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Microbiology

Fighting food pathogens with the help of a soil bacteria

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ABSTRACT

E. coll O157 (EHEC) is a foodborne pathogen associated with limited treatment options. The University of Glasgow and The University of Strathclyde are exploring natural products from the soil bacteria Streptomyces as novel drugs for these infections.

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Enterohemorrhagic Escherichia coli (EHEC) is a notorious foodborne pathogen, typically associated with consumption of undercooked red meat. The infamous 'burger bug', most commonly caused by a subspecies called "O157:H7" is responsible for causing a severe form of food poisoning, which can reach beyond the gut to attack both the kidneys and the brain, with often deadly consequences. Recently, the bug has made headlines after romaine lettuce was banned from restaurants in the USA during a multi-state outbreak. EHEC is particularly troublesome as there are currently no antibiotics recommended for treatment. This is because antibiotics can trigger an 'SOS response' in the bacteria. Just as the name suggests, an SOS response is a signal that the bacteria are under threat, causing them to produce more toxins, leading to the escalation of the infection. Therefore, other avenues for treatment must be explored.

EHEC and other important pathogens of the gut utilise many 'virulence factors' to enhance their ability to colonize and survive the human host. These often include toxins, antibiotic resistance genes, and mechanisms of attachment to the host. One of the most important virulence factors in EHEC is the Type Three Secretion System (T3SS), a needle-like apparatus responsible for injecting proteins from infecting bacteria into cells of the gut, which is required for EHEC establish an infection on the gut

lining of the host. Therefore, we aimed to inhibit this system in a new approach to remove the infection from the host without causing these unwanted side effects. In our research, we proposed this 'anti-virulence' strategy for the treatment of EHEC, where, in contrast to traditional antibiotics, the aim is not to kill or inhibit the growth of the infecting bacteria, but simply to prevent the bacteria from harming the host, by neutralising their weapons. Hence, we intended to inhibit EHEC from attaching to the cells of the gut by inhibiting the T3SS, in theory, allowing the body to pass the infection naturally and without harm.

In our work, we were able to inhibit this process by treating the cells with a compound known as Aurodox. This compound was not designed by us to specifically inhibit this process, but is in fact, a natural product of the soil bacterium, *Streptomyces goldiniensis*. The source of the compound is unsurprising, as approximately 60% of our clinically used antimicrobial compounds are based on the naturally occurring molecules of *Streptomyces,* which have evolved the ability to produce these molecules to gain an ecological advantage over their neighbours while contesting for resources. In our research, we exploited this natural phenomenon and were able to use very small doses of the compound to cause a >7000 fold reduction in the ability of EHEC to attach to epithelial cells. We were also able to demonstrate that the compound did not physically block the secretion system, but prevented the system from being triggered in the first place.

Besides, it was of great importance that we analysed the effect of Aurodox on toxin production, as induction of the bacterial SOS response or increase in toxin production by the compound could make Aurodox unsuitable for use as a treatment for EHEC. Therefore we analysed the expression of SOS response-associated genes and the production of toxin after treatment with Aurodox and found that there was no effect of the compound on toxin production. The results of this experiment are promising, and represent the first steps in the development of an anti-virulence strategy, the first of its kind for EHEC, and a novel redirection of strategy in the antimicrobial drug discovery process.