MEETING AMERICAN ASSOCIATION OF PHYSICAL ANTHROPOLOGISTS

Studying Humans—and Their Cousins and Parasites

KANSAS CITY, MISSOURI—More than 1000 researchers presented 500 papers at the 70th Annual Meeting of the American Association of Physical Anthropologists here, from 28 to 31 March. The talks covered diverse aspects of human and ape evolution, including a genetic study of primates, new dates on an important site for early human fossils, and the evolution of a malaria resistance gene.

The Least Diverse Ape

On our planet of the apes, humans are by far the most successful primate, easily outnumbering all other great apes. But despite our stunning reproductive success, we have very little genetic variation compared with other primates, according to a study presented in Kansas City. When researchers compared DNA sequences at the same six regions in the genomes of humans, chimpanzees, bonobos, and gorillas, they found that humans had far less nucleotide variation at almost every region. In only one case—on the Y chromosome of gorillas—were the apes genetically less diverse than humans.

The new study and similar work by geneticists in Germany are the first to look at a wide range of DNA in all the great apes, and they help resolve earlier, contradictory reports (*Science*, 5 November 1999, p. 1159). The findings confirm what some previous studies had suggested: We are all descended from a small founding population whose offspring multiplied rapidly in the past 200,000 years. The lack of diversity in humans is now so striking that it strongly supports the theory that our ancestors survived a "bottleneck" that quickly winnowed a larger, genetically diverse population into a smaller, homogeneous one. "This is startling; it shows that the bottleneck we went through must have been profound," says Linda Vigilant, a molecular anthropologist at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany.

Studies have shown for a decade that chimpanzees have three to four times as much genetic diversity in their maternally inherited mitochondrial DNA (mtDNA) as humans do. But are chimpanzees exceptionally diverse, or humans exceptionally alike? No one had sequenced enough DNA from other apes to find out, until a study reported in February in *Nature Genetics*. Geneticists Svante Pääbo and Henrik Kaessmann of the Max Planck Institute for Evolutionary Anthropology compared a 10,000-base-pair stretch of noncoding DNA on the X chromosome in humans, chimpanzees, gorillas, and orangutans. They found that humans had not only much less genetic variation than all other great apes, but also had relatively few of the mutations that accumulate in noncoding regions of the genome at a relatively steady rate. That's a signal that humans underwent a major expansion starting 190,000 to 160,000 years ago, says Pääbo.

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The lucky one. This gorilla, Titus, fathered almost all the offspring in his group, giving them all the same Y chromosome.

Meanwhile, two other teams of molecular anthropologists had joined forces to study six regions in both nuclear DNA and mtDNA, in humans, chimpanzees, bonobos, and western and eastern gorillas. In geneticist Ken Kidd's lab at Yale University, graduate student Michael Jensen-Seaman, now at the Medical College of Wisconsin in Milwaukee, and geneticist Amos Deinard focused on four noncoding loci in nuclear DNA inherited from both parents. They found that chimpanzees had the most diversity, whereas humans had the least.

At the same time, graduate student Tasha Altheide, in evolutionary geneticist Michael Hammer's lab at the University of Arizona in Tucson, focused on regions of the paternally inherited Y chromosome and mtDNA. Again, she found that humans had the least variation in mtDNA and little in their Y. But, surprisingly, gorillas had the most variation in mtDNA—and none in the Y.

That exception doesn't shake the pattern of overall low human diversity; rather, it's a clear reflection of gorilla mating habits, gorilla experts say. Gorillas have a haremlike social structure, explains Yale primatologist David Watts: "Relatively few gorilla males in each generation contribute genes to the next one." Indeed, another paper at the meeting by Brenda Bradley, a graduate student in Vigilant's lab, documented this pattern in mountain gorillas at the Karisoke Research Center in Rwanda. The group had more than one adult male, as is common, but the DNA showed that one male, Titus, had fathered all but one of the 10 offspring. "This is a nice reflection of the effect of the mating system on genetic diversity," says geneticist Lynn Jorde of the University of Utah in Salt Lake City.

