Perspectives

Proteases immobilized by extracellular reminiscent of NETs. The abundance of elastase and the age. Endogenous soluble inhibitors may contribute to focusing the activity of proteases by precluding their diffusion. Although not addressed in the paper, it is also possible that NETs sequester cytokines in the local environment of the neutrophil, preventing uncontrolled dissemination of the inflammatory response and thus minimizing damage to surrounding host tissues (7).

The proposed antimicrobial role of NETs seems to be at odds with the use of DNase in mucolytic therapy for treating patients with cystic fibrosis. The hallmark of this common inherited lung disease is tenacious and purulent sputum, whose components include a complex of DNA and elastase (6), reminiscent of NETs. The abundance of proteases immobilized by extracellular DNA in the sputum would appear to be ideally suited to limiting the chronic respiratory infections suffered by cystic fibrosis patients. Hence, degradation of DNA in the sputum by inhaled DNase (which destroys NETs) would be expected to aggravate the disease, not only by impairing these bactericidal tools, but also by releasing elastase and other mediators that could exacerbate the inflammatory condition (7). Paradoxically, therapy with inhaled DNase reduces the symptoms of cystic fibrosis and improves pulmonary function (8). It is possible that excessive NET formation may be counterproductive, preventing proper mechanical clearance of the airways, which is driven by ciliary motion. The cilia themselves may get tangled in the NETs.

The discovery of NETs raises a number of other questions. Do all activated neutrophils make NETs, and if not, what determines which ones do? At what stage of the activation cascade are the NETs “woven”? These questions are important because the notion of activated neutrophils laying down a dense web of extracellular fibers is difficult to reconcile with their need to migrate by chemotaxis toward sites of infection. Indeed, NETs could conceivably act as a barrier to the recruitment of more white blood cells and thereby impede the clearance of chronic infections, as is the case with the formation of abscesses. Along the same lines, it is not apparent how NETs might be dismantled when the infection has been cleared.

The observations of Brinkmann et al. suggest the crucial nature of extracellular killing of bacteria by neutrophils. Whether this antimicrobial action is the result of an active, targeted process by live neutrophils or an altruisitic post mortem contribution to the well-being of the organism remains to be defined. Complex though these NETs may be, they should yield to further unravelling during future studies.

References

Anthropology

The Earliest Hominins—Is Less More?

David R. Begun

Fossil and molecular evidence are converging on a consensus that the human lineage diverged from that of the chimpanzee between ~6 and 8 million years ago (Ma). Recent fossil discoveries in Africa are consistent with this conclusion and are beginning to paint a picture of the pattern of speciation that led to the origin of our lineage. On page 1503 of this issue, Haile-Selassie et al. (1) announce a new late Miocene African hominin (2) species, the third in the past 3 years (1, 3, 4). Ardipithecus kadabba is a nearly 6-million-year-old hominin (2) that Haile-Selassie and colleagues elevate to the species level from Ardipithecus ramidus kadabba. The new discovery renews discussion of the number of taxa that lived shortly after the human lineage diverged from that of chimpanzees, and may shed new light on the very nature of the first humans (2). Although Haile-Selassie and co-workers argue that all known African hominids between ~7 and 4.4 Ma may belong to one genus and see little taxonomic diversity near hominin origins, they may in fact have evidence of more diversity than previously recognized (see the figure).

The new evidence, discovered in the Middle Awash region of Ethiopia, is a handful of teeth including premolars and canines that are indeed distinct from A. ramidus (1, 5, 6). But the relationship of this older and smaller sample of specimens to A. ramidus is uncertain. A. ramidus from the Middle Awash study area (locality of Aramis) has been dated at 4.4 Ma, whereas the morphologically distinctive A. kadabba sample from Asa Koma and several other localities also in the Middle Awash study area is older, 5.6 to 5.8 Ma (one specimen, an enigmatic foot phalanx, is dated to 5.2 Ma) (7, 8). On the basis of their interpretation of a gradual transformation from ape-like to humanlike canine/premolar morphology, and the expectation of high levels of diversity within genera or even species, Haile-Selassie et al. argue that A. kadabba represents an early phase in the development of human anterior teeth. They suggest that A. kadabba represents a transition between chimpanzees (with large, dagger-like canines) and A. ramidus, Australopithecus, and Homo (with unimpressive canines that wear down from the tips). Two other late Miocene hominins, Orrorin tugenensis and Sahelanthropus tchadensis, show predictable variability in this evolving lineage. This is a plausible scenario. However, Ardipithecus, Orrorin, and Sahelanthropus offer evidence of striking diversity. Orrorin has modern-looking thickly enameled molars and robust jaws but has postcranial morphology that is distinct from that of Pliocene hominins (the epoch following the Miocene when clearly bipedal humans are found) (3, 9). Sahelanthropus is also quite distinct from Pliocene hominins in craniofacial and dental morphology (4, 10). Do these samples represent stages in early hominin evolution or discrete lineages? In other words, how many taxa are represented by these fossil samples?

