involved in the primary events of breast carcinogenesis, although only in a minor subset of sporadic breast cancers.

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A View of the Neolithic Demic Diffusion in Europe through Two Y Chromosome–Specific Markers

To the Editor:

The farmer economy originated in different places of the world. One of the most important (probably the first) is in the Middle East, in the so-called Fertile Crescent, from which farming spread toward Europe, North Africa, Arabia, East Africa, and southwestern Asia (Indus valley) (Cavalli-Sforza et al. 1994).

Two models, the cultural and the demic, were proposed to explain the neolithic expansion of the early farming to Europe. According to the first, this expansion might have occurred by transmission of new technologies without movements of farmers and then without changes in the genetic makeup of the preexisting populations. According to the second, the spread of the farming economy might have occurred through the migration of farmers who progressively admixed with local paleolithic hunter-gatherers. As a direct consequence, a change of allele frequencies should have taken place for those genes that differentiated the old inhabitants from the newcomers. The model of demic diffusion, called "the wave of advance" by Ammerman and Cavalli-Sforza (1984), is the most accepted, at least for Europe, where it is also supported by archaeological records (Menozzi et al. 1978). It implies clines of the farmers' gene frequencies, which decrease with increasing distance from the area of origin.

By performing principal components analysis on numerous classical markers, synthetic maps were constructed for Europe and the Near East (Menozzi et al. 1978), which show the Near East as the center of concentric clines of decreasing gene frequencies and give value to the theory of demic spread of agriculture.

Further support to this theory is given by a large population survey we carried out on some Y-specific polymorphisms. Two markers have been found, the distribution of which illustrate well the process of "wave of advance."

We studied the *Taq*I Y-specific RFLPs detected by p12f2 (DYS11) and 49a,f (DYS1) probes in ~3,000 subjects of different populations, mainly from Europe (particularly from the Mediterranean basin) but also from Africa and Asia.

Table 1

Frequencies of the *Taq*I, p12f2-8-kb Allele and 49a,f-Ht 15 in Different Populations

	p12f2-8-kb ALLELE			49a,f-Ht 15		
POPULATION[a]	No.	%	Reference	No.	%	Reference
Turkish	194	33.0	a	208	1.4	a
Lebanese	87	43.7	b	88	0	b
Sephardi Jewish	80	40.0	b	251	2.4	b, o
Ashkenazi Jewish	124	41.1	b, c	277	7.2	b, c, o
Other Jewish communities	247	32.0	c	220	.9	c
Egyptian		nt		34	0	p
Tunisian	91	34.1	a	85	2.3	a
Algerian	92	28.3	a, d	58	3.4	a
Greek	154	27.3	a, e	90	3.3	a
Albanian	72	20.8	a	56	0	a
Southern Italian:						
Apulian	119	29.4	a	89	15.7	a
Calabrian	53	18.9	a	91	17.6	a
Sicilian	114	23.7	a, f	84	13.1	a
Other southern Italian	21	42.9	g		nt	
Central Italian	103	14.6	a	112	37.5	a
Northern Italian	69	17.4	h	171	28.1	q, r
Continental Italian		nt		20	25.0	p
Northcentral Italian	46	8.7	g		nt	
Sardinian	253	13.0	a, i	263	13.7	a, s
Spanish		nt		85	41.2	o
Andalusian	35	8.6	a	35	31.4	a
Catalan	30	3.3	l	28	35.7	l
Spanish Basque	44	0	l	52	53.8	l
French Basque	46	13.0	l	44	63.6	l
Bearnais[b]	25	8.0	l	25	56.0	l
French	26	3.8	m	196	38.8	r
English		nt		21	23.8	p
Dutch	29	3.5	a	33	51.5	a
Northwestern European		nt		57	49.1	t
Czechoslovak	100	6.0	b	105	11.4	b
Hungarian	48	4.2	a	47	6.4	a
Hindu	62	6.5	a	76	0	a
South African Indian		nt		63	0	t
Other Indian		nt		99	11.1	u
Tharus	71	14.1	a	96	0	a
Ethiopian	59	25.4	n	69	0	n