When it comes to humans, however, mating behavior can't explain the lack of variation at virtually every genetic region studied. Thus, the new data support the idea that a relatively small number of breeding humans survived a bottleneck (*Science*, 6 January 1995, p. 35), perhaps caused by a speciation event, disease, or changes in climate and habitat. Surviving populations then expanded rapidly but carried no more genetic variation than their ancient founders. The end result: "We really look like one subspecies of chimpanzee that has spread and taken over the world," says Pääbo.

New Old Dates for Humans in Java

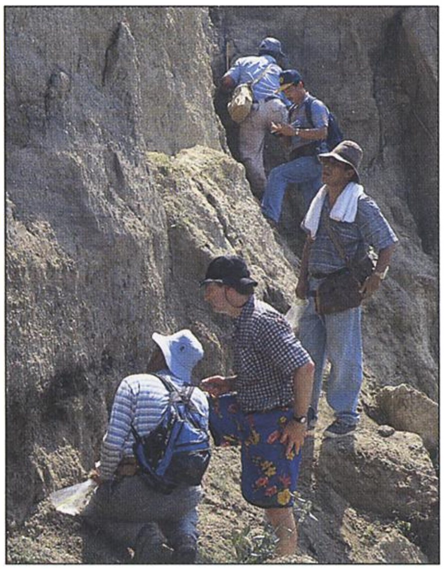
When scientists announced in 1994 that an early human, *Homo erectus*, had lived in Java, Indonesia, as early as 1.6 million to 1.8 million years ago—a million years earlier than expected—anthropologists were stunned (*Science*, 25 February 1994, p. 1118). Because *H. erectus* arose in Africa only 2 million years ago, the dates implied that these early humans had spread 10,000 kilometers long before anyone thought they had even ventured out of Africa. Not surprisingly, other researchers were cautious about rewriting human colonization history and raised serious questions about the dates.

Now, another team of researchers has redated the same fossil beds at one of the Java sites and also finds that *H. erectus* was there 1.5 million years ago. In Kansas City, the team concluded that nearly all the *H. erectus* fossils found in the famed Bapang Formation of Sangiran are at least 1 million years old, with some dating back 1.5 million to 1.6 million years. *H. erectus* was there "for at least a half-million years, beginning 1.5 million years ago," say paleoanthropologist Russell Ciochon and geoarchaeologist Roy Larick of the University of Iowa in Iowa City, coauthors of a report in the 24 April *Proceedings of the National Academy of Sciences*.

But although many researchers are impressed with the team's 3-year geologic study, no one is yet rewriting textbooks. Geochronologist Carl Swisher of Rutgers University in New Brunswick, New Jersey, is pleased his radiometric dates have been confirmed but admits: "There are issues that still need to be addressed to put this thing to rest."

Ever since Dutch anatomist Eugene Dubois found the first specimen of *H. erectus* on the banks of Java's Solo River in 1891, the island has been a treasure trove of early human fossils. Local villagers have found more than 80 *H. erectus* fossils in the Sangiran Dome—an exposed bluff between two volcanoes in central Java—alone. But these fossils have been notoriously difficult to date, because it's hard to pinpoint where local people found them, and because they may have been moved by water or volcanic activity.

The new team worked with Indonesian geologists to put the fossils in geological context, then mapped and dated the sedimentary layers—"comprehensive" work that is well-regarded by other geologists, says Marco Langbroek, an archaeologist at Leiden University in the Netherlands. The team then sampled volcanic pumice at five sites plus the one Swisher dated, just above the layer where fossils were found. They sent the samples to geochronologist Matthew Heizler of the New Mexico Bureau of Mines and Mineral Resources in Socorro, who used the ratio of the decay of argon-40 to argon-39 to date



***Homo erectus*'s haunt.** Sangiran is full of fossils but hard to date.

the hornblende. His dates matched both Swisher's 1994 dates and new, unpublished argon/argon dates.

