ments, currently in progress, will determine whether deletions of the ELN gene are consistently involved in this disease.

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Cystic Fibrosis Carrier Screening in Hispanics

To the Editor:

A recent paper in the *Journal* discussed cystic fibrosis (CF) mutations in Hispanic individuals (Grebe et al. 1994). It is our contention that the "Hispanic" designation is of limited value in genetic analyses, such as those involved in CF-carrier risk assessment. In calculating CF-carrier risk in persons with no family history of the disease, race and ethnic origins are usually considered, because the incidence of CF and the frequencies of individual CF mutations vary between races and ethnic populations. However, "Hispanic" refers neither to a race nor to a defined ethnic subgroup. Rather, it is a geographic label, referring to persons who come from Latin America.

Latin America, in turn, includes >44 governmental entities in the Caribbean and Central and South America, and >400 million people. The region is populated by descendants of European settlers, native peoples, and Blacks, as well as by admixtures of the different races, with significant differences between the proportions of each subgroup in each country (table 1).

We have studied 24 CF affecteds whose families come from Latin America (table 2). For 22, the countries of origin of the parents/grandparents were known. Two patients were lost to follow-up; the specific countries of origin are unknown, but as Latin Americans, their mutations can be included in our tabulation.

We screened each patient with a panel specific for 15 CF mutations (R117H, 621+1, R334W, deltaI-507, deltaF-508, 1717-1G>A, G542X, G551D, G551S, R553X, R560T, R1162, W1282X, N1303K, and 3849+10kbC>T).

When the 24 Latin American CF affecteds are subdivided into their countries of origin, eight countries are specified, reflecting the heterogeneity in countries of origin possible in any Hispanic series (table 2). There are significant differences between the rates of CF-mutation identification in affecteds from individual countries: the highest rates are in countries in which the European contribution to the gene pool is presumed to be the highest, and the lowest are in countries where native peoples and mestizos predominate (tables 1 and 2).

Table 1

Demographics of Selected Latin American Countries

Country	Percent Descending from Population					
	European	Native	Black	Mestizo[a]	Mulatto[b]	Reference[c]
Dominican Republic	15	0	15	0	70	1
Puerto Rico	>95[d]	0	0	0	0	2
Jamaica	3	2	76	4[e]	15	3
Mexico	16	29	0	55	0	4
Costa Rica	96	1	3	0	0	3
Panama	10	6	14	70	0	3
Colombia	20	2	4	60	14	2
Venezuala	21	2	10	67	0	3
Bolivia	15	55	0	30	0	3
Ecuador	10	40	10	40[f]	...	1
Argentina	85	0	0	15	0	1

[a] Racial mix of European and native.
[b] Racial mix of European and Black.
[c] 1 = Banks (1993); 2 = national census data (supplied by UN missions); 3 = Universal Almanac (1994); and 4 = Hunter (1993).
[d] Census data: most Puerto Ricans claim European descent; no breakdown given as to black or mixed races; no native population.
[e] East Asian.
[f] Mix: predominantly Mestizo; small percent Mulatto.

Our results are different from those reported by Grebe et al. (1994; summarized in table 3) and are instructive because of that. In our series, of the total of 48 CF chromosomes from Latin Americans, 32 (67%) are defined with regard to responsible mutations. Of this total, 23 (48%) are mutation deltaF-508 (tables 2 and 3). Grebe et al. identified only 58% of total mutations in their series, using a 22-mutation panel. They attribute this low rate to the introduction of novel CF mutations of Native American origin.

However, Grebe et al. appear to overlook the contribution of Blacks to the total Hispanic population. Though the authors do not report the racial or race-mixture breakdown of their patient sample, Blacks and mulattos constitute a significant population fraction of many Latin American countries; the incidence of CF is higher in Blacks than in Asians (from whom Amerindians are derived) (Wright and Morton 1968; Kulczycki and Schauf 1974; Cann 1994); and the mutation panel Grebe et al. used will detect $\leq$50% of total CF mutations in Blacks (Cutting et al. 1992). It is, therefore, likely that the undefined mutations in the Grebe series not of Caucasian origin are largely derived from the Black African gene pool.

Our results can also be compared with several published series of CF in southern Europeans (Gasparini et al. 1991, 1993; Nunes et al. 1991) (table 3). Our data are consistent with southern Europeans as the major source of CF mutations in Latin America. The mutation detection rate (67%) and the contribution of deltaF-508 to this total (48% of all mutations) are similar to values reported for southern Europe but different from values for the rest of Europe or the world. We also identified mutations N1303K and R334W on three chromosomes each, in our affecteds; both mutations have been reported more frequently in southern Europeans than in the rest of Europe or the world. (The failure of Grebe et al. to find N1303K in their series led them to propose that the absence of this mutation distinguishes CF in Hispanics from southern Europeans; however, we found the mutation in our series at a frequency consistent with southern European studies.)