NOTE.—a = A. S. Santachiara-Benerecetti, unpublished data; b = Santachiara-Benerecetti et al. (1993); c = Ritte et al. (1993); d = 32 samples from Casanova et al. (1985); e = 62 samples from Mitchell et al. (1993); f = 27 samples from Mitchell et al. (1993); g = Mitchell et al. (1993); h = Brega et al. (1987); i = 34 samples from Casanova et al. (1985) and 115 samples from Brega et al. (1987); l = O. Semino, J. Bertanpetit, A. Cambon-Thomases, M. Fellows, and A. S. Santachiara-Benerecetti, unpublished data; m = Casanova et al. (1985); n = G. Passarino, O. Semino, and A. S. Santachiara-Benerecetti, unpublished data; o = Lucotte et al. (1993); p = Persichetti et al. (1992); q = Torroni et al. (1990); r = Lucotte and David (1992); s = 48 samples from Persichetti et al. (1992); t = Spurdle and Jenkins (1992); and u = Lucotte et al. (1990). nt = not tested.

[a] When more sets of data exist for a population, and they do not significantly differ from each other, they are pooled.

[b] French population closely related to the Basques.

The p12f2/*Taq*I RFLP is an insertion/deletion polymorphism with two allelic fragments of 8 and 10 kb (Casanova et al. 1985). The 8-kb allele was not found in African Blacks (Casanova et al. 1985; Brega et al. 1987; Excoffier et al., in press), in Orientals (Liu et al. 1994), and in Native Americans (Torroni et al. 1994). It appears therefore to be a Caucasoid allele.

The 49a,f/*Taq*I RFLP consists of numerous polymorphic bands: at least eight can be present, absent, or dif-

