

the medium after cell growth indicated that a component required for THI4p activity might be missing. However, addition of iron(II) (Fe^{2+}) to the minimal-growth medium markedly increased the formation of compound 3 (Fig. 1). The reaction is extremely selective for Fe^{2+} , so the authors concluded that Fe^{2+} must be necessary for the sulphur-transfer reaction.

The thiazole-forming reaction could now be reconstituted *in vitro* from NAD using intact THI4p protein. The reaction showed conversion of NAD through to compound 1 (Fig. 1), and addition of Fe^{2+} completed the transformation to the final thiazole product, 3. Chatterjee *et al.* found that each molecule of THI4p accounted for the production of a single molecule of thiazole, observing a clear 1:1 correlation between the loss of sulphur from THI4p and formation of the thiazole product.

The deployment of a protein as such a metabolic reagent is extremely rare in biology. One

of the few well-characterized examples is the protein Ada, which repairs methylated lesions in DNA³. Reactivation of THI4p containing the Dha residue has so far proved impossible. Experiments with cultured cells show that thiamine and THI4p accumulate in a 1:1 ratio during growth, consistent with THI4p functioning as a 'one-shot' reagent and not being recycled by the cellular machinery. The reaction results in the build-up of inactivated (Dha 205) THI4p until it comprises about 1.5% of total cellular protein⁴.

These observations¹ raise interesting questions, such as why a protein should be used as a sulphur donor and why the inactive protein should not undergo rapid degradation and its amino acids be recycled. As Chatterjee *et al.* note, this accumulation of THI4p implies that the inactive protein has another cellular function. Indeed, inactivated THI4p has been implicated in DNA protection and other stress responses^{5–7}. The biochemical mechanism linking the biosynthetic and stress-response

roles of THI4p is as yet unknown, but one possibility posed by Chatterjee *et al.* is that the protein helps to mop up any excess intracellular Fe^{2+} , thereby preventing chemical reactions that can produce damaging reactive oxygen species. ■

Peter Roach is at the School of Chemistry, University of Southampton, Southampton SO17 1BJ, UK.

e-mail: p.l.roach@soton.ac.uk

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from Earth as Earth is from the Sun. Eris is the most distant Solar System object to be successfully observed by this technique, a notable achievement.

The authors find that Eris has a radius of $1,163 \pm 6$ kilometres, which is smaller and has significantly less margin of error than the previous measurements of $1,200 \pm 100$ km (ref. 3) and $1,500 \pm 200$ km (ref. 4). Ironically, Sicardy and colleagues' results cannot definitively state whether Eris is larger than Pluto. The ambiguity is due to the fact that Pluto's atmosphere prevents accurate measurement of its surface location, rather than being due to any deficiency in the Eris observations. A more interesting result from the authors' study⁵ is the possibility that Eris has a collapsed atmosphere (frozen to the surface), or a localized atmosphere under certain conditions.

Sicardy *et al.* demonstrate that Eris has no atmosphere at present and that a surprisingly large amount of light is reflected from its surface. This unusually bright surface is difficult to reconcile with the idea that objects in the outer Solar System become darkened by cosmic rays and micrometeorite impacts over time. The new observations could thus support a long-standing theory that, as a large, icy, Kuiper-belt object approaches the Sun during its orbit, a putative atmosphere could sublimate and then condense out as the object moves farther away. Eris is currently far away from the Sun in its 557-year orbit, and although the results do not prove that an atmosphere ever existed, the bright surface could indicate relatively recent condensation.

The discovery of Eris and other Kuiper-belt objects allows Pluto, a seemingly unique object for so many years, to be placed in a broader perspective. Investigation of the bulk properties of a large number of Kuiper-belt objects

PLANETARY SCIENCE

Eris under scrutiny

A stellar occultation by the dwarf planet Eris provides a new estimate of its size. It also reveals a surprisingly bright planetary surface, which could indicate the relatively recent condensation of a putative atmosphere. SEE LETTER P.493

AMANDA GULBIS

Pluto has long reigned as the smallest and most distant planet in our Solar System. In 1992, the discovery¹ of another body in roughly the same region proved that Pluto was not alone and launched a new frontier of study in planetary science — the Kuiper belt, the region at and beyond Neptune's orbit in which the two bodies reside. More than 1,000 Kuiper-belt objects have since been discovered. These objects consist mainly of ices and are typically located away from Earth at 30–50 times the distance between Earth and the Sun. One particular object, later named Eris, caught the attention of astronomers because initial size estimates based on proposed values for its surface reflectance showed that it was probably larger than Pluto². Subsequent direct imaging suggested³ that Eris was about 5% larger than Pluto, whereas detection of Eris's thermal radiation indicated⁴ that the planet was substantially larger than Pluto. On page 493 of this issue, Sicardy *et al.*⁵ use the powerful technique of stellar occultation to derive the most detailed information to date on Eris's size and other physical traits.

The discovery² of Eris in the Kuiper belt sparked the realization that more planets in the outer reaches of the Solar System were

probably awaiting detection. A great debate ensued as to whether Eris and other large, yet-to-be-detected Kuiper-belt objects — even Pluto itself — should be considered planets. This debate forced the astronomical community to rethink the definition of a planet. As a result, the definition was changed in 2006 and both Pluto and Eris were reclassified as dwarf planets. Rarely in the course of modern research has an astronomical discovery generated such widespread debate and emotional reaction among both scientists and the general public — it turns out that Eris was aptly named after the Greek goddess of strife and discord.

