

tors" is to an image that sociobiology has created for itself. The field in fact has a good deal of internal housekeeping to do in figuring out what has been solidly established, what are current active research questions, what is speculation, and what is just plain nonsense parading as "science." These questions should be dealt with if the concerns of people who fear resurgence of 19th- and 20th-century "scientific" racism are to be dealt with.

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References

1. P. Kitcher, *Vaulting Ambition: Sociobiology and the Quest for Human Nature* (MIT Press, Cambridge, MA, 1985).



Future Tritium Supply

I hope my editorial of 13 September (p. 1475) and the letters about it (25 Oct., pp. 481-483) will be the beginning of an open discussion of the relative advantages of the options the United States will have in

order to ensure a tritium supply for the future.

An analysis by Richard Garwin (1) shows the following.

According to the Record of Decision in the *Federal Register* 12/12/95, the accelerator production of tritium (APT) approach would have a discounted total life cycle cost of \$5.1 [billion], while the purchase of an existing LWR [light water reactor] would cost \$4.1 [billion] (reduced to \$1.4 [billion] when one includes revenue to the federal government from the sale of electricity), and to "purchase irradiation services" would be \$1.2 [billion] total life cycle cost.

If one assumes that payments for the Russian option would average \$40 [million] per year beginning in the year 2003 (presumably some earlier purchases to exercise the contract, compensated by reduction in later purchases), the program cost discounted to 1996 at 4.9% per year would be about \$0.57 [billion].

These costs are preliminary, but do show that the cost differentials are significant.

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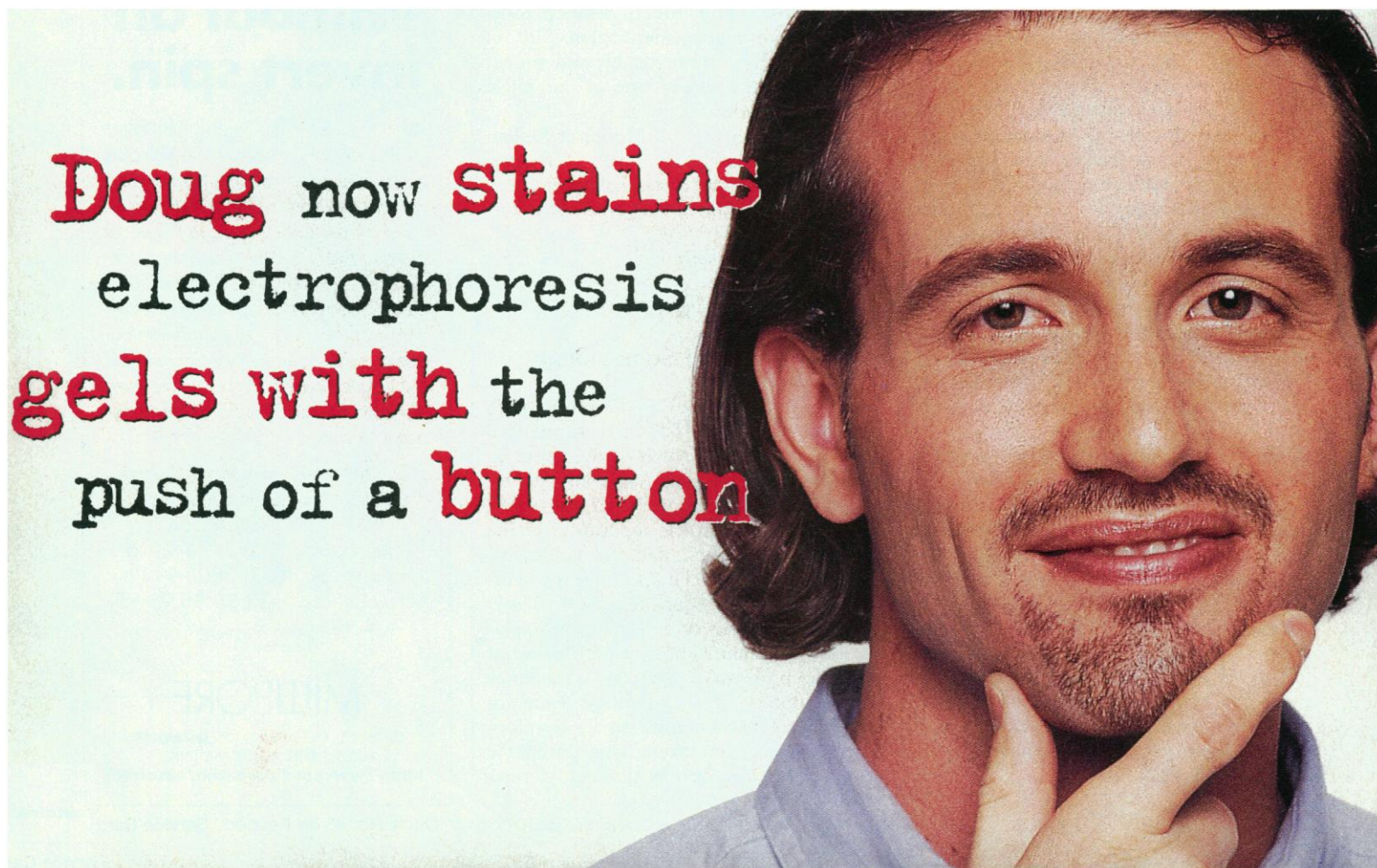
References