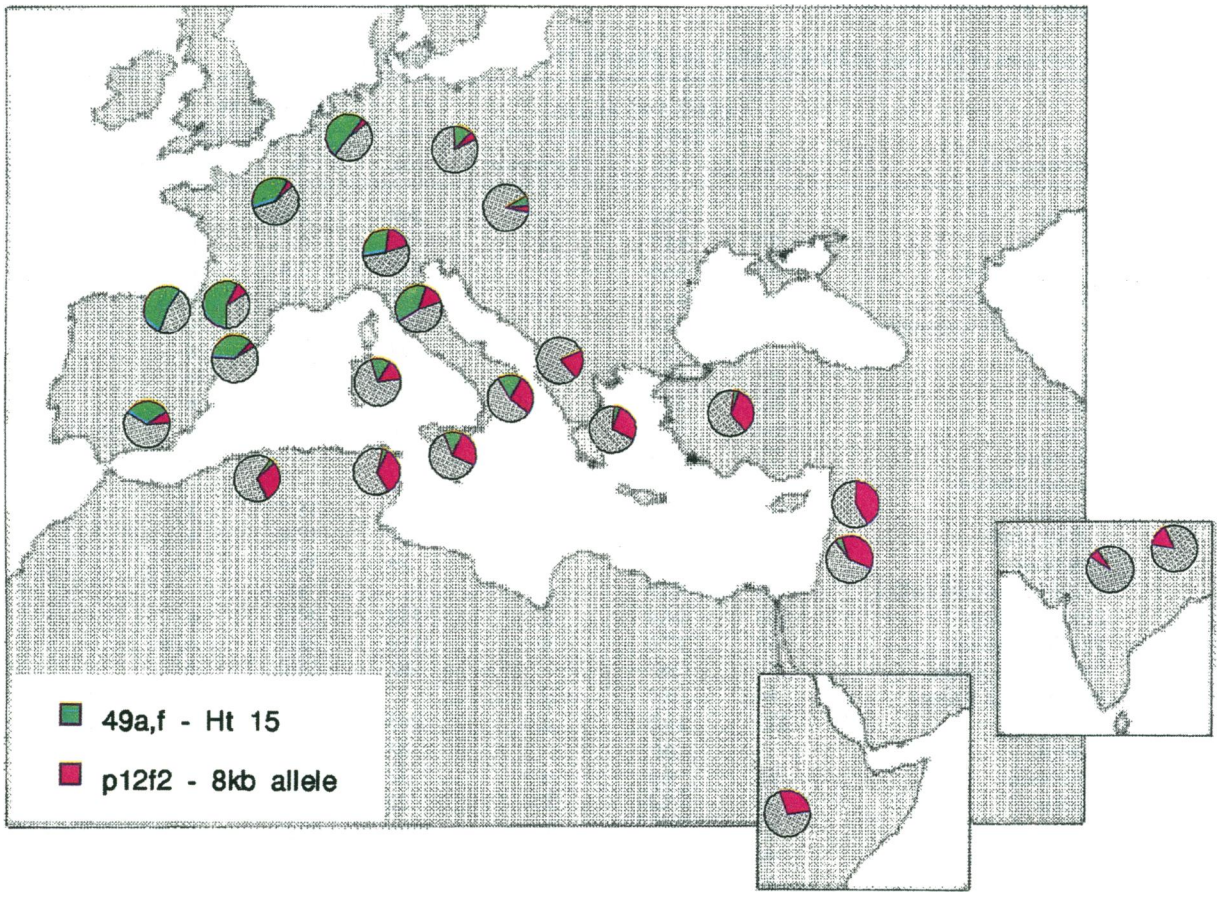

Figure 1 Frequency distribution of the Y chromosomes carrying the p12f2-8-kb allele (purple area) and the 49a,f-Ht 15 (green area) in the populations examined for both systems (see table 1). Calabrians and Apulians have been pooled as southern Italians; Bearnais and French Basques, living in the same area and showing similar frequencies, have also been pooled.

fering in size and represent distinct loci (Ngo et al. 1986). From the combination of these polymorphic bands many haplotypes (Ht) are defined, some of which turned out, either qualitatively or quantitatively, to be population specific (Breuil et al. 1987; Torroni et al. 1990, 1994; Persichetti et al. 1992; Spurdle and Jenkins 1992; Santachiara et al. 1993). Of particular interest in the present context is Ht 15, which is a European haplotype, since it has been found outside Europe only in populations that have had contacts with Europeans (Lucotte et al. 1990; Spurdle and Jenkins 1992; Spurdle et al. 1994; Torroni et al. 1994).

In table 1 are reported the frequencies of the p12f2-8-kb allele and of the 49a,f-Ht 15 for many Caucasoid populations, for Tharus (Nepal) and Ethiopians. Figure 1 is a map showing the frequencies for those populations in which both markers were analyzed.

A cline of decreasing frequencies from the Near East to northwestern Europe, with its maximum value in the Lebanese (44%) and in Jews (41%), is displayed by the 8-kb allele. This makes the 8-kb allele an indicator of the neolithic demic diffusion of the farming culture in Europe. It is worth noticing that, outside Europe, this allele was only found in areas where migrations from the Near East took place, (Tunisia and Algeria for the Phoenician migration, India for the Indo-European, and Ethiopia for that of Geeze speakers) (Renfrew 1989; Cavalli-Sforza et al. 1994).

On the other hand, the 49a,f/*Taq*I-Ht 15, which is only sporadically found outside Europe, shows a gradient of frequencies opposite in direction to that of the 8-kb allele, having its maximum value in northwestern Europeans. The geographic distribution of this haplotype is quite similar to the first sinthetic map for Europe, which, according to Cavalli-Sforza et al. (1994), is that of the preneolithic European gene pool. It is intriguing that its highest frequency (60%) was observed among Basques (Santachiara-Benerecetti et al. 1994), a very ancient European population that has been in the present place for a long time, evading contact with neolithic and subsequent migrations (Aranzadi 1889; Bosch-Gimpera 1943; Cavalli-Sforza 1988; Piazza 1988; Bertranpetit

and Cavalli Sforza 1991). The 49a,f-Ht 15 can therefore be considered a proto-European haplotype, which was diluted by the gradual mixing with the neolithic newcomers. It is worth noticing that in ~300 observations of Ht 15 we have never found this haplotype on Y chromosomes carrying the p12f2-8-kb allele.

