in Qian and colleagues' experiments. Moreover, in both studies, the hearts of treated mice showed improved function compared with those of control mice.

A key challenge for the authors was how to distinguish pre-existing cardiomyocytes from those derived from reprogrammed fibroblasts. To address this, both groups used mice that had been genetically manipulated so that a fluorescent protein was permanently produced only in fibroblasts and their descendants (including those that became cardiomyocytes). The specificity of this lineage-tracing technique depended on the use of certain regulatory sequences, or promoters, that had been taken from genes encoding either periostin or FSP1 — two proteins that are typically produced by fibroblasts, but not cardiomyocytes. In cells in which the promoter was active, a genetic rearrangement led to permanent activation of the gene encoding the fluorescent protein.

Such lineage-tracing approaches are state of the art, but they are not perfect. The biggest pitfall would be activation of the fibroblast promoter in pre-existing cardiomyocytes, so that these would then be mistaken for reprogrammed cells. Neither periostin nor FSP1 is specific to fibroblasts[11,12] (although we know of no evidence for their expression in cardiomyocytes). For these reasons, Song *et al.* carried out further experiments in which they controlled the timing of the fibroblast-marking event using a 'genetic pulse–chase' technique. They report that no cardiomyocytes were marked unless they expressed the transcription-factor cocktail. This finding enhances confidence that true reprogramming had occurred.

Interestingly, both studies found that, although some of the cells had been only partially reprogrammed, others were morphologically and functionally indistinguishable from normal cardiomyocytes. In particular, fibroblast-derived cardiomyocytes in short-term culture were able to contract when stimulated electrically and had electrochemical activities typical of this cell type, including action potentials and electrical coupling. Both research groups used non-invasive diagnostic procedures (echocardiography and magnetic resonance imaging) to identify the improved functional performance and reduced scar area of the treated mice when compared with untreated animals.

The finding of enhanced heart function is certainly important, but how is this happening, and can it be improved on? Although the authors' results suggest that the treatment generated new, functional cardiomyocytes that directly improved pump performance, it is important to remember that the reprogrammed cells constituted only a fraction of the cardiomyocytes in the infarct border zone, which is by nature ill-defined and forms only a fraction of the injured area. Can such a small number of cells directly account for a global increase in heart function? Researchers in stem-cell therapy have encountered similarly disproportionate benefits of cellular grafts in the heart. This therefore raises the possibility that grafted or reprogrammed cells may produce growth factors, cytokines or other signalling molecules that improve the performance of pre-existing cells by enhancing blood flow or cell survival[13].

Going forward, it will be necessary to validate the authors' results in independent labs using different lineage-tracing approaches, and the efficiency of cell reprogramming must be increased. Also, for clinical applications, reprogramming must be achieved without inserting the transcription-factor genes into the fibroblasts' chromosomes, to prevent complications such as malignant transformation. Moreover, are cardiomyocytes the best choice of outcome for reprogramming, or would immature progenitors of cardiomyocytes (which have greater proliferative ability) be better?

Although clinical trials are probably far off, the studies by Qian *et al.* and Song *et al.* open up a new line of investigation in cardiovascular translational medicine. If we can understand the reprogramming mechanisms correctly, regenerative therapy might simply involve inducing the heart to reprogram its own cells after injury. ■

Nathan J. Palpant *and* **Charles E. Murry** *are in the Departments of Pathology, Bioengineering and Medicine/Cardiology, Center for Cardiovascular Biology, Institute for Stem Cell and Regenerative Medicine, University of Washington School of Medicine, Seattle, Washington 98109, USA.*
e-mail: murry@uw.edu

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EVOLUTIONARY ANTHROPOLOGY

Homo 'incendius'

An analysis of microscopic and spectroscopic features of sediments deposited in a South African cave one million years ago suggests that human ancestors were using fire much earlier than had been thought.

RICHARD G. ROBERTS & MICHAEL I. BIRD

Humans have long been captivated by the flickering flames of the campfire. But when did our ancestors first master the use of fire, and which ancient human species was the first to do so? In *Proceedings of the National Academy of Sciences*, Berna and colleagues[1] report that they have found fragments of burnt bone and ashed plants in one-million-year-old sediments at Wonderwerk Cave, Northern Cape province, South Africa. This evidence of fire occurs in the same sedimentary layers as Acheulian stone tools, usually considered the handiwork of *Homo erectus*. Their discovery more than doubles the accepted antiquity of the habitual use of fire by humans[2,3], and highlights the benefits of using microscopic and molecular techniques to identify 'cryptic combustion' at sites of human occupation — whatever their age*.

Controversy has dogged previous claims for the early use of fire by hominins (primates more closely related to humans than to chimpanzees), such as australopithecines or *H. erectus*. The discovery[4] in the 1940s of apparently charred bones at a 3-million-year-old fossil site in South Africa inspired pioneering Australian palaeoanthropologist Raymond Dart to dub these 'proto-humans' *Australopithecus prometheus* — a new australopithecine species named after the giant in Greek mythology who stole fire from the heavens. However, chemical analysis by English palaeoanthropologist Kenneth Oakley[5] showed that the bones were not burnt, but coated in black oxides of iron and manganese.