1. R. L. Garwin, personal communication (19 September 1996).

Interpretations of Multiregional Evolution

The question of a unique African origin for modern humans, the "Eve" theory, is discussed by S. A. Tishkoff *et al.* in their article "Global patterns of linkage disequilibrium at the CD4 locus and modern human origins" (8 Mar., p. 1380). Tishkoff *et al.* appear to incorrectly interpret the multiregional model, which seems to influence their conclusions.

Multiregional evolution does not predict "roughly equivalent time depth and genetic diversity in all parts of the world," as Tishkoff *et al.* state. For instance, some regions outside of Africa, such as Europe north of the Pyrenees (1), have been inhabited for half the time that others have been inhabited (2). The whole linking of time depth and genetic diversity is wrong because the links are *within* a species composed of internally diversified populations; the pattern of genetic diversity among these populations does not reflect differences in time depth, but rather, differing regional histories of selection, genic exchanges, and demographic variation (3). Multiregional evolution began with the hypothesis that, as the world outside of Africa was first colonized, a pattern of genetic diversity developed that



contrasted greater amounts of genetic variability at the center of the human range with greater, though differing, homogeneities at the sparsely inhabited edges (4, 5). We anticipated (4, 5) that Africa, the original center, was a much more densely occupied region. Therefore, while recognizing that gene flow is always multidirectional, the multiregional model proposed that, for most of human evolution, its expected direction was often asymmetrical, largely outward from the center (6). A corollary of this is the expectation that genetic variation in Africa was always greater than elsewhere because of the larger populations, reduced selection at the species' center, and the ecological variation created by Africa's geographic spread from north to south (7). Variation in the more peripheral human populations reflected small, oscillating, population sizes. Nearly all subsequent genetic analyses, mitochondrial and nuclear, have confirmed these expectations.

Multiregional evolution does not contend that "non-African populations... have been diverging since *Homo erectus* emerged from Africa," as Tishkoff *et al.* state. Such an interpretation ignores the central role of genic exchanges in the model. Genic exchange is not a force preventing internal diversification, and there-

fore of small magnitude, but is part of its cause. Human populations have been constantly merging and dividing in a pattern described as "ethnogenesis" (8). Clearly, the multiregional model does not treat diversity as the result of constantly dividing populations, nor are haplotype histories population histories.

In fact, the distribution pattern reported for the CD4 locus is fully consistent with the multiregional model, if one assumes that the genetic evidence of marked population expansions within the last 100,000 years is correct (9) and that these genetic studies accurately show that beginning African populations were larger than others and began expanding earlier (10). The multiregional model does not deny that there has been gene flow out of Africa; such genic exchanges are considered a continuous and significant process and part of how we understand the way genetic diversity is maintained (4, 5). Multiregional evolution differs from the "Eve" theory and similar theories generally called "out of Africa" in that its validity depends on continued mixture, while the others, in various guises, are replacement theories and cannot be correct if mixture between the emerging Africans and native populations took place (11). Continued

efforts to refute the multiregional evolution model are welcome, but the model tested should be the one proposed.

