

Scientists find single letter of genetic code that makes African Salmonella so dangerous

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Abstract image of African Salmonella expressing PgtE in the bloodstream.
Credit: Eliza Wolfson

Scientists at the University of Liverpool have identified a single genetic change in Salmonella that is playing a key role in the devastating

epidemic of bloodstream infections currently killing around 400,000 people each year in sub-Saharan Africa.

Invasive non-typhoidal Salmonellosis (iNTS) occurs when *Salmonella* bacteria, which normally cause gastrointestinal illness, enter the bloodstream and spread through the human body. The African iNTS epidemic is caused by a variant of *Salmonella* Typhimurium (ST313) that is resistant to antibiotics and generally affects individuals with immune systems weakened by malaria or HIV.

In a new study published in *PNAS*, a team of researchers led by Professor Jay Hinton at the University of Liverpool have identified a specific genetic change, or single-nucleotide polymorphism (SNP), that helps the African *Salmonella* to survive in the human bloodstream.

Professor Hinton explained: "Pinpointing this single letter of DNA is an exciting breakthrough in our understanding of why African *Salmonella* causes such a devastating disease, and helps to explain how this dangerous type of *Salmonella* evolved."

SNPs represent a change of just one letter in the DNA sequence and there are thousands of SNP differences between different types of *Salmonella*. Until now, it has been hard to link an individual SNP to the ability of bacteria to cause disease.

Using a type of RNA analysis called transcriptomics, the scientists identified SNPs that affected the level of expression of important *Salmonella* genes. After studying 1000 different SNPs, they found a single nucleotide difference that is unique to the African ST313 strain and causes high expression of a virulence factor called PgtE that prevents *Salmonella* being killed in the bloodstream.

The scientists then used an advanced genetic technique to switch the

SNP found in the African strain to the version found in the type of Salmonella that causes food poisoning and gastroenteritis globally. Finally, they used an animal infection model to show that the bacteria with the altered SNP had lost their ability to cause disease.

Professor Hinton added: "We've developed a new investigative approach to understand bacterial infection, which is the culmination of six years of work. This combination of genomics and transcriptomics could bring new insights to other important pathogens, and prepare us for future epidemics."

Professor Melita Gordon, a University of Liverpool clinician-scientist working in Malawi, who was involved in the project, said: "The ability of iNTS Salmonella strains to cause such serious disease leads to devastating and frequently fatal consequences for very young children, and for adults who may be the chief breadwinners in their homes and communities. We see iNTS disease placing an enormous burden on thinly-stretched local health facilities and hospitals in Malawi, particularly because diagnosis is difficult, and treatment options are limited. It is now urgent that a vaccine is developed to combat this dangerous infection."

More information: Disa L. Hammarlöf et al, Role of a single noncoding nucleotide in the evolution of an epidemic African clade of Salmonella, *Proceedings of the National Academy of Sciences* (2018). [DOI: 10.1073/pnas.1714718115](https://doi.org/10.1073/pnas.1714718115)

Provided by University of Liverpool

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