

donor stem-cell transplant meant that the vast majority of cells (such as immune cells called CD4⁺ T cells) that could harbour HIV were of donor origin and resistant to the HIV strains in the patients. Interestingly, when individuals with HIV have received stem-cell transplants to repopulate their immune cells from donors with wild-type copies of the *CCR5* gene, HIV is initially undetectable in the patients' bodies, but eventually rebounds if antiretroviral therapy is stopped^{6–9}. In such cases, the viral rebound takes many months, rather than the usual two to four weeks, after antiretroviral therapy is withdrawn^{10,11}. This suggests that if a person's HIV-infected immune cells become mainly replaced by uninfected immune donor cells that are protected from infection by antiretroviral treatment, the total burden of HIV in the body can be substantially reduced. However, to tip the balance of such a reduction into a situation of permanent HIV remission, what seems to be needed is the establishment of immune cells that are resistant to the HIV strains present in the body.

In the 2009 study, the patient required an intensive set of therapies, including a second stem-cell transplant when their cancer recurred, and they also underwent irradiation treatment. By contrast, the patient studied by Gupta and colleagues underwent a less-intensive treatment regime for their cancer and did not require irradiation. This is of interest, because it had been unclear whether the intense cancer treatment in the earlier study might have contributed to the successful HIV remission. Another difference is that, in the 2009 study, the patient already had the $\Delta 32$ mutation in one of their two copies of *CCR5*, which might have affected their total HIV burden before transplantation. Although these factors might have had a role in achieving the long-term HIV remission in the case reported in 2009, what seems to be the most important aspect linking the cases is a donor transplant of cells lacking functional *CCR5* on the cell surface.

What has been learnt from these two reports that might guide future efforts towards HIV eradication or remission? A simple answer might be 'not too much'. In some ways, the case presented by Gupta and colleagues is mainly a repeat of a procedure that confirms the previously reported outcome. Substantial efforts are already under way to modify *CCR5* or other genes that facilitate HIV infection or replication in approaches to modify patients' own immune or stem cells. The knowledge gained from this second case of HIV remission is unlikely to cause a change in direction of strategies being developed for tackling HIV. Donor stem-cell transplantation is expensive, fraught with risks and requires intensive effort to tailor the treatment to specific individuals — as such, it cannot be scaled up easily. By contrast, the standard HIV treatment regimen of one or two pills per day is accompanied by relatively minimal adverse effects; therefore,

it is not practical to consider replacing it with a procedure that might risk disease or death, and that creates the need for long-term immunosuppression.

Extremely low levels of residual HIV DNA or RNA have been intermittently detected using sensitive assays on blood cells taken from the patient in remission in Gupta and colleagues' study, and in the earlier study of the patient who underwent HIV remission¹². Although these fleeting hints of persistent HIV are probably clinically insignificant, there is a remote possibility that the person studied by Gupta *et al.* will eventually relapse. Modelling suggests that the possibility of rebound becomes less likely the longer that HIV remains undetectable in the absence of antiretroviral treatment, so, in another six months' time, the long-term remission status of this patient should be clearer. For these and other reasons, such cases are usually called long-term HIV remission, rather than a cure, an analogy borrowed from the cancer field.

The impact of the news of a second case of HIV remission might be overlooked by some in the scientific community because the report simply confirms previous results and shows a lack of obvious scalability for treatment. However, the effect this news has had on the wider public, especially for people living with HIV, should not be forgotten. This case has certainly generated interest, and might have instilled a sense of hope in some individuals. Such cases

also provide motivation to continue working on and refining research endeavours, even if scalable approaches to achieve long-term HIV remission might be many years away. Optimism does not need to be in conflict with rationalism. ■

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PALAEANTHROPOLOGY

Unknown human species found in Asia

Excavations in southeast Asia have unearthed a previously unreported hominin species named *Homo luzonensis*. The discovery has implications for ideas about early hominin evolution and dispersal from Africa. [SEE ARTICLE P.181](#)

MATTHEW W. TOCHERI

Homo sapiens is the only living species of a diverse group called hominins (members of the human family tree who are more closely related to each other than they are to chimpanzees and bonobos). Most extinct hominin species are not our direct ancestors, but instead are close relatives with evolutionary histories that took a slightly different path from ours. On page 181, Détroit *et al.*¹ report the remarkable discovery of one such human relative that will no doubt ignite plenty of scientific debate over the coming weeks, months and years. This newly identified species was found in the Philippines and named *Homo luzonensis* after Luzon, the island where bones and teeth from individuals of this species were

excavated from Callao Cave. Specimens of *H. luzonensis* were dated to minimum ages of 50,000 and 67,000 years old, which suggests that the species was alive at the same time as several other hominins belonging to the genus *Homo*, including *Homo sapiens*, Neanderthals, Denisovans and *Homo floresiensis*.

