absolute devil to get it out."

By late last year, Clarke's team had removed enough bones to reconstruct more than 90% of the skeleton — making it the most complete *Australopithecus* so far. On 29 November, they posted two papers on Little Foot to the bioRxiv preprint server — one on the age of the specimen[2], the other on the limbs and locomotion[3].

On 4–5 December, the team posted third and fourth papers, on the skull and the potential relationship of the specimen to a known hominin species[4], as well as on the arms and an injury Little Foot received during her life[5]. Further papers, on the hand, teeth and inner ear, are expected in the near future, says Crompton. Most will ultimately appear in a special edition of the *Journal of Human Evolution*.

A NEAR-COMPLETE PUZZLE

The bioRxiv papers crystallize ideas that emerged in earlier publications about the age of the fossil. They also cover new ground, suggesting that Little Foot was an adult female and stood about 130 centimetres tall — just 10 centimetres shorter than the average woman in some modern-human populations. "Little Foot was quite big," says Crompton. The paper covering limbs and locomotion[3] reveals that Little Foot's legs are longer than her arms, similar to modern humans, making her the oldest hominin for which we can be sure of that feature, says Crompton. This means that Little Foot was better adapted to walking upright on the ground than were many other australopiths.

Little Foot's skull, bones and teeth are so unusual that Clarke and his team have categorized her as the distinct species[4] *Australopithecus prometheus*, a name first suggested in 1948 on the basis of a skull fragment found roughly 250 kilometres north of Johannesburg[6] and that remains controversial. They also suggest that *A. prometheus* is an ancestor of a group of hominins called *Paranthropus*[4], which co-existed with early *Homo* species for about one million years.

But Lee Berger, an archaeologist also at Wits University, disagrees with the decision to resurrect *A. prometheus*. In a paper scheduled to be published in the *American Journal of Physical Anthropology*, he argues that the name *A. prometheus* was never properly defined. If Little Foot constitutes a distinct species, Berger thinks, a new name is needed.

He is also disappointed by the lack of solid information in the papers on the age and locomotion — he would have liked to have seen detailed measurements of the fossil bones. "There's no data — there are almost no measurements of the fossils," he says. Berger hopes to provide those data in his own publications — although he is still at an early stage of his analysis of Little Foot.

Crompton responds that the locomotion paper is an overview that attempts to reconstruct how Little Foot moved by drawing on the more-solid data in the team's other papers. Gabriele Macho, an anthropologist at the University of Oxford, UK, agrees that the locomotion paper is light on solid data, but says the team acknowledges the gap. She looks forward to seeing more-detailed papers soon. "The positive thing is this skeleton is tremendously important," she says. "No question about it." ■

1. Bruxelles, L., Clarke, R. J., Mairee, R., Ortega, R. & Stratford, D. *J. Hum. Evol.* **70**, 36–48 (2014).
2. Bruxelles, L. *et al.* Preprint at bioRxiv https://doi.org/10.1101/482711 (2018).
3. Crompton, R. H. *et al.* Preprint at bioRxiv https://doi.org/10.1101/481556 (2018).
4. Clarke, R. J. & Kuman, K. Preprint at bioRxiv https://doi.org/10.1101/483495 (2018).
5. Heile, A. J., Pickering, T. R., Heaton, J. L. & Clarke, R. J. Preprint at bioRxiv https://doi.org/10.1101/486076 (2018).
6. Dart, R. A. *Am. J. Phys. Anthropol.* **6**, 259–284 (1948).

GENETICS

Machine learning hunts for cause of paralysing illness

Scientists hope that probing the immune system will identify the cause of a polio-like disease.

BY SARA REARDON

Infectious-disease researchers hunting for the cause of a mysterious illness that is paralysing children are combining machine learning with a new gene-sequencing technique to pin down the culprit.

The disease, called acute flaccid myelitis (AFM), causes limb weakness and paralysis that resembles the symptoms of polio. The US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, has confirmed 134 cases of AFM in the United States so far this year. Many of those who develop the illness never recover.

Most of the evidence suggests that an enterovirus called EV-D68 is causing the illness[1], but researchers haven't been able to find the pathogen in the spinal fluid of children with the disease. Scientists are trying to identify the culprit by using a combination of host-response diagnostics — which look at how the immune system responds to pathogens — and machine-learning analysis. The approach could lead to better diagnostics and provide hints about new treatments.

Host-response diagnostic tests haven't been used in the clinic yet. But researchers are developing similar tests to help pinpoint other conditions that can be tricky to diagnose, including tuberculosis and bacterial meningitis.

"We've never really had a smoking gun."

This year's AFM outbreak started in October, and is the third in a series of outbreaks in the United States that have occurred every other year since 2014. Researchers have yet to find a definitive explanation for the pattern. It is also taking scientists an unusually long time to determine the cause of the illness, says William Weldon, a microbiologist at the CDC.

Blood samples taken from many of the people with AFM contain the virus. But many people who never developed AFM symptoms also have the virus in their blood.