Could all of these fossils belong to the same genus, or even the same species? This is implied by Haile-Selassie et al. but seems unlikely to me. Comparisons among these taxa are difficult because they preserve little in common. Nonetheless, we know that Orrorin has mandibular and molar morphology similar to that of australopithecines, but female canines resembling those of apes (3, 11). Sahelanthropus has a unique combination of superficially modern-looking facial and periornital morphology, primitive-looking teeth and braincase,
and a probably homologous hominin suite of features of the basicranium (4, 10). A. kadabba is distinctive in having canines that appear to partly hone or sharpen against the lower first premolar (P3 by paleontological convention), not as much as in apes but more than in humans. In crown cross section and shape, however, the canines are more hominid-like than the more chimpanzee-like Ororrin canines. But Ororrin has australopithecine-like thickly enameled teeth, usually associated with a diet requiring powerful chewing forces, whereas Sahelanthropus, A. ramidus, and A. kadabba have intermediate-thickness enamel (less thick than in other hominins, but much thicker than in African apes) (5). Miocene hominins range from thinly enameled chimpanzee-like molars, as in Dryopithecus, to Australopithecus-like thickly enameled molars, as in Sivapithecus and Orrorin tugenensis, and it is unclear which among these or the intermediate condition in Ardipithecus and Sahelanthropus represents the ancestral condition for hominins. Differences in enamel thickness often distinguish taxa at the genus level and usually reflect dietary adaptation rather than phylogeny.

Ororin is said to share hominin synapomorphies (newly evolved, shared characteristics indicating a recent common ancestry) of the lower limb related to bipedalism (3, 9), but this is far from established. The most important features suggesting bipedalism either are found in nonbipeds (the groove for the obturator externus muscle) or appear different enough from the morphology of known bipeds to call the functional homology of these features into question (the linea aspera, which is unusually laterally displaced in Ororin, or the asymmetric femoral neck cortical bone, which is less asymmetric than in known bipeds) (12). A. kadabba also lacks synapomorphies of A. ramidus and Australopithecus in canine, premolar, and last molar morphology, which suggests that the Asa Koma and other older samples belong to another genus (note that A. ramidus was originally named Australopithecus ramidus because of an understandable hesitation to name a new human genus, and was later elevated to a new genus when no Australopithecus-Homo synapomorphies were discovered).

It is tempting to see evidence of analgesia (unilinear evolution) in the late Miocene hominin record in part because continuity is suggested by claims for some evidence of bipedalism in all known taxa. The evidence from Ororin is ambiguous (see above), whereas that from Sahelanthropus is indirect, based only on the position of the foramen magnum. The region is severely distorted in the only cranial specimen of Sahelanthropus, and even the describers recognize the uncertainty (4). A. kadabba is interpreted as a biped on the basis of a single toe bone, a foot proximal phalanx, with a dorsally oriented proximal joint surface, as in more recent hominins (6). However, the same joint configuration occurs in the definitely nonbipedal late Miocene hominin Sivapithecus (13), and the length and curvature of this bone closely resembles those of a chimpanzee or bonobo. In addition, the specimen is 400,000 to 600,000 years younger than the rest of the A. kadabba sample, 800,000 years older than A. ramidus, and from a locality that is geographically much closer to Aramis than to Asa Koma. It may or may not be from a biped, and if it is, which biped?

Another issue is the canine/premolar complex. Tall crowned interlocking canines are usually associated with agonistic (aggressive) displays typical of primate societies characterized by strong male competition (14). A shorter canine crown in humans is interpreted as an indication of greater levels of male coalitional behavior, or at least reduced competitiveness. Chimpanzee males are intermediate between humans and most other great ape males in canine crown height and competition levels, and bonobos are intermediate between chimpanzees and humans. But the remarkable reduction of canine crown height in humans is thought to signal a dramatic increase in the degree of male cooperation, cited as a hallmark of human origins [e.g. (15)]. The diversity of canine/premolar morphology described by Haile-Selassie et al., from chimpanzee-like to humanlike, represents a striking and unlikely degree for a single genus, especially in an anatomical complex strongly correlated to an aspect of socioecology that is considered to be a primary distinction between apes and humans.

