

protease opens up to allow the products to escape. The findings of Shen *et al.*¹ suggest that this final enzyme-opening step limits the rate of the overall reaction, so that mutations that facilitate this opening process activate IDE.

Shen and colleagues' results¹ excitingly suggest that drug molecules might also be able to activate IDE by mimicking the latch-disrupting mutations. Of course, designing a molecule that targets the latch system may prove challenging. On the other hand, the new structures of IDE will undoubtedly facilitate the development of inhibitors targeting IDE's active site. The potential use of IDE inhibitors for the treatment of diabetes should not be dismissed out of hand, because transient pharmacological inhibition of IDE might yield different results from the life-long, pan-cellular defects present in the genetically altered rodent models discussed above. Moreover, any risk of exacerbating Alzheimer's disease (by elevating amyloid- β -protein levels) might be avoided by using compounds that do not cross into the brain. Whether inhibition or activation of IDE is ultimately prescribed, Shen and colleagues' crystal structures herald the dawn of a rational, structure-based approach to the pharmacology of this ubiquitous protease. ■

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PALAEOANTHROPOLOGY

Return of the last Neanderthal

Eric Delson and Katerina Harvati

New finds from Gibraltar date Mousterian tools to as recently as 28,000 years ago. By inference, their Neanderthal makers survived in southern Iberia long after all other well-dated occurrences of the species.

The last Neanderthals were participants in one of the most dramatic events in the story of human evolution. At a time of increasing climatic instability and environmental deterioration, they would have had to have survived in ever-smaller groups, confined to less environmentally hostile refugia on the coast of the Mediterranean, and competing for access to resources with modern humans pressing on their territory.

These conditions are widely thought to have led to the Neanderthals' extinction within a relatively short time after the colonization of Europe by modern humans¹. But in a paper² on page 850 of this issue, Finlayson *et al.* revise that model considerably*. They produce dating results from Gorham's Cave, Gibraltar, that might indicate that a group of Neanderthals survived extinction in this part of southern Iberia until at least 28,000 years ago — thousands of years after anatomically modern humans had firmly established themselves as the inheritors of the European continent.

Neanderthals inhabited western Eurasia from a time in the Middle Pleistocene between 500,000 and 160,000 years ago (depending on the definition of the earliest members of the Neanderthal group^{3,4}) until approximately 30,000 years ago (Fig. 1). They were characterized by a suite of specialized morphological features, many of them unique to the group, that together make them highly distinct from modern humans. Their skeletal remains are often found associated with 'Mousterian' stone tools, named after the Le Moustier site

*This article and the paper concerned² were published online on 13 September 2006.

in France. In Europe — but not in northwest Africa or southwest Asia — such tools are exclusively found with Neanderthals, and are presumed to have been made by them.

Neanderthal remains discovered from times near the end of their existence are sometimes found with tool assemblages resembling those produced by early modern humans. This is possibly a result of acculturation or imitation of modern human technology⁵. Although there is still some discussion over the Neanderthals' taxonomic status and their relationship to modern humans, it is now widely recognized that they represent a distinct, Eurasian evolutionary lineage. They shared a common ancestor with modern humans in the early Middle Pleistocene or before^{3,6,7}, but became isolated thereafter from the rest of the Old World. Glacial climatic conditions are considered at least in part responsible for this isolation and for the evolution of some distinctive features of Neanderthal morphology, especially their short limbs and heavy trunks. These are similar to, but more extreme than, features of cold-adapted modern populations such as the Inuit^{8,9}.

The interaction between Neanderthals and modern humans after the arrival of the latter in Europe around 40,000 years ago is among the most interesting topics in European palaeoanthropology. Did they meet? Did they compete? If so, in what ways? Did they interbreed? If they did, did the Neanderthals become assimilated into the modern-human gene pool, or was theirs a union without issue⁴?

Until recently, the interval of coexistence of the two groups in Europe was thought to be as long as 8,000 to 10,000 years. Although it has

ASTRONOMY

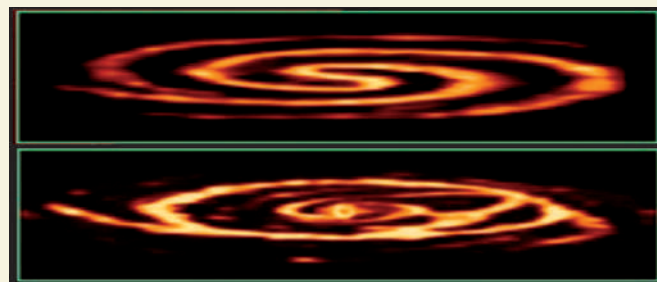
Andromeda's troubled past

It would have been quite a collision. Around 210 million years ago, galaxy M31 — better known as Andromeda — and its smaller neighbour M32 met almost head-on, leaving the battered structure of M31 seen today. This striking proposal is made by D. L. Block *et al.* on page 832 of this issue (*Nature* **443**, 832–834; 2006).

The story is summed up by the two snapshots, each roughly

120,000 light years across, included here. They show the results of Block and colleagues' numerical simulations, with (top) a serene M31 some 35 million years before the collision, and (below) the dishevelled M31 of today.

