remarkable, as is the analogy to cystic fibrosis (CF), a recessive disease. We certainly have no such evidence for carrier advantage, and indeed have evidence for significant selection against affected carriers. Selection dynamics against CF are regulated through the affected homozygote, rather than the rare heterozygote with congential absence of the vas deferus. Further, heterozygote advantage for CF is far from clear[19], and the cholera hypothesis unconfirmed[20]; nor does the geographic distribution of CF mimic that of cholera.

The Ashkenazim are subject to at least a dozen genetic diseases at high frequency that are uniqueto this population; none of these mutations is common among the non-Jews living in proximity to Jews. While heterozygote advantage poses many difficulties in explaining this distribution, founder effect of recent mutations in a rapidly expanding population from a limited number of founders offers a simple, parsimonious solution.

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A major founder Y-chromosome haplotype in Amerindians

Sir — The original peopling of the Americas remains shrouded in mystery. Two facts appear settled: (i) migration occurred from Asia through a land bridge in Behringia[1] and (ii) the first peopling occurred sometime in the Pleistocene[1,2]. The nature of the ancestral populations and the number and timing of the migrations are matters of considerable dispute[3–7]. We have decided to approach this problem with the use of Y-chromosome polymorphisms which, because of haploidy and lack of recombination, establish long-lasting patrilineages, remaining unaltered from generation to generation until a mutation supervenes. Our study of 12 widely different Amerindian populations from South and Central America shows the existence of a major, perhaps single, Y-chromosome founder haplotype. This has obvious implications for the identification of the ancestral Asian populations.

We haplotyped Y-chromosomes with two different PCR-based DNA polymorphisms. The first was the tetranucleotide microsatellite, *DYS19* (*Y-27H39*) which has five common alleles (A to E) and a gene diversity of 0.66 in Caucasians[8]. The other was based on sequence variation in alphoid repeats located in the Y centromeric region, typed by heteroduplex analysis[9]. There are 23 different alphoid haplotypes (αh), numbered from I to XXIII, which together with *DYS19* enable us to distinguish at least 37 different Y-chromosome haplotypes worldwide (Table 1).

Table 2 summarizes our data with 12 different Amerindian populations of diverse geographical origins (ranging from Argentina to Mexico) and from several linguistic groups. The haplotype IIA (combination of αhII and *DYS19* allele A) was seen in 74% of the individuals. By excluding the Mapuches, with the highest level of miscegenation, the frequency of the IIA haplotype rises to 0.91. Our data are supported by studies in Yanomamis, where 10 out of 11 males had the *DYS19* A allele[10]. Haplotype IIA thus apparently identifies the predominant, and perhaps single, founder Y-chromosome in Amerindians.

Why should such low variability occur in Amerindian Y chromosomes while much higher polymorphism is seen in mtDNA (Table 2)[5–7]? The population dynamics of matrilineages

Table 1 Y-chromosome haplotypes in three distinct populations

Haplotype	Populations Number and (frequency)		
	Brazilian[a] Caucasians 100	African[b] Pygmies 17	Mongolians[c] 46
I A	2 (0.02)		1 (0.02)
I B			2 (0.04)
I C	2 (0.02)		
I D	1 (0.01)		
I E	1 (0.01)		
II A	10 (0.10)		
II B	38 (0.38)		2 (0.04)
II C	8 (0.08)		2 (0.04)
II D	1 (0.01)		1 (0.02)
II F			2 (0.04)
III A		1 (0.06)	
III B	6 (0.06)		3 (0.07)
III C	5 (0.05)	1 (0.06)	
III D	2 (0.02)	2 (0.12)	1 (0.02)
III E		1 (0.06)	2 (0.04)
IV C	7 (0.07)		1 (0.02)
IV D	2 (0.02)		
V A	2 (0.02)		
V B	2 (0.02)	1 (0.02)	
V C	2 (0.02)	1 (0.02)	
IX C	1 (0.06)		
IX D	1 (0.01)	4 (0.23)	
IX E		4 (0.23)	
XII A	1 (0.01)		
XIV B	1 (0.01)		
XV A	2 (0.02)		
XVI A	2 (0.02)		
XVI B	1 (0.01)		
XVII B	1 (0.01)		
XVIII B		1 (0.02)	
XVIII C			9 (0.20)
XVIII D			10 (0.22)
XIX B			1 (0.02)
XX B			6 (0.13)
XXI B		1 (0.06)	
XXII A		1 (0.06)	
XXIII D		1 (0.06)	

[a]This random sample has been described elsewhere[8]. [b]Gift from L.L. Cavalli-Sforza from the Department of Genetics, Stanford University. [c]Mongolian individuals were from the following ethnic groups: Khalkha (40), Buryad (4), Darigamga (1) and Durved (1).