Although no one doubts that the two groups got the right age for the volcanic rock, the new team faces the problems that have plagued others in Java. Namely, how much time passed between the formation of the dated volcanic layer and the deposition of the fossils, and was the old pumice transported into younger, fossil-bearing layers? Langbroek also notes that the results are at odds with the dates of two tektites—shock-melted crystals formed by a huge meteor impact 800,000 years ago—from the fossil beds.

Larick and Heizler respond that their dates are in proper stratigraphic order, with old dates below younger ones, making it "improbable that the pumice is reworked." Furthermore, the tektites were found and analyzed more than 20 years ago, and some researchers question whether they really came from fossil-bearing layers—and indeed whether they are tektites at all. "The ever-increasing number of early radiometric [dates] calls the published context of these two artifacts into question," says Larick.

All the same, the authors will need "tektite-proof helmets" to prove that *H. erectus* set foot in Java 1.5 million years ago, says Langbroek. He concludes: "We need more than a new set of radiometric dates to clear the problems at Sangiran."

The Evolution of Malaria Resistance

Malaria kills between 1 million and 3 million humans, mostly children, every year, making it the leading cause of death from an infectious disease (*Science*, 20 October 2000, p. 428). It has plagued humans for at least 3000 years, when an Egyptian mummy was entombed with antigens to malaria in its blood. But scientists still don't know when the deadliest form of malaria—*Plasmodium falciparum*—arose and first spread in humans. "Studies of the malaria parasite seem to show that it's been around a long time, since the split from chimpanzees," says biological anthropologist Jonathan Friedlaender of Temple University in Philadelphia. "But when did it become this ubiquitous killer in humans?"

Now, in a paper at the Human Biology Council's meeting in Kansas City, an international team of geneticists has examined humans' evolutionary response to malaria to help answer that question. By tracing two genetic mutations that give people anemia but also confer resistance to malaria, the team concludes that the disease first began to have a severe effect on humans in the past 11,000 years, says lead author Sarah Tishkoff of the University of Maryland, College Park. The paper offers "the first estimate for actual dates for the occurrence of human genetic mutations associated with malaria protection," says Friedlaender.

The work confirms, in part, a longstanding theory that the disease first hit humans severely when agriculture was introduced in the past 10,000 years, although mild forms of malaria have existed since our ancestors split from apes. The new work

How old a plague? Malaria, carried by *Anopheles* mosquitoes, may have ravaged humans since the birth of agriculture.

also pushes back the date for the initial spread of *P. falciparum* in western Africa by several thousand years, from 2500 to 4000 years ago to a time 12,000 to 7000 years ago, when climate changes in sub-Saharan Africa triggered changes in human lifestyle.

Several groups have looked for clues to the origins of malaria by tracing the genetic evolution of the malaria parasites—*P. falciparum* and *P. vivax*—or the *Anopheles* mosquitoes that transmit them, but Tishkoff's team examined the human genome. They zeroed in on a common genetic disease—glucose 6-phosphate dehydrogenase (G6PD) deficiency, which affects 400 million people. Those with the deficiency have anemia, but they also have roughly half the risk of getting severe malaria as do most humans.

The team focused on two of the many variants of G6PD deficiency—the A– variant, found only in Africa, and the Med variant, found in the Mediterranean, the Middle East, and India. Both variants are the result of a single nucleotide substitution in the G6PD gene, and both are found in strong association with certain microsatellite markers in the noncoding region of the gene. This association and low variation indicated to Tishkoff that the variants were both independent and young, as otherwise the microsatellite association would have broken down over time.

The age of the variants was calculated by population geneticist Andrew Clark of Pennsylvania State University, University Park. He counted mutations and estimated the mutation rate by taking into account recombination, selection pressure, and the microsatellites' mutation rate. After also determining

CREDITS: (TOP TO BOTTOM) SINCLAIR STAMMERS/WHO/TDR; RUSSELL CIOCHIN the frequency of the mutations in different populations, the team concluded that the A– variant arose in Africa within the past 3840 to 11,760 years, and the Med allele arose between 1600 and 6640 years ago in the Middle East or Mediterranean.

Both mutations then spread rapidly through regions where malaria is endemic, despite the fact that they cause anemia. That shows that the mutations were strongly favored by natural selection, suggesting that malaria suddenly had a severe effect on humans at these times, says Tishkoff.