Subsequent claims for early fire use have received a similarly cool reception. Some studies have suggested that australopithecines or *H. erectus* had tamed fire by 1.4 million years ago in southern and eastern Africa[6,7], and that cooking has played a pivotal part in the evolution of early *Homo* species[8]. These proposals have been contested, however, either because the burnt remains are not in their original depositional context or because they are found at open-air sites where bush fires ignited by volcanic activity or lightning strikes cannot be ruled out. Acheulian toolmakers were using

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Figure 1 | The crucible of combustion. View inside Wonderwerk Cave, South Africa, from the bottom of excavation 1, looking towards a massive stalagmite formed 30 metres inside the cave entrance. The photograph was taken before the deepest archaeological layer (stratum 12) had been excavated. Berna *et al.*[1] analysed the *in situ* remains of ashed plants and burnt bones from stratum 10, which occurs mid-profile in the section shown in the right foreground. The ghostly grid pattern in the photo is due to the string lines used to demarcate the excavation in 1-yard (approximately 0.9-metre) horizontal intervals, and their vertical projections towards the floor. (Photo courtesy of P. B. Beaumont.)

fire almost 800,000 years ago in Israel[9], but evidence for its habitual use does not emerge until after 400,000 years ago[2,3]. This later date places pyrotechnology (the intentional use and control of fire) in the hands of only Neanderthals and *Homo sapiens*, leaving *H. erectus* and earlier hominins out in the cold.

The Earlier, Middle and Later Stone Age deposits inside the 140-metre-long Wonderwerk Cave have been excavated[10] since the 1940s. Excavation 1 — the deepest of the six in the cave — is sheltered behind a massive stalagmite (Fig. 1) and comprises 12 archaeological strata. Berna *et al.*[1] studied stratum 10, one of the Earlier Stone Age layers that contains Acheulian stone tools and that was deposited between 1.1 million and 1 million years ago, as indicated by measurements of radionuclides produced by cosmic rays and of magnetic polarity[11,12]. The authors observed that this layer also contains a variety of pyrogenic features visible to the naked eye, including bones and teeth with charred surfaces and a whitened appearance that indicates their thermal decomposition. Using a technique known as Fourier transform infrared (FTIR) spectroscopy[13], the researchers found that the bones and adhering sediments had been heated to 400–700 °C. Moreover, the surfaces of many of the stone tools had dimpled, 'pot-lid' fractures, which are typically created at high temperatures[9]. But the authors' most compelling proof of *in situ* combustion was found under the microscope and from direct chemical analysis of intact blocks of sediment.

Examination of intact sediments at the microscopic scale — the 'micromorphology' — provides a powerful means of investigating site formation processes and post-depositional alterations in an undisturbed context[14]. Micromorphological analysis has previously been used to support suggestions of fire use in Israel 400,000 years ago[2], and to refute claims of similar antiquity for the 'Peking Man' site at Zhoukoudian in China[15]. These studies used FTIR spectroscopy to identify burnt materials, but Berna *et al.*[1] take this technique a step further by coupling micromorphology to FTIR spectra measured on burnt materials still embedded in resin-impregnated blocks of undisturbed sediment. For this purpose, they used a FTIR spectrometer attached to an infrared microscope. This analysis revealed *in situ* combustion features that are invisible to the naked eye, including abundant and well-preserved remains of ashed plants and angular fragments of burnt bone.

Berna *et al.* emphasize that extracting this 'smoking gun' evidence required the application of both microscopic and molecular techniques to study intact, undisturbed deposits. Their results represent a call to arms for archaeologists to make *in situ* analyses at other sites to search for cryptic traces of anthropogenic burning and to gain insight into site formation processes more generally. Complementary techniques can also be used to investigate the human history of fire use. For example, many minerals undergo structural transformation when exposed to high temperatures, and this can be recognized using established physical and chemical techniques[13]. The magnetic and thermoluminescent properties of sediments and stone tools can also provide records of ancient heat treatment[16] (thermoluminescence is the release, upon heating, of previously absorbed radiation energy as light). And the abundance and isotopic composition of pyrogenic carbon — from the macroscopic to the molecular in scale[17] — can help to establish combustion conditions in archaeological deposits and identify the most promising strata for further micromorphology and FTIR-microscopy investigations.

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With the pyrotechnology pendulum swinging back to 1 million years ago, the fire-making credentials of *H. erectus* have begun to be restored. Widespread acceptance of controlled burning at such an early date will require the establishment of a pattern of ancient fire use at multiple sites, as observed in Europe after 400,000 years ago[3]. The evidence from stratum 10 at Wonderwerk Cave should ignite the search for such a pattern in Africa using *in situ* and other microanalytical techniques.

And what of stratum 12, the deepest archaeological layer in the cave? This stratum, which was deposited more than 1.4 million years ago along with Oldowan stone tools[1,10–12], has been reported[10] to contain wood ash, charred and whitened bones, and stones with pot-lid fractures. Berna *et al.* examined the purported ash and concluded that it is weathered rockfall and flowstone[1], but work now under way on the bones and stones may yet produce further fireworks from *Homo* 'incendius'. ■

Richard G. Roberts *is at the Centre for Archaeological Science, University of Wollongong, Wollongong, New South Wales 2522, Australia.* **Michael I. Bird** *is at the Centre for Tropical Environmental and Sustainability Science, James Cook University, Cairns, Queensland 4870, Australia.*
e-mails: rgrob@uow.edu.au; michael.bird@jcu.edu.au

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