MOLECULAR EVOLUTION

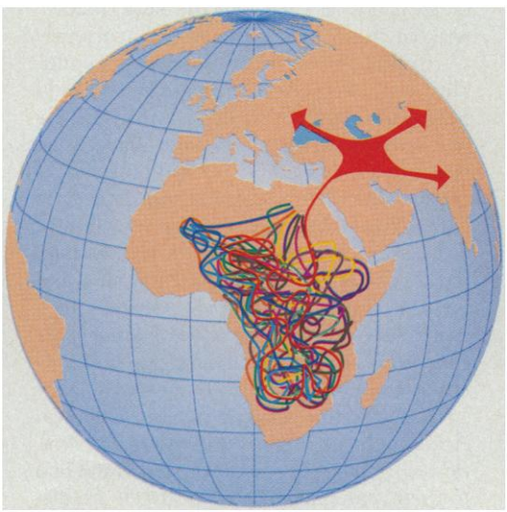
Evidence Mounts for Our African Origins—and Alternatives

Last year a genetic "Adam" took his place beside "Mitochondrial Eve." Genes passed down from fathers to sons suggested modern humans arose within the past 200,000 years and then swept around the globe, replacing remnants of an earlier, million-year-old migration; "Eve's" mitochondrial DNA, inherited by daughters from mothers, indicate that the modern group started in Africa. But genes do not equal whole populations, and with each pedigree limited to just a small stretch of DNA from each sex, some researchers still argue that the older populations in far-flung regions may not have been replaced. Instead, those groups produced modern humans—with an ancient heritage—themselves.

Now, on page 1380, an international team has tried to round out the picture with one of the largest studies to date of nuclear DNA, which can track the travels of both sexes—and the data trace them back to Africa, about 100,000 years ago. The DNA, a piece of chromosome 12, has a great variety of patterns in sub-Saharan Africa, loses many patterns in Northeast Africa, and is dominated by just one type in the rest of the world. This looks like a series of small populations repeatedly "budding off" from larger ones, losing variety as they go. And the group that left northeast Africa hasn't had enough time to recreate it through mutations. "It really looks to me like the rest of the world emerged from the northeast corner of Africa," says co-author Neil Risch, a Stanford University geneticist.

Mary Ellen Ruvolo of Harvard University and other anthropologists agree. "This is strong evidence for an out-of-Africa bottleneck," says Ruvolo, adding that it fits with other studies, both of genes and fossils, pointing to a recent migration date. But other researchers say that the new results don't settle the issue. The data could also support the ancient multiregional scenario, because changes in population size outside of Africa can reduce genetic diversity. "This is very nice work, and it's a believable story," says Michael Hammer, a geneticist at the University of Arizona, Tucson, and a chronicler of the genetic Adam. "But their data don't yield a test that can prove African replacement false or true."

The team, coordinated by geneticist Ken Kidd's lab at Yale University, thinks this particular stretch of DNA—examined in 1600 people in 42 populations—is more informative than critics charge. It consists of two segments, located only a short distance apart on the chromosome but mutating at different rates. The slow-evolving marker allows researchers to trace common ancestry; the faster-evolving one differentiates among populations. The first segment, known as Alu, comes in just two forms: an intact one and a truncated version that has lost most of its 285 base pairs (bp). The second segment,



SOURCE: S. TISHKOFF

Up and out? A genetic feature known as an Alu deletion has various patterns in Africa, but only one *(red)* seems to have made it out; a recent population migration could explain this.

a series of nucleotides repeated a varying number of times, or a short tandem repeat polymorphism (STRP), has 12 forms. The combination yields 24 possible varieties.

Outside of Africa, the researchers found that just one truncated Alu type predominated: the one linked to a 90-bp-long STRP. In Ethiopia and Somalia, there was somewhat more variety. But "to my complete surprise, when I started typing the [sub-Saharan] Africans, I came up with almost all the variations," says Yale graduate student Sarah Tishkoff. "Overall, there is very high diversity. So we're proposing a two-step process. Some diversity was lost in northeast Africa. There was a further loss when a small population left Africa, and by chance, the one Alu deletion variant that remained with them was the one with the 90-base-pair STRP."

And when did all this occur? The Alu deletion provides a timing mechanism. The researchers think it first occurred sometime within the last 5 million years, after we split off from the other great apes; the deletion isn't found in nonhuman primates. And it probably occurred on a chromosome with the 90-bp STRP, because that combination appears most often in more populations. Since then, the STRP has had time to mutate into the other versions in Africa. But outside the continent, the link between the deletion and the 90-bp STRP is 40 to 50 times stronger. Assuming a roughly constant mutation rate, the researchers argue that people moved beyond the continent only recently, leaving a proportionately shorter amount of time for mutations to occur. And that calculation yields a variety of recent dates for the migration, perhaps 100,000 years ago or even sooner.

This fits rather well with other studies on different parts of the genome, says Ruvolo, citing various analyses of mitochondrial DNA, the male-inherited Y chromosome (*Nature* vol. 378, pp. 376–378, 1995), as well as work tracing genetic markers on chromosomes 13 and 15 (*Proceedings of the National Academy of Sciences* vol. 92, pp. 6723–6727, 1995). Stanford geneticist Luigi Cavalli-Sforza, who heard the study presented last year at a meeting in Barcelona, Spain, says he "was very impressed."

But other scientists note that the genetic diversity in a population isn't just a reflection of when it originated. A small long-standing one outside of Africa could create a similar genetic picture, says Oxford University geneticist John Clegg. Small populations tend to lose genetic diversity, and a series of contractions and subsequent expansions would produce widespread uniformity, he explains. "You can't assume the genetic pattern reflects historical events in these populations," says Alan Templeton, a geneticist at Washington University in St. Louis. Some anthropologists also note that similarities in fossil faces from Asia spanning millions of years support regional continuity.

Tishkoff, however, argues that if separate small populations outside Africa were long-standing, they wouldn't all develop the same kind of genetic uniformity—there would be time for mutation and recombination to increase the Alu deletion diversity. "You just wouldn't expect to see the same pattern in all these populations," she says.

The scientists do agree that a truly complete story of human origins—and a test of whether those origins are recent or ancient—isn't going to happen until many more genetic loci are studied. "Some traits could have a long regional time depth, while others could flow out of Africa," Templeton says. Preliminary data from loci on chromosomes 19 and 11, and 8, Tishkoff says, show patterns similar to that on chromosome 12. Clegg's lab is now tracking mutations on beta-globin genes, which could produce a chapter with yet a different ending. The trick will be to fit all these chapters within the same book.

–Joshua Fischman