Rapidly changing knowledge about hominin evolution in Asia is forcing the re-examination of ideas about early hominin dispersals from Africa to Eurasia. Hominins appear in the fossil record about 6 million to 7 million years ago in Africa, and the earliest hominin fossils in Eurasia are about 1.8 million years old². Explanations for the earliest hominin dispersals from Africa fall under what is known as the Out of Africa I paradigm³. Modern humans only come into focus in the Out of Africa II

paradigm, which refers to the early dispersals of *H. sapiens* from Africa to Eurasia that first occurred in the past 200,000 years⁴.

Ever since *Homo erectus* was discovered in the early 1890s in Indonesia on the island of Java, this species has essentially been the only character of interest in the Out of Africa I dispersal events. The conventional viewpoint is that this intrepid hominin began to stride gallantly towards far-off places around 1.5 million to 2 million years ago (a dispersal that enabled it to ultimately occupy territory across Africa and Eurasia)³. Meanwhile, the other hominin species around at that time stayed in Africa, living on borrowed time and facing imminent extinction. Compared with *H. erectus*, these species — for example, other early *Homo* species such as *Homo habilis*, as well as the australopiths (hominins not in the genus *Homo*), which include *Paranthropus* and *Australopithecus* — had smaller brains and an anatomy that is less similar to that of modern humans. Indeed, as this simplified old story goes, how could such species possibly compete given the anatomical and probable behavioural advantages that *H. erectus* possessed?

Certain discoveries have challenged these entrenched ideas by raising the possibility that other hominins besides *H. erectus* dispersed from Africa to Eurasia during the Early Pleistocene (a period that occurred 2.58 million to 0.78 million years ago)⁵. Stone tools found in China are 2.1 million years old⁶, but no fossils as old as that have been attributed to *H. erectus*. It is also under debate whether *H. erectus* is the ancestor of *H. floresiensis*⁷, a species that lived on the Indonesian island of Flores. *H. luzonensis* provides yet more evidence that hints that *H. erectus* might not have been the only globe-trotting early hominin.

Détroit and colleagues have assigned seven teeth, two hand bones, three foot bones and one thigh bone to *H. luzonensis*. These remains, including one bone that was found previously⁸, came from at least two adults and one child. The teeth include two premolars and three molars from an individual's upper jaw (Fig. 1). Overall, these teeth and bones have a striking combination of characteristics never before reported together in a hominin species.

When compared with the molars of other hominin species, *H. luzonensis* molars are astonishingly small, and the simplified surfaces of their crowns and their low number of cusps are features that look similar to the molar crowns and cusps of *H. sapiens*. Yet the shapes of *H. luzonensis* teeth share similarities with the teeth of *H. erectus* from Asia, and the size ratio of *H. luzonensis* premolars to molars is similar to that of *Paranthropus*, species of which are known for their massive jaws and teeth. The authors also used 3D imaging to examine the enamel–dentine junction (EDJ), which is an internal region of the tooth where dentine material meets the enamel layer. *H. luzonensis* premolar EDJs have a form that is distinct from that of hominins other than