The stellar-occultation technique, in which a star is observed to pass behind a foreground object (in this case, Eris), has proven to be an effective method for discovering and characterizing features of Solar System bodies. Only a handful of large Kuiper-belt objects have been observed to occult stars, and each occultation has revealed something new and interesting, such as an unexpectedly bright surface on Kuiper-belt object 55636 (ref. 6), or waves in the upper atmosphere of Pluto^{7,8}. These results have led to reconsideration of ideas about how objects in the outer Solar System are formed and evolve. Sicardy *et al.*⁵ predicted and observed the occurrence of a stellar occultation when Eris was nearly 100 times as distant

has provided insight into the formation, evolution and dynamical histories of these bodies. We now expect that there are hundreds of objects that will eventually be classified as dwarf planets. Because Eris is the only body similar to Pluto for which detailed stellar-occultation data are available, Sicardy and colleagues' results⁵ represent a major step forward in our knowledge about large Kuiper-belt objects.

Future attempts will certainly be made to

obtain additional stellar-occultation data for Eris as well as for other Kuiper-belt objects. Whether they are called planets or not, there is clearly still much to learn about these distant, icy bodies. ■

Amanda Gulbis is at the Southern African Large Telescope and South African Astronomical Observatory, 7935 Cape Town, South Africa.
e-mail: amanda@salt.ac.za

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GENOMICS

Plague's progress

The Black Death was one of the most devastating pandemics in human history. The first complete genome sequence of the causative *Yersinia pestis* bacterium provides a fresh perspective on plague evolution. SEE LETTER P.506

EDWARD C. HOLMES

The Black Death was a pandemic of almost unprecedented scale. It is estimated that 30–50% of Europe's population perished from the plague between 1347 and 1351. As might be expected from such a remarkable level of mortality, this pestilence had a profound impact on medieval society. For example, it greatly influenced the depiction of death in art (Fig. 1), and acted as the driving force for the establishment of some of the first public-health measures, although these were generally futile. It has long been supposed that the Black Death, like all plague epidemics since, was caused by the bacterium *Yersinia pestis* in a transmission cycle involving fleas, rats and humans. But the evolutionary relationships between *Y. pestis* strains from different plague epidemics have been less clear. On page 506 of this issue, Bos *et al.*¹ describe the first complete genome sequence of *Y. pestis* from Black Death victims, and show that this pandemic was a pivotal event in plague evolution.

Obtaining bacterial DNA that is almost 700 years old presents a number of challenges, prominent among them the risk of inadvertent contamination by DNA from other sources^{1,2}. Bos *et al.* extracted bacterial DNA from five teeth of plague victims taken from a burial pit at East Smithfield (ES) in London, which was established at the height of the pandemic in 1348–49. The key methodological advance in their work was the use of a molecular capture assay that assisted in the detection of *Y. pestis* DNA amid a background of host and environmental DNA. The stringent laboratory procedures used by the authors, the observed patterns of mutational damage in the DNA, and the finding that the ES strain is ancestral to all contemporary *Y. pestis* strains on



Figure 1 | The last rites. In this fourteenth-century picture, a victim of the Black Death is attacked by a devil, while a priest reads the last rites and God watches from above.

phylogenetic trees, strongly suggest that the obtained genome sequence is an authentic representative of the Black Death pathogen.

The ES strain is significant for several reasons. First, in combination with studies of partial genome sequences of *Y. pestis* from Black Death victims³, it demonstrates beyond doubt that *Y. pestis* was the true cause of the Black Death, despite claims to the contrary⁴. Second, the fact that the ES strain falls at the base of a phylogenetic tree that links contemporary *Y. pestis* genomes suggests that the Black Death was a crucial event in plague evolution that

generated all later lineages of *Y. pestis*, including those responsible for the 'Asian' (or modern) plague pandemic that has spread globally since the nineteenth century. Interestingly, the greatest genetic diversity of *Y. pestis* is observed⁵ in China, suggesting that most plague epidemics originated in this region. Third, Bos *et al.*¹ suggest that the genetic similarity between the ES strain and contemporary strains of *Y. pestis* that are associated with less severe epidemics indicates that the high mortality of the Black Death was not simply a function of the bacterial strain involved. Given the small sample size of the authors' study, this assertion must be treated with caution, but the availability of a complete genome of *Y. pestis* from the Black Death should make the hypothesis experimentally testable.

Although the recovery and sequencing of the ES strain confirms the role of *Y. pestis* in the Black Death, it also raises questions about the cause of two earlier major disease pandemics previously assigned to *Y. pestis*: one that spread through parts of Africa, Asia and Europe in AD 541–542, during the reign of the Roman emperor Justinian and, more tentatively, the plague of Athens (430–426 BC), which was evocatively described in the writings of the Greek historian Thucydides. Bacterial DNA has purportedly been recovered from both of these epidemics, although in the case of the plague of Athens, the DNA was attributed⁶ to the *Salmonella enterica* serovar Typhi bacterium that causes typhoid fever, rather than to *Y. pestis*. However, the Athenian *Salmonella* strain is not actually closely related to that responsible for typhoid⁷, suggesting that the ancient DNA had been contaminated by DNA from a modern, soil-living *Salmonella* species. The cause of the plague of Athens therefore remains a mystery.

The DNA supposedly from the Justinian plague is certainly that of *Y. pestis*, but the close similarity between the 'Justinian' DNA and that of modern *Y. pestis* variants⁸ suggests that the former strain may not be authentic. Importantly, if all contemporary strains of *Y. pestis* are derived from the Black Death, as suggested by Bos and colleagues¹, then both of the earlier epidemics were caused either by a strain of *Y. pestis* that has left no contemporary descendants, or by an entirely different organism. Ancient DNA may be central to resolving this question.

The analysis of ancient DNA is a powerful