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References and Notes

1. W. Roebroeks and T. van Kolfschoten, *Antiquity* **68**, 489 (1994).
2. C. C. Swisher III *et al.*, *Science* **263**, 1118 (1994).
3. A. R. Templeton, *Am. Anthropol.* **95**, 51 (1993).
4. A. G. Thorne, in *Proceedings of the 8th Pan African Congress of Prehistory and Quaternary Studies, Nairobi, September 1977*, R. E. Leakey and B. A. Ogot, Eds. (TILMIAP, Nairobi, Kenya, 1981), pp. 180-181.
5. M. H. Wolpoff, Wu Xinzhi, A. G. Thorne, in *The Origins of Modern Humans: A World Survey of the Fossil Evidence*, F. H. Smith and F. Spencer, Eds. (Liss, New York, 1984), pp. 411-483.
6. ———, in *ibid.*, pp. 452-455; M. H. Wolpoff, *Human Evolution* (McGraw-Hill, New York, 1995). The first publications on the multiregional model: cited E. Mayr in *Populations, Species and Evolution* (Belknap, Cambridge, 1970), who discusses this point at length, noting that gene flow is increasingly directional as the peripheries of a species are approached, and R. Sokal, in *Syst. Zool.* **22**, 360 (1973), who observes that marginal populations receive most of their gene flow from more central ones.
7. A. G. Thorne, M. H. Wolpoff, R. B. Eckhardt, *Science* **261**, 1507 (1993); R. B. Eckhardt, M. H. Wolpoff, A. G. Thorne, *ibid.* **262**, 973 (1993).
8. J. H. Moore, *Am. Anthropol.* **96**, 925 (1994).

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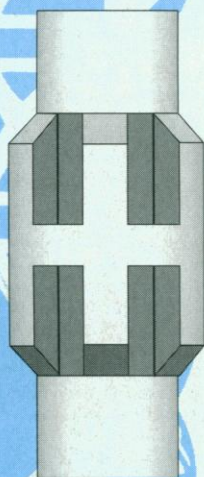
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9. J. H. Relethford and H. C. Harpending, *Cur. Anthropol.* **36**, 667 (1995).
10. J. H. Relethford, *Evol. Anthropol.* **4**, 53 (1995).
11. D. W. Frayer, M. H. Wolpoff, F. H. Smith, A. G. Thorne, G. G. Pope, *Am. Anthropol.* **95**, 14 (1993); D. W. Frayer, M. H. Wolpoff, A. G. Thorne, F. H. Smith, G. G. Pope, *ibid.* **96**, 424 (1994).
12. I thank J. Hawks and J. Relethford for suggestions and insight.

Response: While we may have misrepresented the current incarnation of the multiregional model of recent human evolution, that is primarily because of shifting definitions by its advocates. The multiregional model is a general hypothesis as advocated by Wolpoff. We described the heart of the multiregional model as "a continuous transition among regional populations from *H. erectus* to *H. sapiens* . . . [that] could have been achieved by considerable amounts of gene flow between populations." Wolpoff emphasizes the role of gene flow from Africa, the proposed center of human diversity, outward into the more sparsely inhabited edges. The critical distinction between a "multiregional" model and an "out-of-Africa" model is the relative contribution of the earlier, pre-*H. sapiens* non-African populations to the current populations in Europe and Asia. The "out-of-Africa" model states that all (or nearly all) genes in all modern populations are derived from migration out of Africa by anatomically modern *H. sapiens*. The multiregional model originally postulated that most genes in Asian populations derived from *H. erectus* populations living in the area for more than a million years. Recently, however, the model has become more vague and less quantitative, and allows for considerable contributions of genes recently flowing out of Africa. This current version of the multiregional model is merely a restatement of the assimilation models proposed by Smith *et al.* (1) and Bräuer (2). The crux of the problem is the amount of gene flow. As pointed out by Stoneking (3), complete replacement out of Africa and completely independent origins from previously separated populations are the extremes of a continuum of hypotheses, with the modern African contribution varying from 100% to 0%.