The simulations offer telling support for the authors' scheme of events, which hinges on two dust rings in the galaxy's disk



(See Fig. 1 on page 832). One, at a radius of about 33,000 light years, is well known; the other, much closer in, was identified only recently with NASA's Spitzer Space Telescope. The two rings emerge from the

simulations — precise in both position and orientation — as a consequence of a head-on galaxy-galaxy impact, with M32 being the likely culprit.

Tim Lincoln

been suggested that modern humans arrived in most areas after Neanderthals had already become locally extinct⁸, most researchers found it difficult to imagine that the two groups never interacted during those millennia. The most recent review of the dating evidence¹, however, has proposed that the duration of coexistence was much shorter than thought, and limited to as little as 2,000 years in some places.

Such a short interval points to a relatively fast Neanderthal extinction and a competitive edge for modern humans. That edge came perhaps from cultural practices such as improved clothing and more effective social networks, as documented by finds of personal ornamentation^{9,10}. The short time span also limits the scope for interaction, whether cultural or genetic, between the two groups. This view is consistent both with genetic evidence pointing to very little, if any, Neanderthal contribution to the modern-human gene pool, and with the paucity of potential hybrid skeletal remains.

Finlayson and colleagues' evidence² adds yet another dimension to the story of coexistence. It indicates that at least one group of Neanderthals in Gibraltar was able to survive the deteriorating climate and competition from modern humans, while continuing to use Mousterian (Middle Palaeolithic) technology, until 28,000, and possibly 24,000, years ago. Such a late survival would reinforce the importance of southern Iberia as a refuge area at a time when modern humans were expanding and diversifying culturally across mid-latitude Europe.

Finlayson *et al.* are rightly cautious in their treatment of their very late dates for the last Mousterian occupation at Gibraltar. Their dating sequence (their Fig. 1 on page 851 and Table 1 on page 852) shows several cases where samples lower down in their dig have produced ages that are younger than those above them. This violates the basic rule of stratigraphic superposition, that younger layers overlie older ones. The authors state that such reversals are due to the reuse and cleaning of what is assumed to have been the hearth area, suggesting that dates within the main part of the hearth (which has 24,000 above 26,000 above 30,000 years ago) are more trustworthy than areas alongside it. But there are just too many instances of dates younger than 28,000 years that are out of order, implying that these dates might not be reliable. More extensive sampling of the *in situ* hearth and surroundings might resolve this issue.

If the evidence for Neanderthal survival until 24,000 years ago were to hold water, it might also put other findings in a new light, in particular the Lagar Velho child. This purported Neanderthal-modern hybrid was found in Portugal with Upper Palaeolithic artefacts, and dated¹¹ to 24,500 years ago. Until now, one of the main objections to the acceptance of this find as a possible hybrid — aside from its juvenile morphology, which makes it difficult to draw conclusions about the adult form — has been its chronology. The specimen dates to several millennia after the Neanderthals were thought to



Figure 1 | Principal late Neanderthal/Mousterian sites across western Eurasia. Finlayson and colleagues' find² of Mousterian tools in Gorham's Cave, Gibraltar, might be the most recent indication of Neanderthal settlement yet. Zafarraya (Spain) and Figueira Brava (Portugal) have yielded southern Iberian putative late Neanderthal fossils, whereas St. Césaire and Arcy-sur-Cure (both France) are slightly older (between 35,000 and 30,000 years old). Also indicated are Le Moustier, the eponymous site for the Mousterian tool industry, and Feldhofer, the site of the initial Neander Valley find of 1856. Vindija (Croatia) and Mezmaiskaya (Russia) are noted by Finlayson *et al.*² as having recently been related to older than 30,000 years ago. Subalyuk (Hungary), Guattari (Italy), Amud (Israel) and Shanidar (Iraq), as well as Feldhofer and Le Moustier, are older than 35,000 years, but they give an indication of the geographical range of the last glacial Neanderthal finds; sites farther east, such as Teshik-Tash (Uzbekistan; not shown), have recently been the subject of questions as to the identity of the fossils recovered.

have disappeared, and was therefore much too recent to be a hybrid¹². This criticism would no longer hold if Finlayson and colleagues' youngest dates could be accepted; for the moment, the consensus is that they cannot.

When considering Finlayson and colleagues' find, it is also important to point out that evidence of Mousterian tools does not in itself indicate that their makers were Neanderthals; this is merely a reasonable assumption. Recovering human fossils from the site would resolve the uncertainty, and possibly shed light on the morphology of late Neanderthals. Until then, we can only be certain that Mousterian toolmakers occupied Gorham's Cave as late as 28,000 years ago. The interval between 28,000 and 24,000 years ago, and the toolmakers' identity, remain in question. Finally, the authors correctly dismiss now discredited late Neanderthal dates from central and eastern Europe, but they may have too quickly rejected some from southern Iberia¹³ that could complement their own evidence for regional refugia.

The late survival of an archaic hominin is not completely unexpected, given the spectacular find of the even later *Homo floresiensis* in Indonesia¹⁴. However, as exciting as the new Gibraltar dates might be, this is not the first claim of the discovery of the last Neanderthal¹⁵. Finlayson and colleagues' date of 28,000 years ago is later than any other well-documented supposed Neanderthal occurrence, proving the importance of this long-term project. Gorham's Cave might well pinpoint the newly extended end of a long lineage of human occupation in Europe. But time will tell. ■

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