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Figure 1 | A mass burial pit created during the Black Death. Klunk *et al.*[2] retrieved DNA from the bones of people who were alive before, during or after the Black Death.

Genetics

Rapid natural selection during the Black Death

David Enard

Human DNA from the Middle Ages reveals that natural selection occurred at pace in survivors of a bubonic plague pandemic, perhaps leaving their descendants at increased risk of autoimmune diseases. **See p.312**

During the Industrial Revolution, the pigmentation of peppered moths (*Biston betularia*) changed in a matter of decades, with natural selection favouring darker moths that were better camouflaged against soot-covered surfaces[1]. This is a classic example of what evolutionary biologists have long known – that natural selection can happen rapidly, given the right conditions. Klunk *et al.*[2] report on page 312 that even humans, with their historically small populations and long intervals between generations, can adapt at remarkable speed. But riding the evolutionary bullet train might come at a cost.

Bubonic plague is a deadly infectious disease caused by the pathogenic bacterium *Yersinia pestis*, which is spread by rodents. In the fourteenth century, a wave of bubonic plague dubbed the Black Death killed up to 50% of people in Europe[3], making it the deadliest pandemic recorded in modern European history. Klunk *et al.* asked a simple question – was the Black Death so deadly that it triggered an episode of natural selection in the genomes of infected individuals? In other words, did survivors carry specific genetic variants that made them more likely to survive than those who were killed?

To answer it, the authors sequenced DNA from people who lived in London or Denmark just before, during or after the Black Death (Fig. 1). The sequencing allowed the team to track genetic variants that had become more common during the pandemic. The authors reasoned that these variants were more likely than other variants to have been naturally selected – people who carried them survived more often than those who did not, and left more descendants who inherited the protective genetic variants. In turn, these descendants would have had more protection during subsequent waves of disease, which occurred every few years for the next four centuries. Indeed, these subsequent waves were typically less deadly than the Black Death[4].

The narrow time window from which samples were taken, and the large number of samples analysed, are selling points of the study, allowing Klunk *et al.* to accurately date natural selection. The authors achieved this using historical records and radiocarbon dating, among other approaches. Even though evolutionary biologists had previously wondered about the possibility of natural selection during the Black Death, proper investigation was not possible without this precise dating of many samples.

Klunk and colleagues found that a striking number of genetic variants were selected for in genes that govern immune defence against pathogens. In just a few generations, tens to hundreds of genetic variants that might potentially be protective against the plague became more common in a detectable way. The authors also found that the four that became most common were selected for at a speed and an intensity never observed before in human genomes. Individuals who carried some or all of these variants probably had immune defences that responded efficiently to *Y. pestis*, and, as a result, had much better odds of surviving infections.

Klunk *et al.* then infected cultures of human cells carrying different genetic variants with *Y. pestis*. These experiments confirmed that the gene variants that were most highly selected for did indeed confer robust immune defences – the cells with those variants were more resistant to *Y. pestis* infection than were cells that did not carry these variants.

It is worth noting that such rapid and strong selection is highly unlikely to occur for human traits other than immune defence. No other set of traits is under such strong evolutionary pressure. Furthermore, the evolution of the immune defence system is unique in the sense that, until the advent of systematic vaccination of the population in the past century, humans had very little control over pathogens. Klunk and colleagues' results therefore cannot be extrapolated to the rest of the human genome.

Finally, there is evidence that the speed at which natural selection occurred during the Black Death might have come at a cost that is still being paid today. Some of the genetic variants identified by the authors increase the risk of autoimmune diseases such as rheumatoid arthritis[5]. Perhaps this increased risk simply did not matter during the Black Death – the urgency of the pandemic might have made the trade-off an inevitable one.

Although the study provides evidence of rapid selection of immune-defence variants, there are caveats to consider. Sequencing DNA from historical samples is challenging, so the authors had to restrict their sequencing efforts to prominent immune-defence genes. Such genes are involved in the response to many other pathogens, and it is still unclear whether any of these could have contributed to the strong natural selection observed. A possible future research avenue will be to sequence entire genomes, to further establish that the burst of natural selection was indeed specific to *Y. pestis*. This could be achieved by showing that natural selection occurred at a specific combination of genes whose modulation as a group is affected only by *Y. pestis*.

Going forward, more studies of ancient DNA could also enable a better understanding of the evolutionary origins of autoimmune diseases. Population migrations can shape the risk of such diseases through 'founder' events, in which, by chance, the founders of a given population happen to carry specific disease-associated variants[6]. Klunk and colleagues' inferences – together with a study by my group that identified a historical epidemic through the natural selection it drove in host genomes[7] – indicate that ancient epidemics are also a force to consider.

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The author declares no competing interests.

Quantum physics

Superfluid system hosts early-Universe dynamics

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A fluid of ultracold atoms has exhibited quantum dynamics similar to those thought to have existed moments after the Big Bang – ushering in a new era of laboratory exploration of the early Universe. **See p.260**

The idea that the early Universe underwent a phase of rapid inflation was originally proposed to address some of the outstanding puzzles of the Big Bang[1]. But scientists soon realized that this theory of inflation could also explain the very origin of the Universe's cosmic structure[2]. Like all events that occurred in the early Universe, the inflationary phase has long been inaccessible to direct experiments, but that doesn't necessarily preclude exploration of the physics involved. On page 260, Viermann *et al.*[3] report a set of neat laboratory experiments that offer a peek at a small segment of inflationary history by examining the dynamics in a system of supercooled potassium-39 atoms.

By cooling the atoms down to just tens of nanokelvin, the authors achieved a state known as a superfluid, which can be thought of as an ideal fluid with zero viscosity. Superfluids exhibit excitations, called phonons, consisting of sound waves that are restricted to discrete energy levels[4]. Viermann and colleagues' superfluid was shaped like a pancake, so the phonons propagated in two dimensions. Once excited, they were free to roam through the superfluid, and their speed determined how long it took them to propagate from one side of the pancake to the other. The authors manipulated this speed, and the shape of the pancake, to mimic wave propagation in a particular space-time geometry (known as the Friedmann–Lemaître–Robertson–Walker, or FLRW, geometry). This geometry encodes the gravitational field of the whole Universe, meaning that it can represent different cosmological scenarios, including inflation[5].

To establish the link between wave propagation in their superfluid pancake and the dynamics of the early Universe, Viermann *et al.* carried out two kinds of test. First, they excited short bursts of sound waves (wavepackets) in the centre of their superfluid, and studied how these wavepackets spread out when the wave speed was manipulated to simulate an inflationary Universe (Fig. 1). The sound speeds were modified by varying external magnetic fields, which influenced the interactions between atoms. The authors found that the wavepackets propagated in an