The dates for the A– variant fit loosely with a well-known hypothesis by geneticist Frank Livingstone of the University of Michigan, Ann Arbor, who proposed in 1958 that sickle cell anemia and malaria took hold when farmers first used iron tools to clear forest and live in dense settlements near mosquito breeding grounds. But Livingstone's dates were just 2500 to 4000 years ago, more recent than Tishkoff's dates. Tishkoff consulted Alison Brooks, an expert on African prehistory at George Washington University in Washington, D.C., who noted that archaeological evidence has been accumulating for a dramatic lifestyle change in Africa starting 12,000 years ago, when a climate shift transformed the Sahara from an arid wasteland into a green savanna with many lakes and ponds. Africans fished and herded animals and for the first time moved into denser communities on the lakeshore—next to the breeding grounds of *Anopheles* mosquitoes. Conditions were perfect for the parasite. Presumably in response to the disease's devastating effect in this environment, the A– mutation arose and spread rapidly—a vivid example of natural selection in action, says Tishkoff.

The Med mutation came later in the Middle East or Mediterranean, perhaps in response to the more recent spread north of the deadliest malaria, *P. falciparum*. Interestingly, the dates for the rapid spread of the Med mutation coincide with the exploration of Greeks and Macedonians, such as Alexander the Great. "It fits beautifully," says Tishkoff. If the dates hold, she says—and at the moment they have large margins of error—"this is one of the few cases where you can tie in genetics, history, and archaeology."

–ANN GIBBONS

GERMAN RESEARCH MINISTER

Bulmahn Is Bullish on Science Reforms

Edelgard Bulmahn wants to change how the country manages its research institutions, but she's facing vocal opposition from many academics

BERLIN—Ambitious and controversial, Edelgard Bulmahn has been a major force in German science and higher education since becoming research minister in 1998. A member of the "Red-Green" coalition government, Bulmahn has proposed an overhaul of Germany's university rules—seeking merit pay and "junior professorships" that would free young scientists to pursue independent research—that has polarized the academic community (*Science*, 6 April, p. 30). She has also pushed efforts to reverse Germany's brain drain by beefing up fellowship programs and other incentives to attract expatriates and woo international scientists.

But Bulmahn, a political scientist and former member of Parliament, has not restricted herself to academic reforms. She has waded into the debate over embryonic stem cells, emphasizing the use of adult stem cells for now. Bulmahn also is the key negotiator in trying to convince Bavarian state officials to convert a new research reactor to a uranium fuel that could not be diverted by terrorists for making nuclear weapons.

In a 9 April interview with *Science* in her Berlin office, Bulmahn discussed these and other topics in laying out her vision for German research. What follows has been edited for clarity and length.

***Science*:** On becoming minister, you set some ambitious goals to reform the university system and the science system as a whole. In what areas have you made the most progress?

Bulmahn: We have started to modernize our research system to handle today's challenges. … We need to give our young scientists and scholars more and better opportunities to do their research independently within the framework of their universities or research institutions. … We haven't finished everything we started, but that is always the case if you want deep reforms. … Science and research have been priorities of this government. We have increased the budget by 12.5% in the last 2 years, even while the overall federal budget has been decreasing.

***Science*:** More than 3700 professors recently signed a petition complaining about your proposed university reforms, which would allow a performance-oriented salary system, phase out the post-Ph.D. Habilitation requirement to become a professor, and establish "junior professors." How do you respond to their concerns?

Bulmahn: People have become used to this German public-service system after more than 100 years, so of course some people are afraid of these changes. You will always face opposition when you try to change traditional systems.

In their public arguments, opponents have distorted the reform proposals. … They have used the argument that, in the future, young scientists would get a so-called monthly "starting salary" of DM 8500 [US$4200]. That is not true. The starting salary of a young scientist or young professor would be negotiated by them and the university. … As a young scientist, you could get much more money, depending on your performance and

Correcting the record. Bulmahn says opponents "have distorted" the government's proposed reforms.

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