"We've never really had a smoking gun," says Charles Chiu, an infectious-disease researcher at the University of California, San Francisco, who is leading the machine-learning project. He suspects that if EV-D68 causes AFM, it damages the spinal cord quickly and then drops to undetectable levels in the body.

Host-response diagnostics are useful when researchers don't know what they're looking for, says Purvesh Khatri, a computational systems immunologist at Stanford University in California. The composition of the immune system's defences differs depending on which pathogens are present in the body. So instead of looking for the agent itself, Khatri says, researchers could look at what the immune system is seeing.

Most attempts to identify mystery illnesses involve searching for a pathogen's DNA or RNA in areas of the body such as tissue or blood. But the host-response technique takes a blood sample and sequences all of the

23,000 or so human genes present in the blood at any given time.

Chiu's group is analysing these genes — collectively known as the transcriptome — using machine learning. The scientists are searching for similarities between the transcriptomes of people with the illness, and differences between the transcriptomes of those with AFM and people with other, known infections, including those caused by enteroviruses. Once the team knows which genes are relevant to AFM cases, it can test for them directly.

"We're not relying on detecting the virus — we already know we can't detect the virus," says Chiu, who published some of the machine-learning methods in late November[2]. His group hasn't published any results yet because they're still preliminary. But the scientists' data suggest that the expressed genes that are common among people with AFM are those that researchers would expect to see in a person whose immune system is fighting a virus.

"I think it's definitely promising," says Weldon. He says that the CDC has been working with Chiu's group, and is talking with other teams that are pursuing similar experimental tests based on host-immune response.

Khatri stresses that researchers will need to train the machine-learning algorithm with data from diverse populations. Immune responses may vary depending on a person's ethnicity or country of origin, which can determine which pathogens people encounter, he says. Thorough training of the algorithm is especially important if researchers want to use similar host-response diagnostic techniques widely.

One group, led by infectious-disease researcher Christopher Woods at Duke University in Durham, North Carolina, has developed a transcriptomics test that can determine with 90% accuracy whether a bacterium, a virus or an autoimmune reaction is responsible for a person's symptoms[3].

The distinction is important for treatment, Woods says, and could prevent physicians from prescribing unnecessary antibiotics for viral or autoimmune diseases.

Khatri's group has developed a test that predicts whether a person will develop active tuberculosis. About 25% of the world's population harbours the bacterium that causes the illness, but only about 5–10% of these people develop symptoms[4]. The test from Khatri's group could allow researchers to categorize and prioritize people for treatment before the disease becomes severe.

Chiu hopes that the host-immune response approach could also help to explain why only some people infected with EV-D68 develop AFM. His group is also sequencing the genomes of children with the condition. The researchers hope that this information — combined with the transcriptome data — might provide hints about who could be susceptible to the illness before the next outbreak, which many researchers expect to occur in 2020. "These cases this year provide valuable data for us in evaluating how it might progress in the future if we see additional outbreaks," Chiu says. ■

ARMANDO L. SANCHEZ/CHICAGO TRIBUNE/TNS VIA GETTY

Most of those affected by the outbreak of acute flaccid myelitis are children.

1. Hixon, A. M. *et al. PLoS Pathog.* **13**, e1006199 (2017).
2. Langelier, C. *et al. Proc. Natl Acad. Sci. USA* https://doi.org/10.1073/pnas.1809700115 (2018).
3. Tsalik, E. L. *et al. Sci. Transl. Med.* **8**, 322ra11 (2016).
4. Sweeney, T. E. *et al. Lancet Respir. Med.* **4**, 213–224 (2016).

PUBLISHING

China backs open-access plan

Officials pledge support for 'Plan S', which aims to make papers immediately free to read.

BY QUIRIN SCHIERMEIER

In a huge boost to the open-access movement, librarians and funders in China have said that they intend to make the results of publicly funded research free to read immediately on publication.

The move, announced at an open-access meeting last week in Berlin, includes a pledge of support for Plan S, a bold initiative launched in September by a group of European funders to ensure that, by 2020, their scientists make papers immediately open.

It is not yet clear when Chinese organizations will begin implementing new policies, or whether they will adopt all of Plan S's details, but Robert-Jan Smits, the chief architect of Plan S, says the stance is a ringing endorsement for his initiative. "This is a crucial step forward for the global open-access movement," he says. "We knew China was reflecting to join us — but that it would join us so soon and unambiguously is an enormous surprise."

In three position papers, China's National Science Library (NSL), its National Science and Technology Library (NSTL) and the Natural Science Foundation of China (NSFC), a major research funder, all said that they support the efforts of Plan S "to transform, as soon as possible, research papers from publicly funded projects into immediate open access after publication, and we support a wide range of flexible and inclusive measures to achieve this goal". They add: "We demand that publishers should not increase their subscription prices on the grounds of the transformation from subscription journals to open access publishing."

The government will now urge Chinese funders, research organizations and academic libraries to make the outcomes of publicly funded research free to read and share as soon as possible, says Xiaolin Zhang, chair of the ▶