



UNIVERSITY OF MARYLAND
SCHOOL OF MEDICINE

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Researchers apply large-scale sequencing analysis for detailed reconstructions of historic plague pandemics

A multi-national team of academic, government and industry scientists from Europe, China and the United States published data reconstructing the global evolutionary history of devastating plague pandemics in unprecedented detail. This includes the notorious Black Death epidemic in medieval Europe that greatly affected the peoples and governments of Western Civilization. Published today in the prestigious international journal ***Nature Genetics*** (published online on 10/31/2010), the research reconstructs the fatal global impact of the plague bacterium (*Yersinia pestis*), using the historic and phylogenetic comparison of 17 *Yersinia pestis* isolates from global sources.

Funding from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, contributed in part to the historical analysis research to help scientists and the medical community better trace and prepare for future outbreaks of plague.

The multinational team included Drs. Mark Eppinger and Jacques Ravel from the Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine. Dr. Ravel, Associate Director, Genomics at IGS, and Dr. Eppinger, Research Associate, are experts in microbial genomics and forensics. They sequenced and analyzed several bacterial plague genomes that allowed detailed insights into the dynamic spread of the three plague pandemics recorded in human history. Just as DNA is revolutionizing criminal investigations, it can be used to understand ancient events through the use of evolutionary theory and genomics analysis.

Pandemic infectious diseases have accompanied humans since their origins, and have shaped the form of civilizations. Of these, plague is possibly historically the most dramatic, being among other feats, credited for the fall of the Roman Empire. If these pandemics are something of the past, the plague has never fully disappeared and is currently re-emerging in several parts of the world, particularly in Africa and Madagascar. In addition, it is ecologically established in global animal populations. The work shows that the bacterium responsible for the plague (*Yersinia pestis*) evolved in or near China, and has been transmitted via multiple epidemics that followed various routes, including transmissions to West Asia via the Silk Road and to Africa by Chinese voyages led by the explorer Zheng He between 1409 and 1433.



The last plague pandemic of 1894 spread to India and radiated to many parts of the globe, including the USA, which was infected by a single radiation still persisting today in wild rodents. The work showed that country-specific plague lineages could be identified by unique mutations they have accumulated in their genomes.

The international team, led by Professor Mark Achtman (University of Cork, Ireland) demonstrated that country-specific plague lineages (populations) could be identified by unique mutations that have accumulated in their genomes. These unique mutations will be useful for understanding future disease events involving plague, as this type of DNA fingerprinting can be used to characterize both natural and nefarious plague outbreaks. This is crucial, as plague has been used as a biological weapon in antiquity, as well as modern times.

To avoid sending samples of this major potential bioterrorism agent around the world, the team devised an innovative research strategy of decentralized experiments. The multinational team worked on 17 complete plague genome sequences and on 933 variable sites in the DNA of the largest global collection of plague isolates ever assembled. This information allowed the team to track the progress of the historical pandemics throughout the world and to calculate the age of the different waves of this devastating disease. Most of these dynamic events could now be linked to known historical records.

Dr. Eppinger, a contributing first author on the project, said: “The sequencing of additional plague bacteria was crucial in identifying subtle, yet important differences in this evolutionary young human pathogen. What was so amazing with the results is that it was possible to use present day genome information to accurately link past plague pandemics to major events in recorded human history”.

Dr. Paul Keim, Regents Professor and Divisions Director from Northern Arizona University (NAU) and the Translational Genomics Research Institute (TGen) notes that “Future epidemiologists can learn from this millennium-scale reconstruction of a devastating disease to prevent or control future infectious disease outbreaks.”

Quotes from non participating Scientists:

Professor Arturo Casadevall, Chair of Microbiology and Immunology, Albert Einstein College of Medicine, Yeshiva University, said, “*Yersinia pestis* is one of those microbes that has changed the flow of history. The mapping of *Yersinia pestis* global diversity is a wonderful human achievement that will allow us to better understand such past cataclysms, as well as prepare for future epidemics.”

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Notes to Editors

This research is published on 31 October 2010 in the journal **Nature Genetics** - Morelli et al., *Yersinia pestis* genome sequencing identifies patterns of global phylogenetic diversity, Nature Genetics (2010) (NG-LE27468R2)

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Contacts at the Institute for Genome Sciences

Media contact: Sarah Pick, spick@som.umaryland.edu 410.707.2543

Dr. Mark Eppinger, meppinger@som.umaryland.edu 410.706.6782

Dr. Jacques Ravel, jravel@som.umaryland.edu 410.706.5674

About the Funder

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<http://www.niaid.nih.gov/Pages/default.aspx>.

About IGS

The Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine is an international research center dedicated to advancing the use of genomics to improve biomedicine. Led by Dr. Claire Fraser-Liggett, a preeminent genome scientist and microbiologist, IGS is located in a BioPark in downtown Baltimore. IGS scientists are pioneers in the expanding fields of genomics, bioinformatics and metagenomics. For more information, see www.igs.umaryland.edu.