Populations with genetic continuity between modern populations and the *H. erectus* populations in the same regions must have chromosomal regions of "roughly equivalent time depth" and potentially "equivalent diversity," subject to subsequent demographic factors. Simple expansion of such a population into an adjacent unoccupied area, such as northern Europe, is largely irrelevant. The CD4 data argue for 100% replacement, with no indication of any pre-existing haplotypes. While it is true that genetic diversity is a function both of time and of the demographic history of a popula-

tion, the data at CD4 cannot be explained simply by differences in population size between Africans and non-Africans or by a general model of gene flow. One of our key points was that African populations have maintained a larger long-term effective population size than non-African populations, as reflected by their much greater genetic diversity. The shared pattern of haplotype diversity and linkage disequilibrium observed in all non-African populations cannot be explained by "small, oscillating, population sizes" in long-standing non-African populations. It is highly unlikely that small populations spread over large continental areas could have existed for a million or more years and have remained strongly connected by gene flow (4). Moreover, the data at CD4 are inconsistent with large amounts of gene flow out of Africa because we found only a small subset of African haplotypes outside of Africa. In particular, we observed predominantly only one type of Alu(-) chromosome outside of Africa, that with a 90-base pair (bp) STRP allele, whereas across Africa we observed three Alu(-) chromosomes with frequencies greater than 25%—those with 90-bp, 85-bp, or 115-bp STRP alleles. Also, the low frequency of the 90-bp-Alu(-) chromosome in Asia argues against large amounts of gene flow from Europe or the Middle East (which have this chromosome at approximately a 30% frequency) into this region. These data argue strongly against a multiregional model, which emphasizes large amounts of gene flow between globally distributed populations.

Although data from one locus cannot exclude all intermediate hypotheses, when they are combined with data from Y chromosome (5), mitochondrial DNA (mtDNA) (6), and other autosomal loci (7), they do strongly argue that all of the genes in modern humans recently came out of Africa—that is, they argue for complete replacement of older human groups outside of Africa by a single group of anatomically modern humans that recently (about 100,000 years ago) left Africa. Also, theoretical work based on mtDNA data (8) argues strongly against a "partial replacement" model with any level of admixture between the migrating population and archaic populations outside of Africa. These data cannot exclude the possibility of other loci supporting Wolpoff's vague hypothesis, but so far no such loci have been found.

A specific, testable, model needs to be specified. No testable model has been proposed by Wolpoff. "Marked population expansions" are not a sufficient assumption to achieve consistency of our CD4 data with a multiregional model. What fraction of the genes in modern non-Africans must have a

premodern, non-African origin if the multiregional model is true? To date, genetic studies have not shown unequivocal evidence for any alleles in modern populations that are not of recent African origin. Although the distribution of CD4 haplotypes cannot be explained except by a recent single migration out of Africa, they are indeed compatible with Wolpoff's newest version of the multiregional model if one postulates a wave of migration and concomitant gene flow such that all CD4 alleles in preexisting non-African populations have been replaced by the alleles that recently came out of Africa with anatomically modern *H. sapiens*. To us, this is the "out-of-Africa" model.

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References

1. F. H. Smith, A. B. Falsetti, S. M. Donnelly, *Yearb. Phys. Anthropol.* **32**, 35 (1989).
2. G. Bräuer, in *The Human Revolution* (P. Mellars and C. B. Stringer, Eds. (Edinburgh Univ. Press, Edinburgh, UK, 1989), pp. 123–154).