In conclusion, this study has revealed two distinct Y-chromosome markers, the p12f2-8-kb allele, specific to Caucasoids and the 49a,f-Ht 15, specific to Europeans, which are valuable to detect genetic admixtures. They show an opposite gradient of frequencies from the Near East to western Europe, illustrating well the "wave of advance" of the neolithic demic expansion in Europe. Moreover, the haploid condition of the Y chromosome, and therefore the absence of recombination, makes the proto-European Ht 15 an important tool in evaluating the contribution of European paleolithic males in the present day populations of Europe.

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Questioning the Need for Anonymous Genetic Counseling and Testing

To the Editor:

In their recent article, "The Need for Anonymous Genetic Counseling and Testing," Mehlman et al. (1996) propose that patients at risk for nontreatable, delayed-onset diseases for which an accurate single-gene test is available should have the option of proceeding with counseling and testing anonymously. We have significant concerns about their proposal for implementation of anonymous genetic testing and its implications for genetic counseling.

Mehlman et al. (1996) predict that with the availability of anonymous testing a greater number of patients would seek testing, since the confidentiality of their results would be solidly protected from insurers, employers, family members, and other interested third parties. As evidence of the need for anonymous testing, they cite the fact that, at their center, anonymous testing for Huntington disease (HD) is requested by one in five patients. To maintain anonymity, the authors suggest that medical records the patient provides for counseling purposes be copied with the identifying information removed, that the patient be assigned a coded number that would not reveal personal information, and that the patient consider renting a post-office box under a pseudonym to facilitate future contact with the genetics staff when new treatments or pertinent information about their disease needs to be communicated.

At our weekly adult genetics clinic, we counsel patients at risk for HD, hereditary cancer syndromes, and other adult-onset neurological conditions for which genetic testing may or may not be available. Since 1994, when direct testing for HD became clinically feasible, we have seen 71 at-risk patients, 37 (52%) of whom have already completed the presymptomatic testing protocol and had genetic testing for this condition.

Mehlman et al. (1996) reported that 20% of their patients seeking presymptomatic testing for HD had inquired about anonymous testing, but the authors did not provide their sample size. Only 3 (4%) of the 71 patients we have seen, to date, have inquired about anonymous testing, which is significantly less than the 20% cited by Mehlman et al. (1996). Our lower numbers may reflect the fact that we do not currently offer anonymous testing as an option. In order to establish whether the availability of anonymous testing would have made a difference in the decision to be tested, it will be important to survey at-risk individuals who did not proceed with presymptomatic testing, to formally assess why they chose not to be tested and ascertain their thoughts about anonymous testing. However, it should be noted that at-risk individuals often have personal reasons rather than insurance concerns that predominantly figure into their decision not to be tested, which will not be solved by anonymous testing.

In a study by Quaid and Morris (1993), 66 individuals at 50% risk for HD completed a mailed questionnaire that asked them to rate a list of 17 reasons why an at-risk individual might decline genetic testing for HD by using a seven-point Likert-type scale where 1 is "extremely unimportant" and 7 is "extremely important." The five most important reasons individuals cited for not proceeding with presymptomatic testing were (1) increased risk to children if the individual tested positive (mean = 5.29), (2) lack of a cure (mean = 4.92), (3) potential loss of health insurance (mean = 4.29), (4) no plans for having more children (mean = 4.15), and (5) financial costs of genetic testing (mean = 4.09).

In proposing anonymous genetic testing, Mehlman et al. (1996) cite the success with anonymous HIV testing. While Mehlman et al. (1996) acknowledge the limitations in comparing HIV testing with genetic testing, they fail to mention that a large part of the stigmatization surrounding knowledge of HIV status likely stems from