Both clade (synapomorphies) and grade (diet, locomotion, and socioecology) criteria suggest more rather than fewer taxa among the earliest possible hominins. Why the different interpretations? Evidence is scarce and fragmentary, and uncertainty predominates. Interpretations rely especially heavily on past experience to make sense of incomplete evidence. Haile-Selassie and colleagues interpret diversity in fossil hominins in terms of variability and gradual evolutionary change in an evolving lineage. Others see clades as opposed to ancestor-descendant relations (see the figure).
of opinion inevitable. The solution is in the mantra of all paleontologists: We need more fossils!

References and Notes
2. The terms hominid, hominin, and even human are in flux among paleoanthropologists. Here I refer to all great apes and humans as hominids (a family), and all taxa more closely related to living humans than to chimpanzees as hominins (a tribe). In this context, human is synonymous with hominin.

Astronomy

Watching Black Holes Spin
Stéphane Corbel

By definition, black holes cannot be observed directly. Their effects on nearby light and matter, however, have been seen so often that we are forced to conclude that black holes really do exist. To some extent, we can even understand how they are created. When a massive star dies, it leaves behind a “compact object.” If the mass of the residual compact object is more than about three times the mass of the Sun (the so-called Oppenheimer-Volkov limit), then nothing can hold back gravity and the residual core of the death star becomes a black hole (1).

These strange beasts can be found in x-ray binaries in which the black hole (with a typical mass of 10 $M_\odot$, where $M_\odot$ is the mass of the Sun) is accreting material from a companion star (similar to the Sun, for example) via an accretion disk. Black holes can also be very massive (from $10^6$ to $10^9 M_\odot$) and are found at the center of galaxies (2). Another population of intermediate-mass black holes (tens to thousands of solar masses) may also exist in the so-called ultraluminous x-ray sources (ULXs) (3). For stellar-mass black holes in an x-ray binary, the mass can be measured accurately with spectroscopic optical and/or near-infrared observations of the companion star (4). Similarly, the mass of the black hole Sgr A* at the center of our own Galaxy has been estimated as $3.6 \times 10^6 M_\odot$ by looking at the motion of stars very close to the black hole (5). Alternative methods (2) also exist for measuring black hole mass in active galactic nuclei (AGN).

In addition to their mass, black holes are also characterized by their spin. The existence of radio pulsars demonstrates that stellar remnants are spinning rapidly when formed, so it seems likely that all stellar-mass black holes are spinning, at least initially. The rotation (6) of black holes is quantified by the dimensionless spin parameter $a^* = Jc/GM^2$, where $J$ and $M$ are the angular momentum and mass of the black hole, respectively, $c$ is the velocity of light, and $G$ is the gravitational constant. Gas flowing toward the black hole slowly reaches the innermost stable circular orbit (ISCO). However, the frequencies of these QPOs could also be related to diskoseismic oscillations (QPOs) in the x-ray power density spectra of stellar-mass black holes (8, 9). Usually, these QPOs are detected when the soft x-ray emission is very high, which is when the accretion disk is very close to the black hole. How close is a matter of debate, as it is directly relevant to the spin of the black hole. However, the frequencies of these QPOs correspond to an orbital radius that cannot be smaller than the ISCO (7). The ISCO of a Schwarzschild (non-rotating) black hole corresponds to a maximum orbital frequency of $220 [M/(10 M_\odot)]^{-1} \text{Hz}$ (where $M$ is the black hole mass). To date, the Rossi X-ray Timing Explorer (RXTE), with its unprecedented time resolution and collecting area, has detected high-frequency QPOs above this frequency in several black hole candidates (8, 9). Such findings could indicate significant spinning of the black hole if these oscillations are related to the orbital frequency of accreting gas at the ISCO. However, the identification of the physical mechanism behind these oscillations is ambiguous. Indeed, these QPOs could also be related to diskoseismic oscillations in which the disk acts as a resonant cavity under influence of general relativity effects (10) or to relativistic dragging of the black hole inertial frame (11). In any case, both of these models also imply significant spinning of the black hole.

Recently, near-infrared flares (possibly associated with emission of nonthermal

The author is at the University of Paris 7 Denis Diderot and Service d’Astrophysique, CEA, CE-Saclay, 91191 Gif-sur-Yvette, France. E-mail: corbel@discovery.saclay.cea.fr

http://www.sciencemag.org on March 31, 2008

References and Notes
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