3. M. Stoneking, in *Human Genome Evolution*, M. S. Jackson, G. Dover, T. Strachan, Eds. (Bios Scientific, Oxford, UK, in press).
4. J. H. Relethford, *Evol. Anthropol.* **4**, 53 (1995); A. Rogers and L. Jorde, *Hum. Biol.* **67**, 1 (1995); H. Zischler, H. Geisert, A. von Haeseler, S. Pääbo, *Nature* **378**, 489 (1995); J. H. Relethford and H. C. Harpending, *Am. J. Phys. Anthropol.* **95**, 249 (1994); J. S. Wainscoat *et al.*, *Nature* **319**, 491 (1986).
5. M. F. Hammer, *Nature* **378** (1995); R. L. Dorit, W. Akashi, W. Gilbert, *Science* **268**, 1183 (1995).
6. L. Vigilant, M. Stoneking, H. Harpending, K. Hawkes, A. C. Wilson, *Science* **253**, 1503 (1991); R. L. Cann, M. Stoneking, A. C. Wilson, *Nature* **325**, 31 (1987).
7. J. A. Armour *et al.*, *Nature Genet.* **13**, 154 (1996).
8. E. J. Manderscheid and A. R. Rogers, *Am. J. Phys. Anthropol.* **100**, 1 (1996).

Mona with Cigar?

The cartoon by Kazuko Ashizawa (4 Oct., p. 43) illustrating the contents and introduction to "Science in Japan: Competition on campus" is a close adaptation (without credit) of the theme and general form of one of the most dynamic woodblock prints of the great Japanese *ukiyo-e* artist Toshusai Sharaku. The print shows the actors Otani Oniji II and Ichikawa Omezo in the kabuki drama "Nihon-matsu Michinoku-sodachi" ("The Countryman from Nihonmatsu in the North") performed in August 1794.

Sharaku is the ephemeral mystery man of Japanese art history about whom little is known. His work was produced in a 10-month period around 1795, after which he disappeared suddenly (1). The cartoon is analogous to Leonardo da Vinci's "Mona Lisa" depicted smoking a cigar.

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References

1. R. Lane, *Images from the Floating World: The Japanese Print* (Tabard, New York, 1978), pp. 122–127.

Letters to the Editor

Letters may be submitted by e-mail (at science_letters@aaa.org), fax (202-789-4669), or regular mail (*Science*, 1200 New York Avenue, NW, Washington, DC 20005, USA). Letters are not routinely acknowledged. Full addresses, signatures, and daytime phone numbers should be included. Letters should be brief (300 words or less) and may be edited for reasons of clarity or space. They may appear in print and/or on the World Wide Web. Letter writers are not consulted before publication.

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Poster Session Topics 5:30–6:30 p.m.

Neurotrophins and Growth Factors

- Evaluating growth factors in the Cytosensor System (NGF, EGF, TGF- α , GM-CSF)
- CNTF directly activates metabolic rate increases in SH-SY5Y cells
- BDNF signal transduction activation of the truncated trkB isoform, trkB.T1

G-protein Coupled Receptors

- Evaluating β -adrenergic, D_1 – D_4 dopaminergic, and M_1 – M_2 muscarinic receptors

Agonist and Antagonist Profiling

- Use of a single assay system to assess functional coupling of a variety of receptors for agonist and antagonist profiling

Ligand-gated Ion Channels

- Glutamate receptors: direct measurement of neurotransmitter activation of cellular metabolism in cultured hippocampal neurons
- Nicotinic receptors: Long-term exposure of TE671 cells to PMA induces a change in metabolic and calcium responses to nAChR activation.

Signal Transduction Elucidation

- Evaluating signal transduction pathways and other metabolic processes using the Cytosensor System

Immune Factors

- Characterization of the functional activity of CC and CXC human chemokine receptors: functional activity of a novel chemokine receptor, CC-CKR5, identified using microphysiometry.
- Stimulating peripheral blood T cells with anti-CD3 and anti-CD28 results in sustained increases in extracellular acidification rate

Scientific Talks 6:30–7:30 p.m.

Structural Determinants of Cholecystokinin Receptors for Interregulation and Desensitization.

Stephen Wank, M.D.

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Use of the Cytosensor Microphysiometer System for *In Vitro* Toxicology

Drs. Mohyee and Amira Eldefrawi

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