(mtDNA) and patrilineages (Y chromosomes) differs. Probably among the early settlers of America, gender-specific activities such as hunting and fighting caused higher mortality in men, leading to a smaller effective number of males than females. Moreover, presumably some males, such as the headman, contributed disproportionately to the Y-chromosome pool due to polygyny. These factors could combine to promote low levels of patrilineage variability with higher levels of matrilineage diversity.

We have hitherto analysed 46 individuals from Mongolia and although we found 17 different Y-chromosome haplotypes, we did not see any case of haplotype IIA (Table 1). This is in agreement with the observations of Gomolka *et al.*[11] who studied *DYS19* in 215 Asians from eight populations and found only one instance of the A allele. Together, these data suggest that the IIA haplotype is not prevalent in Asia. Thus, the finding of Y-chromosome haplotype IIA in a given Asian population should select it as an Amerindian ancestor candidate.

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Acknowledgements
This work was funded by CABBIO, by CNPq and FINEP of Brazil, by CONICET, CIC and Antorchas Foundation of Argentina and by FONDECYT (Project # 1931028) of Chile. Correspondence should be addressed to S.D.J.P.

Table 2 Y-chromosome haplotypes in Amerindian populations

Amerindian population	Country of origin	Linguistic group	Number of individuals studied	Estimated admixture[a]	Number of different mitochondrial haplotypes in sample[b]	Number and proportion of the IIA Y haplotype in sample[c]
Mapuche[d]	Argentina	Mapudugun	20	<12%	8	8 (40%)
Wichi[d]	Argentina	Mataco/Mataguayo	27	<3%	4	24 (89%)
Chorote[d]	Argentina	Mataco/Mataguayo	6	<3%	4	6 (100%)
Chulupi[d]	Argentina	Mataco/Mataguayo	1	<3%	1	1 (100%)
Toba[d]	Argentina	Huaycurú	6	<3%	2	5 (83%)
Huilliche[e]	Chile	Mapudugun	3	<5%	2	0 (0%)
Atacameño[e]	Chile	Kunza	1	<3%	1	1 (100%)
Surui[f]	Brazil	Tupi	3	Not done	Not done	3 (100%)
Karitiana[f]	Brazil	Tupi	2	Not done	Not done	2 (100%)
Quechua[f]	Peru	Quechua	1	Not done	Not done	1 (100%)
Auca[f]	Equador	Huaorani	1	Not done	Not done	1 (100%)
Maia[f]	Mexico	Yucatec	2	Not done	Not done	2 (100%)
Total			73		10	54 (74%)

[a]Caucasian gene admixture was calculated through the ADMIX program[12], using the ABO, Rh, Kell and Lutheran blood groups, with the allele frequencies estimated by the MAXLIK[13] program. The gene admixture in Mapuches was computed using an expanded battery of blood groups that included MNSs, P, Kidd, Duffy and Diego, in addition to the others listed above. [b]Mitochondrial RFLP haplotypes were determined as described[8]. The following ten different haplotypes were found in the sample: A_1, A_2, B, C_1, C_2, D_1, D_2, E_1, E_2, B/D. [c]The other Y chromosome haplotypes seen were, in decreasing order of frequency, IIB (eight individuals), IIIB (3), IIIC (2), XIIA (2), IIC (1), IVC (1), VB (1) and IXE (1). All these haplotypes were seen in Brazilian Caucasians or Africans (Table 1) and thus their presence could conceivably be explained by admixture. Haplotype IIB, but not the other ones, can also arise by a single mutation from haplotype IIA. [d]Samples collected by Dr. F.R. Carnese. [e]Samples collected by Dr. F. Rothhammer. [f]Samples from the Human Mutant Cell Repository (Camden, NJ).