

# ANCIENT DNA TRACES ORIGIN OF BLACK DEATH

Plague-causing bacteria from Kyrgyzstan are direct ancestors of those that sparked medieval pandemic.

By Ewen Callaway

surprising things to me is that these *E. coli* have been in a very constant environment, yet their genomes have not shrunk much.

Lenski: I think part of the issue on the genome shrinkage is that that's a slow process. Thirty years and 75,000 generations — it's a drop in the evolutionary bucket. So I would guess that if we could come back — in one million years or whatever, the bacteria probably would have extremely reduced genomes. That's a reason to keep it going.

## Why did you decide to pass the torch?

Lenski: I'm not going to be around forever. I think it's better to do those things now, to plan them carefully and thoughtfully. So it just made sense. I'm 65 years old, and although I don't plan to retire any time in the next few years at least, the lab is getting smaller. And one of the important things for keeping the long-term lines going is this daily rhythm. I think a lab that has half a dozen or more people is ideally suited to the weekend and holiday coverage that the experiment benefits from.

So I asked Jeff, maybe in 2018 or 2019. I have a National Science Foundation grant to run the experiment, and Jeff is now a co-principal investigator on that.

## Why did Jeff take it on?

Barrick: I'm a big proponent of open science. This is a great resource that I want to support and share and continue. It's become kind of a common touchstone for a lot of stories about bacterial evolution. And something that people can take in so many directions. I'm excited about supporting the community.

## Rich, what's your advice for Jeff?

Lenski: Keep calm and carry on. Frustrating things will happen. But the experiment is quite forgiving. As long as my brain is working, I'll be really excited to see what new spin-off experiments he and collaborators generate, what new analyses he and the broader community generate to make sense of what's going on with the long-term lines. Probably the most important thing Jeff will have to think about in 20 or 30 years is, who's next?

## Interview by Ewen Callaway

This interview has been edited for length and clarity.

**A** Silk Road stopover might have been the epicentre of one of humanity's most destructive pandemics.

People who died in what is now Kyrgyzstan in the fourteenth century were killed by strains of the plague-causing bacterium *Yersinia pestis* that gave rise to the pathogens responsible for the Black Death several years later, shows a study of ancient genomes.

"It is like finding the place where all the strains come together, like with coronavirus where we have Alpha, Delta, Omicron all coming from this strain in Wuhan," says Johannes Krause, a palaeogeneticist at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, who co-led the study, published on 15 June in *Nature* (M. A. Spyrou *et al.* *Nature* 606, 718–724; 2022).

## A pestilence's roots

Between 1346 and 1353, the Black Death laid waste to western Eurasia, killing up to 60% of the populace in some places. Historical records

suggest that the bubonic plague emerged from the east: Caffa, on the Crimean peninsula, experienced one of the earliest-recorded outbreaks of plague during a 1346 siege by the army of the Mongol Empire. The Caucasus and other locales in Central Asia have been put forward as potential epicentres.

China hosts some of the world's greatest genetic diversity of modern *Y. pestis* strains, hinting at an East Asian origin for the Black Death. "There were all kinds of hypotheses in the literature. And it was not really known where it exactly came from," says Krause.

## Signs of the plague

Several years ago, Philip Slavin, an economic and environmental historian at the University of Stirling, UK, and a co-lead author of the study, came across records from a pair of fourteenth-century cemeteries in Kyrgyzstan that, he thought, might hold clues to the origins of the Black Death. The cemeteries, known as Kara-Djigach and Burana, held an unusually high number of tombstones dated to 1338 and 1339, ten of which made explicit reference to a pestilence.

"When you have one or two years with excess mortality, it means something funny is going on there," Slavin said at a press briefing.

To determine whether the burials held any relevance to the later Black Death, Slavin worked with Krause to track down the remains from the Kyrgyz cemetery — which had been excavated in the 1880s and 1890s and moved to St Petersburg, Russia. The team, led by archaeogeneticist Maria Spyrou at the University of Tübingen, Germany, sequenced ancient DNA from seven people whose remains were recovered, discovering *Y. pestis* DNA in three burials from Kara-Djigach.

A pair of full *Y. pestis* genomes gleaned from the data showed that the bacteria were direct ancestors of strains linked to the Black Death, including a *Y. pestis* sample from a person who died in London that Krause's team sequenced in 2011. The Kara-Djigach strain was also an ancestor of the vast majority of *Y. pestis* lineages around today — a sign, Krause says, of an explosion in *Y. pestis* diversity shortly before the Black Death. "It was like a big bang of plague," he said at the press briefing.

Other evidence also puts the origins of the Black Death in this part of Central Asia. Among



An engraved tombstone of a person who died from the Black Death, from the Kara-Djigach cemetery in what is now Kyrgyzstan.

modern strains of *Y. pestis* bacteria, those sampled from marmots and other rodents in Kyrgyzstan, Kazakhstan and Xinjiang in northwest China, surrounding the Tian Shan mountain range, were most closely related to the Kara-Djigach strain. “We can’t really say it’s that village or that valley, but it’s likely that region,” says Krause.