If it is accepted that the CF mutations in Latin America are predominantly of southern European origin, then any mutation panel one would use in screening persons from Latin America would include the most common mutations listed in table 3. With these mutations in the screen, one would only expect to detect ~70% of all mutations, since this is the detection rate currently achieved in southern European surveys. The remaining 30% of CF mutations in affecteds from this region (southern Europe) are presently undefined.

Thus, in calculating CF-carrier frequency for any individual from Latin America, one would optimally take into account that person's racial and ethnic background and the demographics of his or her country of origin. In Mexico, for example, 16% of the population is of European ancestry, and 55% are of mixed native-European descent (table 1). Under the assumption of an equal contribution of each race to any mixed-race individual, the proportion of total Mexican chromosomes that might be of European origin is ~44%. A CF-carrier frequency of 1 in 25 in southern Europe and the fact that any contribution to the CF-mutation pool by the

Table 2

CF Mutations Defined as to Country of Origin

Family	Country of Origin[a]								
	Dominican Republic (9/11; 92%)	Puerto Rico (7/9; 77%)	Cuba (0/1; 0%)	Mexico (3/6; 50%)	Colombia (3/5; 60%)	Ecuador (4/9; 44%)	Peru (1/1; 100%)	Chile (1/1; 100%)	NS[b] (3/4; 75%)
1	508/508								
2	508/508								
3	508/508								
4	508/508[c]								
5	508/unk								
6	508/unk								
7		508/334							
8		508/1303							
9		508/unk							
10		508/unk							
11		508[d]	unk[d]						
12				508/508					
13				542/unk					
14				unk/unk					
15					508/1303				
16					508/unk				
17						508/334			
18						551/unk			
19					unk[e]	508			
20						unk/unk			
21						unk/unk			
22							508[f]	508[f]	
23									553/1303
24									334/unk

NOTE.—unk = undefined mutation.

[a] Data following country of origin are proportion and percent of chromosomes defined as to responsible mutations. The overall total was 32/48 (67%).

[b] NS = not specified as to Latin American country of origin.

[c] Child of Dominican Republic/Colombian parent; excluded from Dominican Republic total but included in overall total.

[d] Child of Puerto Rican/Cuban couple.

[e] Child of Colombian/Ecuadoran couple.

[f] Child of Peruvian/Chilean couple.

Table 3

Mutations in Selected Populations

Series	Total No. of Chromosomes	Percent of Total and (No. of Chromosomes) for Mutation[a]								
		508	542	551	553	334	1303	1282	3849	1162
Present study[b]	48	48 (23)	~2 (1)	~2 (1)	~2 (1)	~6 (3)	~6 (3)	0	0	0
Series (a)[c]	129	46 (59)	5.4 (7)	0	.8 (1)	1.6 (2)	0	.8 (1)	2 (3)	1.6 (2)
Series (b)[d]	597[e]	50	6	.25	.1	.5	3.24	.5	nd	3.6
Worldwide (a)[f]		67	3.4	2.4	1.3	<1	<1	2.1	?	<1

[a] nd = not tested; ? = no value given.

[b] Our series; mutations defined in 67% of all Latin American CF chromosomes.

[c] Grebe et al. (1994); mutations defined in 58% of all Latin American CF chromosomes.

[d] Nunes et al. (1991); mutations defined in 64% of all southern European CF chromosomes (from Spain, Italy, Greece, etc.).

[e] Different numbers of chromosomes (from 123 to 597) tested for each mutation.

[f] From series (a); mutations defined in 85% of all CF chromosomes worldwide (using a 22-mutation panel).

native population or Blacks will be negligible lead us to estimate a CF-carrier frequency of ~1 in 56 in Mexico overall.

Similar calculations of CF-carrier frequency can be made for each country for which population data are available, on the basis of the proportion of European chromosomes contributing to the population total. Confirmation that these estimates are correct can only come after population screening to determine CF-carrier frequencies has been carried out in the individual Latin American countries.

The CF-carrier frequency calculated in this manner would be for a country overall and for persons from that country about whose ancestry not much is known. However, for an individual of European descent who is not a mulatto or mestizo, it may be more accurate to quote a CF-carrier frequency that reflects his or her origins. For a person whose ancestors came from southern Europe to Latin American, then, a CF-carrier frequency of 1 in 25 would be an appropriate estimate.

We conclude that, because of significant differences in the racial composition of each country in Latin America, for the purposes of CF-carrier risk calculation, one should not consider Hispanics as a single category but rather as many distinguishable subpopulations. For any one individual, it is possible to use family history to determine the subpopulation in which he or she best fits—e.g., of Dominican origin versus Dominican of European extraction, or from Ecuador versus Ecuadoran mestizo. One can, then, use the demographic data already available for each country in Latin America to estimate CF-carrier frequency for the subpopulation in question. The more complete the demographic data, the more accurate the estimates of CF-carrier frequency are likely to be. Confirmation of the above hypotheses and suggested approach to calculating CF-carrier risk awaits the results of more extensive screening to detect CF-carriers among those considered Hispanic in the United States.

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