Choreographed stages of Salmonella infection revealed

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This is Professor Jay Hinton, University of Liverpool. Credit: University of Liverpool

Scientists have used a new method to map the response of every

salmonella gene to conditions in the human body, providing new insight into how the bacteria triggers infection.

In a world first, the scientists exposed salmonella to 22 lab environments that mimic conditions that the bacterium finds when it enters the human body and discovered the effects of these conditions on individual genes in the bacteria.

After people eat salmonella, the microbes enter the stomach, and intestine, and then invade human cells. The researchers mimicked these changing environments by altering levels of acidity, oxygen and nitric oxide in lab experiments.

The researchers from the University of Liverpool and Trinity College Dublin examined the effect of each of these environments on the 4,742 genes in the bacterium and determined which conditions 'turned on' each gene. The results paint an accurate picture of the 'choreography' of gene expression that is required when this dangerous bacterium infects people.

Soon after entering the body, exposure to oxygen-limited conditions causes the activation of genes which enable the bacteria to stick a syringe-like structure into the gut wall to cause diarrhoea. Once inside the lining to the gut, immune defence chemicals prompt salmonella to be engulfed by macrophages – the cells that normally kill other bacteria. Unusually, the bacteria have evolved to thrive inside these protective cells, by switching on genes that neutralise the lethal abilities of macrophages.

Salmonella can survive in stressful environments and even hijack the body's own defences. In people with weakened immune systems, such as the young, old or those with HIV, infection by salmonella can prove fatal, with an estimated 160,000 deaths each year across the world.

Doctors are reluctant to use antibiotics to treat all but the most extreme cases of salmonellosis in order to avoid creating resistant strains of the bacterium. Instead, the usual advice is for people to rest and drink fluids. Ideally a vaccine would be developed to eliminate the need for antibiotics entirely.

The results of the new study, which reveals the specific genes used during salmonella infection and growth, and the triggers which activate them, have implications for the future design of drugs and vaccines which could be specifically targeted against the strategies used by salmonella to become active inside the human body.

The method used by the scientists is transferrable to all bacteria and, given time, many more diseases could be studied using the same approach.

Professor Jay Hinton from the University of Liverpool's Institute of Integrative Biology led the study. He said: "These findings show that salmonella goes through a complex choreography of different stages while infecting different parts of our bodies.

"We've started using this approach with salmonella as it's a well understood organism with a significant global impact, and we hope that the same technique will now be used to gather more information from a variety of other dangerous bacteria."

More information: All of the data sets have been uploaded to a free-to-use website: bioinf.gen.tcd.ie/cgi-bin/salcom.pl

Provided by University of Liverpool