Rodents are the natural reservoir for *Y. pestis*, and humans develop bubonic plague only when a vector such as a flea passes on the infection. Krause suspects that humans’ close contact with infected marmots sparked the Kyrgyzstan epidemic, whereas immunologically naive rat populations in Europe fuelled the Black Death.

Tian Shan makes sense as an epicentre for the Black Death, says Slavin. The region is on the ancient Silk Road trade route, and the Kyrgyzstan graves were found to contain pearls from the Indian Ocean, corals from the Mediterranean and foreign coins, suggesting that faraway goods passed through the area. “We can hypothesize that trade, both long-distance and regional, must have played an important role in spreading the pathogen westward,” Slavin said.

### Medieval ‘death certificates’

Obtaining genomes from plague bacteria ancestral to those behind the Black Death is “a tremendous breakthrough”, says Monica Green, a medieval historian and independent scholar in Phoenix, Arizona. “The headstones are as close as we will ever come to ‘death certificates’. So we know this lineage of *Y. pestis* was in existence then.” But she’s less sure of the study’s conclusion that the plague’s ‘big bang’ occurred at around the time of the Kyrgyzstan deaths in 1338–39. Green has hypothesized, on the basis of genetic, ecological and historical evidence, that the thirteenth-century expansion of the Mongol Empire catalysed the spread and diversification of *Y. pestis* strains responsible for the later Black Death.

Sharon Dewitte, a bioarchaeologist at the University of South Carolina in Columbia, says the work opens the door to studying the Black Death – and the wider outbreak it was part of, known as the second plague pandemic – beyond Europe. She’s keen to compare demographic and mortality patterns from people in Kara-Djigach who died of the plague with those from European Black Death cemeteries.

“Having more plague samples from ancient Asia and China will be super-interesting in terms of adding even more evidence to the Asian origin of the first and second [plague] pandemics,” adds Simon Rasmussen, a computational biologist at the University of Copenhagen who has analysed ancient *Y. pestis* sequences.

Krause hopes to analyse remains from China to see how a pandemic that so scarred Europe reverberated in East Asia, he says. “We would really like to get the Eastern part of the story.”

# AFRICAN RESEARCHERS LEAD CAMPAIGN FOR COLLABORATION EQUITY

Statement on research partnerships between the global north and south highlights unethical practices.

By Holly Else

**R**esearchers at the seventh World Conference on Research Integrity, in Cape Town, South Africa, have been hammering out the equity issues plaguing science partnerships that span the global north–south divide. Several sessions at the event were dedicated to the design of a soon-to-be-published document called the Cape Town Statement on fostering research integrity. The conference ran from 29 May to 1 June.

The statement will offer guidance on how researchers from low- and middle-income countries can become equal partners in international projects. The organizers hope that having a set of principles for fair and equitable partnerships will help scientists from the global south to speak out against unfair practices. These include not being properly credited and pursuing research questions imposed by collaborators from the global north that do not benefit local communities.

Although not all international collaborations are problematic, unfair and inequitable practices are rife, says Lyn Horn, who heads the Office of Research Integrity at the University of Cape Town. She is formulating the statement together with a group of researchers and ethicists. “Even people and funders with very good intentions perhaps don’t understand how entrenched some of their practices and processes are,” she says.

Researchers in low- and middle-income countries often work with peers from wealthier ones. This can bring advantages in the form of secure funding, which might not be available locally, and better career prospects as a result of working with prestigious institutions. Their partners benefit, too, because they gain access to local communities and expertise.

But these collaborations can be fraught with inequity. Sometimes, the research is funded and led by overseas scientists who arrive with a fully formed research question that either doesn’t address the issues of local people, or disregards their customs and traditions. Local researchers often have little involvement outside data collection and fieldwork, and are not always given fair credit for their contributions. In the worst cases, local researchers are not involved at all – foreign scientists simply fly in,



Social-justice researcher Thuli Madonsela at the World Conference on Research Integrity.

do the study and leave, a phenomenon called helicopter science – or do work that would not be ethically approved in wealthier countries, a situation known as ethics dumping.

“The statement is going to open up space for people to proactively engage on these issues,” says Francis Kombe, director of EthiXPERT, an organization in Pretoria, South Africa, that promotes ethical research, and who is contributing to the Cape Town statement.

On 16 May, a paper outlining the issues and possible solutions was published for discussion at the conference (L. Horn *et al.* Preprint at OSF Preprints <https://doi.org/hz46>; 2022). It includes a preliminary list of key values and principles – such as accountability, mutual respect and fairness – that are important for fostering equality and could be incorporated in the statement. The document also proposes actions that funders, research-team leaders, institutions, journals, publishers and scientists involved in these partnerships can take to redress the balance.

Those leading the discussions at the conference will now finesse the text of the statement, and hope to publish the work in a journal later this year. “The fact that we have contributed to the generation of these principles makes us feel that they are ours – we can lead by them,” says Amos Laar, a public-health researcher at the University of Ghana in Accra.