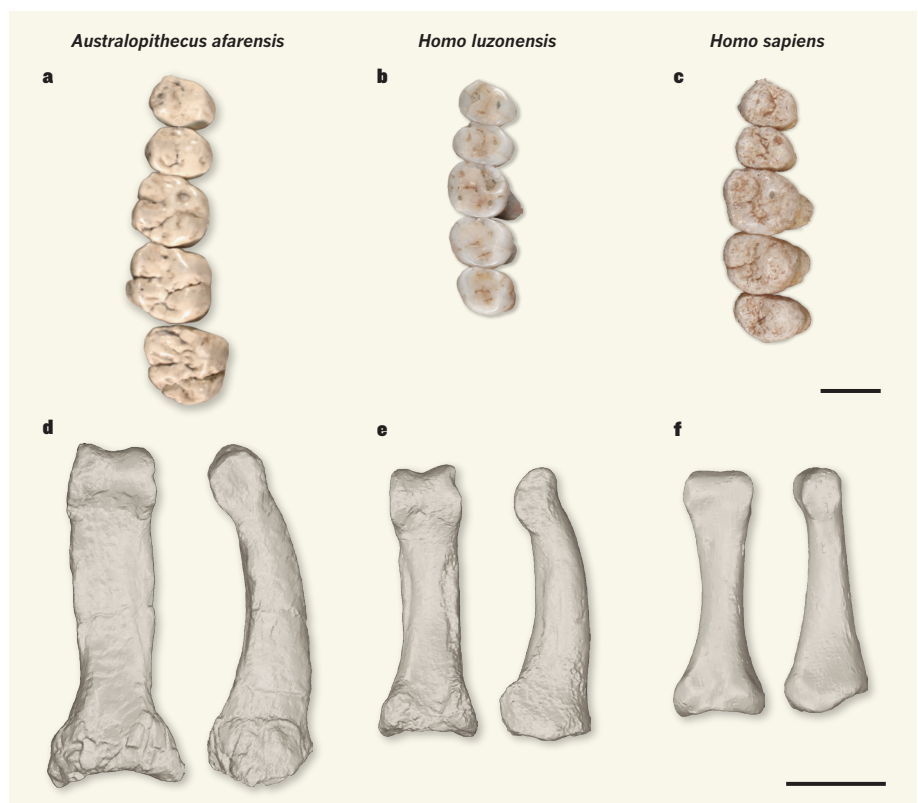


Figure 1 | Hominin teeth and toe bones. Détroit *et al.*¹ report the discovery of a previously unknown extinct human species named *Homo luzonensis*, identified from teeth and bones excavated in the Philippines and dated to at least 50,000 years old. **a–c**, *H. luzonensis* premolar and molar teeth (**b** have a general pattern of a small tooth size and low tooth surface complexity that is typical of premolars and molars from the genus *Homo*, including the teeth of *Homo sapiens* (**c**; a roughly 177,000-year-old specimen from Israel⁴). This pattern contrasts with the larger and more complex surfaces of premolars and molars of some early hominins that do not belong to the genus *Homo*, such as *Australopithecus afarensis* (**a**; a cast of an approximately 3.4-million-year-old specimen from Ethiopia). The teeth in **b** are from the right side of the jaw; those in **a** and **c** are from the left side but are shown mirrored as from the right side for comparison with **b**. **d–f**, A 3D scan of a toe bone from *H. luzonensis* (**e**; bottom and side views shown) is strikingly similar to that of *A. afarensis* (**d**; a 3D scan of an approximately 3.2-million-year-old specimen from Ethiopia) in overall shape and curvature, and unlike the straighter and more slender anatomy of *H. sapiens* toe bones (**f**; a 3D scan of a specimen from the Philippines from the 1800s). The interesting mix of features observed in *H. luzonensis* raises key questions about the species' ancestry and its relationships with other human species. Scale bars represent 1 centimetre.

H. floresiensis. However, depending on the specific *H. luzonensis* molar that was analysed, the EDJs either look like those of *H. erectus* from Asia or like those of *H. sapiens*. This strange juxtaposition of features in a single individual's jaw is completely unexpected and clouds our ability to reasonably assess, at least for now, the exact evolutionary relationships between *H. luzonensis* and other hominin species.

Although attempts to extract DNA from *H. luzonensis* specimens have so far been unsuccessful, the anatomy of the foot and hand bones of *H. luzonensis* strengthens the case that these remains represent a previously unknown hominin species. A foot bone called the third metatarsal has an anatomy in *H. luzonensis* that is distinct from that of other hominin species, including *H. sapiens*⁸. The authors' 3D shape analyses of a *H. luzonensis* toe bone show that its shape is essentially indistinguishable from the toe bones of *Australopithecus afarensis* and *Australopithecus africanus* (Fig. 1), despite the separation of these australopiths

from *H. luzonensis* by at least 2 million to 3 million years of evolution. Similar analyses found that a *H. luzonensis* finger bone most resembles the finger bones of australopiths and species of early *Homo*. Finally, the *H. luzonensis* finger and toe bones are curved, which suggests that climbing was an important part of this species' behavioural repertoire, as was also the case for many species of early hominin⁹.

The discovery of *H. floresiensis* raised the question of whether it evolved from a species of early *Homo*^{7,10}, for which evidence of its existence outside Africa has yet to be documented. Scientists are still struggling to answer this definitively^{11,12}. The question is more pressing with the discovery of *H. luzonensis*, given the need to explain yet another hominin species that, like *H. floresiensis*, was around during part of the Late Pleistocene (defined as a period of time 126,000 to 11,700 years ago), had *Homo*-like teeth but australopith-like hands and feet, and that lived on an island only reachable after a major sea crossing. Perhaps *H. floresiensis* and

H. luzonensis are both descendants of *H. erectus* populations that evolved separately on their respective islands for hundreds of thousands of years, if not more^{13,14}. However, explaining the many similarities that *H. floresiensis* and *H. luzonensis* share with early *Homo* species and australopithecids as independently acquired reversals to a more ancestral-like hominin anatomy, owing to evolution in isolated island settings, seems like a stretch of coincidence too far¹⁵.

