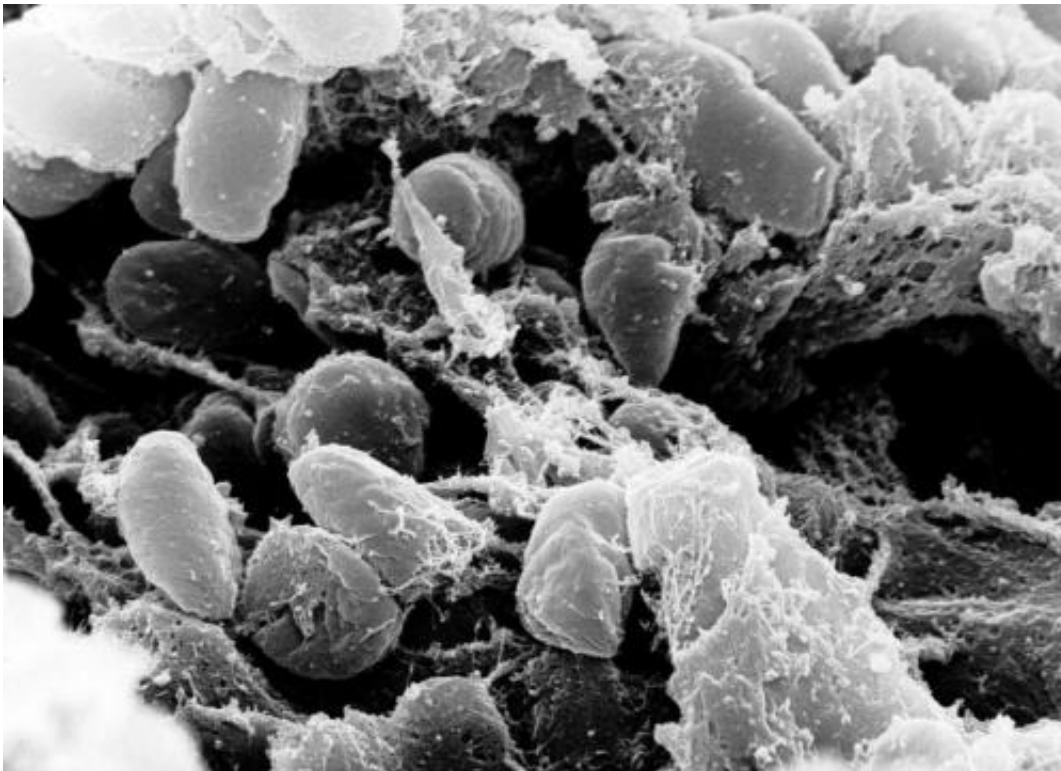


How small genetic change in *Yersinia pestis* changed human history

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A scanning electron microscope micrograph depicting a mass of *Yersinia pestis* bacteria in the foregut of an infected flea. Credit: Wikipedia

While studying *Yersinia pestis*, the bacteria responsible for epidemics of plague such as the Black Death, Wyndham Lathem, Ph.D., assistant professor in microbiology-immunology at Northwestern University Feinberg School of Medicine, found a single small genetic change that

fundamentally influenced the evolution of the deadly pathogen, and thus the course of human history.

In a paper published in *Nature Communications*, Lathem and first author Daniel Zimmler, Ph.D., a Feinberg post-doctoral fellow, demonstrated how the acquisition of a single gene caused the shift of *Y. pestis* from causing a primarily gastrointestinal infection to a more serious and often fatal respiratory disease. They further showed how later modifications of this gene enhanced infections associated with the [bubonic plague](#).

"Our findings demonstrate how *Y. pestis* had the ability to cause a severe respiratory disease very early in its evolution. This research helps us better understand how bacteria can adapt to new host environments to cause disease by acquiring small bits of DNA," Lathem said.

The team examined ancestral strains of the bacteria in mouse models to learn when *Y. pestis* gained the ability to infect the lungs and cause the severe form of the disease known as [pneumonic plague](#).

In the most ancestral of all currently existing *Y. pestis* strains, they showed how the bacteria could successfully colonize the lungs but could not cause the severe disease associated with pneumonic plague. The biggest difference they found between this strain and closely related strains that could cause pneumonic plague was a gene for the surface protein Pla.

Lathem proposed that the bacteria's acquisition of the gene Pla enhanced its ability to cause infection in the lungs and was all that this ancestral strain of *Y. pestis* needed to produce a fatal lung infection.

So Lathem and his team inserted the Pla gene into this strain to observe changes in the health of the lungs. They found the newly mutated strain had gained the ability to cause respiratory infection identically to

modern strains of *Y. pestis* that cause disease today, demonstrating that the Pla gene was necessary for *Y. pestis* to infect the lungs. In addition, they found that no other changes to *Y. pestis* were required, even though the bacteria has continued to gain and lose [genes](#) over the last several thousand years.

The lab also looked at variations of the gene Pla and discovered that a single modification only found in modern strains of *Y. pestis* was a critical adaptation for the bacteria to spread in the body and infect the lymph nodes, a form of the infection that causes bubonic plague. According to Lathem, the surprising conclusion from this aspect of the study is that, contrary to current thinking in the field, *Y. pestis* may have first evolved as a respiratory pathogen before it could cause the more common form of disease, bubonic plague.

Lathem said the new research may explain how *Y. pestis* transitioned from causing only localized outbreaks of plague to the pandemic spread of *Y. pestis* such as the sixth century's Justinian Plague and the fourteenth century's Black Death.

"Our data suggests that the insertion and then subsequent mutation of Pla allowed for new, rapidly evolving strains of [disease](#)," Lathem said. "This information can show how new respiratory pathogens could emerge with only small genetic changes."

More information: *Nature Communications*, [DOI: 10.1038/ncomms8487](#)

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