Toward A Molecular History of *Yersinia pestis*

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Identifying Pathogens in Ancient Remains

1. Identification of species specific nucleic acids (DNA or RNA) in remains by two independent groups.

2. Isolation and identification of species specific non-nucleic acid biomolecules (protein, lipid, carbohydrate).

3. Biological plausibility.
Detecting Non-Nucleic Acids in Ancient Remains


Rapid Diagnostic Test

- Antibody strip test that detects the *Yersinia pestis* F1 antigen, a protein from the capsule.
- Developed for and used in clinical medicine in resource poor areas.

iPCR: Immuno-PCR

Malou et al (2012). *PLoS ONE*, 7(2) DOI: [10.1371/journal.pone.0031744](https://doi.org/10.1371/journal.pone.0031744)

Michel Drancourt, Didier Raoult and the Marseille group

- Pioneers in paleomicrobiology; the first to isolate ancient *Yersinia pestis* DNA in 1998.
- Working hypothesis that plague can be transmitted by the human body louse.
- Developed multi-disease ancient DNA assays and the immuno-PCR assay for protein.
SNP Profiles

- Single Nucleotide Polymorphisms (SNP) = genetic fingerprint based on single base changes
- SNP profiles are necessary because there is so little genetic diversity in the *Yersinia pestis* species.
- Amplification of species specific fragments proves *Y. pestis* identity. Sequence differences place it on the family tree which will eventually allow strain mapping.

DNA of the Black Death


- The sequence of over 90% of the *Yersinia pestis* genome was identified.
- This clone is ancestral to most modern strains.
- There is no obvious genetic rationale for the virulence of the second pandemic.
- Ancient DNA fished out of the specimen by hybridizing to fragments of a modern *Y. pestis* strain on an gene chip.
Simplified Phylogenetic Tree

Biogeography and Phylogenetics

Supplementary Figure 3. Postulated routes of spread. D) A condensed MSTree (Fig. 2) with colored sections that are repeated in parts A–C and E, within which corresponding colors link locations within maps (circles, pie charts) to nodes within the MSTree segment. A) Sources of 1.ANT isolates in Central Africa and routes of navigation (black lines) by Zheng He from China to Africa in 1409-1433. B) Upper left sources of isolates from branch 2 superimposed on a map of Asia. Lower right: sources of 2.MED isolates superimposed on a topographical map of the Silk Road (white lines; 200 BC – 1,400). C) Direction of spread of 1.IN nodes within China from northwest to south. E) Postulated routes of migration of 1.ORI since 1894. I–Ie: Radiations with few isolates. Radiations 1.ORI1 and 1.ORI3 are expanded in Supplementary Figs. 4–5.

Multiple waves of plague in the third pandemic caused by 1.0R1

6th-8th century
14th century
15th-18th century