Given the rich history of the Out of Africa I paradigm, unsurprisingly, *H. erectus* has been the centre of attention in ideas about early hominin evolution and dispersals in Asia. Nevertheless, it is worth considering how different these ideas might be if, in the 1890s,

H. floresiensis or *H. luzonensis* had been discovered rather than *H. erectus*. Because *H. luzonensis* provides the first glimpse of a second hominin species living on a distant island at a time when *H. sapiens* populations from Africa were beginning to spread across the world, one thing can be said for certain — our picture of hominin evolution in Asia during the Pleistocene just got even messier, more complicated and a whole lot more interesting. ■

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OPTICAL PHYSICS

Correlations detected in a quantum vacuum

A vacuum as described by quantum mechanics is perhaps the most fundamental but mysterious state in physics. The discovery of correlations between electric-field fluctuations in such a vacuum represents a major advance. SEE LETTER P.202

ANDREY S. MOSKALENKO & TIMOTHY C. RALPH

A surprising result in quantum mechanics is that a vacuum is not empty. Particles can appear out of nothing for very short periods of time. This phenomenon can be understood as a consequence of the energy–time uncertainty principle, whereby restriction of a measurement to an extremely short time interval leads to large fluctuations in energy in the interval. Although indirect effects of these ‘virtual’ particles are well studied, it is only by probing a vacuum on very short timescales that the particles become ‘real’ and can be directly observed¹. But do these particles appear completely randomly, or are they correlated in space and time? On page 202, Bena-Chelmus *et al.*² provide an answer to this question by finding evidence for correlations between fluctuations in the electric field of a vacuum.

One way to measure correlations in fields is through interference, such as in the double-slit experiment of British physicist Thomas Young³. In this experiment, light waves pass through two slits and interfere with each other to produce an interference pattern on a screen. This simple, but profound, experiment was originally developed to probe wave effects and was later used to illuminate the duality between particles and waves in quantum physics. In the past, variations of the double-slit experiment have been realized for photons, electrons, atoms and large molecules⁴. Current

attempts are even looking for multipath interferences for biological objects, such as viruses⁵.

A comparably counter-intuitive enterprise is to search for interferences between separated parts of a vacuum. Bena-Chelmus and colleagues devoted their experimental study to exactly this task. For a simple, conceptual

physical explanation of their work, consider a version of the double-slit experiment that is based on an instrument called a Mach–Zehnder interferometer⁶ (Fig. 1a). Moreover, let us limit the discussion to temporal correlations and consider the case in which thermal radiation is incident on the interferometer.

In this set-up, the radiation is divided into two equal parts by a beam splitter. The two parts propagate in their own ‘arms’ of the interferometer before passing through a second beam splitter and being collected by two detectors. In one of the arms, there is a device called a delay line, which introduces a variable time delay in the propagation of one part with respect to the other. The correlation properties of the radiation can be determined from the variation in the intensity measured by either of the detectors as a function of the time delay. A perfect interference pattern (one that is at its maximum visibility) is observed if the intensity oscillates between a certain maximum

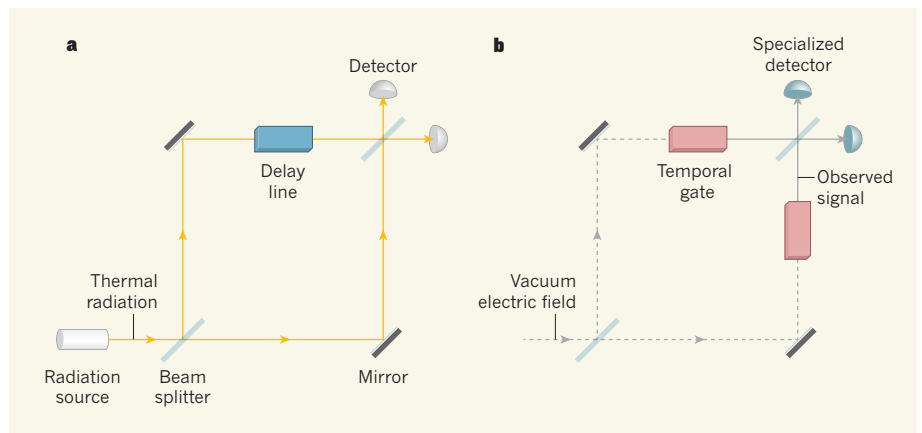


Figure 1 | Standard and modified Mach–Zehnder interferometers. **a**, In a Mach–Zehnder interferometer, thermal radiation from a radiation source is split into two parts by a beam splitter. Each part is directed by a mirror through a second beam splitter and into a detector. A device called a delay line introduces a time delay in the propagation of one part with respect to the other. This set-up can be used to study the correlation properties of the radiation. **b**, Bena-Chelmus *et al.*² report an experiment that can be thought of as a modified Mach–Zehnder interferometer. The radiation and its source are replaced by the electric field associated with a vacuum, and the delay line is substituted with two elements called temporal gates that ‘observe’ electric fields in ultrashort time windows — the two observations differ by a time delay. Specialized detectors analyse the observed signals. The authors used their experiment to measure correlations between electric-field fluctuations in the vacuum.