

## Harnessing the power of predatory bacteria as a 'living antibiotic'

## November 23 2016

A naturally occurring predatory bacterium is able to work with the immune system to clear multi-drug resistant *Shigella* infections in zebrafish, according to a study published today in *Current Biology*.

It is the first time the predatory bacterium Bdellovibrio bacteriovorus has been successfully used as an injected anti-bacterial therapy and represents an important step in the fight against drug-resistant infections, or 'superbugs'.

Shigella infection is responsible for over 160 million illnesses and over 1 million deaths every year - and is a common cause of 'travellers' diarrhoea.' Cases of drug-resistant Shigella are also on the rise as, although the diarrhoea usually clears up without treatment, antibiotics are often used even in mild cases to stop the diarrhoea faster. Resistance to antibiotics has prompted a team of researchers from Imperial College London and Nottingham University to look to the natural environment for creative solutions to this problem.

To investigate Bdellovibrio's ability to control drug resistant Gramnegative infections, researchers injected zebrafish larvae with a lethal dose of Shigella flexneri strain M90T, resistant to both streptomycin and carbenicillin antibiotics. *Bdellovibrio* was then injected into the larvae's infection site, and a decrease in the number of *Shigella* was seen. In the absence of *Bdellovibrio*, zebrafish were unable to control the replication of *Shigella* and levels of the bacteria rose.



Wellcome Research Career Development Fellow Dr Serge Mostowy, colead author from Imperial College London said: "This study really shows what a unique and interesting bacterium *Bdellovibrio* is as it presents this amazing natural synergy with the <u>immune system</u> and persists just long enough to kill prey bacteria before being naturally cleared. It's an important milestone in research into the use of a living antibiotic that could be used in animals and humans."

Bdellovibrio can invade and kill a range of Gram-negative bacteria, such as *E. coli* and *Salmonella*, in the natural environment. Previous research has shown that it can reduce pathogen numbers in the stomach of chickens when taken as an oral therapy, but there is growing need to develop therapies to target infections in wounds and organs. Successful use of Bdellovibrio highlights its potential uses in tackling a range of drug-resistant Gram-negative bacterial infections that can develop in hospital patients.

Professor Liz Sockett, co-lead author from The University of Nottingham said: "This has been a truly ground-breaking collaboration that shows therapeutic *Bdellovibrio* in action inside the translucent living zebrafish. The predatory action of the *Bdellovibrio* breaks the *Shigella*-pathogen cells and this stimulates the white blood cells; redoubling their 'efforts' against the pathogen and leading to increased survival of the zebrafish 'patients'."

Remarkably, *Bdellovibrio* is also able to reduce pathogen load in immunocompromised zebrafish larvae that have been depleted of white blood cells. However, survival is significantly greater in immune-competent zebrafish, showing that Bdellovibrio's maximum therapeutic benefit comes from its ability to work cooperatively with the host's own immune system.

Dr Michael Chew, Science Portfolio Advisor at Wellcome said: "It may



be unusual to use a bacterium to get rid of another, but in the light of the looming threat from <u>drug resistant infections</u> the potential of beneficial bacteria-animal interactions should not be overlooked. We are increasingly relying on last line antibiotics, and this innovative study demonstrates how predatory bacteria could be an important additional tool to drugs in the fight against resistance."

**More information:** 'Injections of predatory bacteria work alongside host immune cells to treat Shigella infections in zebrafish larvae' *Current Biology*, DOI: 10.1016/j.cub.2016.09.067

## Provided by Wellcome Trust

Citation: Harnessing the power of predatory bacteria as a 'living antibiotic' (2016, November 23) retrieved 10 April 2024 from <a href="https://phys.org/news/2016-11-harnessing-power-predatory-bacteria-antibiotic.html">https://phys.org/news/2016-11-harnessing-power-predatory-bacteria-antibiotic.html</a>

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