in vivo was due to the emergence of phage-resistant mutants exhibiting antimicrobial resensitization, followed by targeted treatment with the resensitized antibiotic.

"We believe further research in the field is likely to lead to the discovery of innovative uses of combination therapies using phages and antibiotics in combination, rather than proposing phages as a substitute to antibiotics," said Dr. Barr.

More information: Fernando L. Gordillo Altamirano et al, Phage-antibiotic combination is a superior treatment against Acinetobacter baumannii in a preclinical study, *eBioMedicine* (2022). DOI: 10.1016/j.ebiom.2022.104045

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