the human genome based on 5,264 microsatellites. Nature 380:152–154
Esposito T, Ciccodicola A, Flagiello L, Matarazzo MR, Migliaccio C, Cifarelli RA, Visone R, et al (1997) Expressed STSs and transcription of human Xq28. Gene 187:185–191
Knöll A, Schunkert H, Reichwald K, Danser AHJ, Bauer D, Platzer M, Stein G, et al (1997) Human renin binding protein: complete genomic sequence and association of an intronic T/C polymorphism with the prorenin levels in males. Hum Mol Genet 6:1527–1534
Laan M, Pääbo S (1997) Demographic history and linkage disequilibrium in human populations. Nat Genet 17: 435–438
Nagaraja R, MacMillan S, Kere J, Jones C, Griffin S, Schmatz M, Terrell J, et al (1997) X chromosome map at 75-kb STS resolution, revealing extremes of recombination and CG content. Genome Res 7:210–222
Nelson DL, Ballabio A, Cremers F, Monaco AP, Schlessinger D (1995) Report on the 6th international workshop on X-chromosome mapping. Cytogenet Cell Genet 71:308–342
Peltonen L, Pekkarinen P, Aaltonen J (1995) Messages from an isolate: lessons from the Finnish gene pool. Biol Chem 376:697–704
Sajantila A, Salem A-H, Savolainen P, Bauer K, Gierig C, Pääbo S (1996) Paternal and maternal DNA lineages reveal a bottleneck in the founding of the Finnish population. Proc Natl Acad Sci USA 93:12035–12039
Schneider S, Kueffer J-M, Roessli D, Excoffier L (1997) ARLEQUIN, version 1.1. Genetics and Biometry Laboratory, University of Geneva, Geneva
Slatkin M (1994) Linkage disequilibrium in growing and stable populations. Genetics 137:331–336
Terwilliger JD, Zöllner S, Laan M, Pääbo S (1998) Mapping genes through the use of linkage disequilibrium generated by genetic drift: "drift mapping" in small populations with no demographic expansion. Hum Hered 48:138–154
von Haeseler A, Sajantila A, Pääbo S (1996) The genetical archaeology of the human genome. Nat Genet 14:135–140
Weir BS (1996) Genetic data analysis II. Sinauer Associates, Sunderland, MA

Address for correspondence and reprints: Dr. Svante Pääbo, Max-Planck-Institute for Evolutionary Anthropology and Institute of Zoology, University of Munich, Luisenstrasse 14, D-80333 Munich, Germany. E-mail: paabo@eva.mpg.de

0002-9297/98/6302-0042$02.00

Am. J. Hum. Genet. 63:656–662, 1998

Evidence for a Common Ethnic Origin of Cystic Fibrosis Mutation 3120+1G→A in Diverse Populations

To the Editor:

Cystic fibrosis (CF) is a common recessive disorder in Caucasians, but little is known about its incidence in other populations (Welsh et al. 1995). In a recent study, however, Macek et al. (1997*b*) described a subset of specific CF transmembrane-conductance regulator (CFTR) gene mutations in African American CF patients. One splicing mutation, 3120+1G→A in intron 16, was particularly frequent and accounted for approximately half the "African" CF chromosomes in the group that Macek et al. studied (Macek et al. 1997*b*). This mutation also has been identified in four native African CF patients, on 5/8 chromosomes (Carles et al. 1996). Furthermore, it has been demonstrated that 3120+1G→A is a predominant CF mutation in the Eastern Oasis population of Saudi Arabia (El-Harith et al. 1997). Finally, three Greek CF families have been reported to harbor this mutation (Tzetis et al. 1997). These observations indicate that CF mutation 3120+1G→A is present in diverse populations from different continents.

To examine whether the 3120+1G→A mutation has a common origin in all these populations or whether its widespread distribution is the result of recurrent mutational events, we analyzed DNA samples obtained from 17 unrelated CF patients in four different populations and from 8 unrelated African CF carriers (fig. 1). In the first cohort, six CF patients were of African American descent, three CF patients originated from Saudi-Arabia, three CF patients were of Greek origin, and five CF patients were native Africans (four families came from South Africa, and one family came from Cameroon). In the second cohort, eight native African individuals who had been identified as mutation carriers in a population-based screening in South Africa (C. Padoa and M. Ramsay, unpublished data) were included here as a confirmatory group. The presence of the 3120+1G→A mutation in these different ethnic groups was confirmed by direct sequencing. We have typed six intra- and six extragenic RF40LP markers that had been useful in previous studies to characterize the origins of numerous other CFTR mutations (Estivill et al. 1987; Dörk et al. 1992, 1994; Ramsay et al. 1993; Sereth et al. 1993; Cuppens et al. 1994; Morral et al. 1996). In addition, we investigated the three highly informative intragenic CFTR microsatellites that are located in intron 8 (IVS8CA) and intron 17b (IVS17bTA and IVS17bCA) of the CFTR gene (Zielenski et al. 1991; Morral and Estivill 1992; Morral et al. 1993).

A common extended 3120+1G→A–associated haplotype could be derived in each of the four study populations (table 1). The phasing of haplotypes was based either on homozygosity or on the analysis of parental samples in all African and Arab CF families, as well as in two African American and two Greek CF families. In the remaining single CF patients, other haplotypes for the 3120+1G→A allele than those deduced in table 1 would be formally possible. Three of the four single African American patients, however, were compound

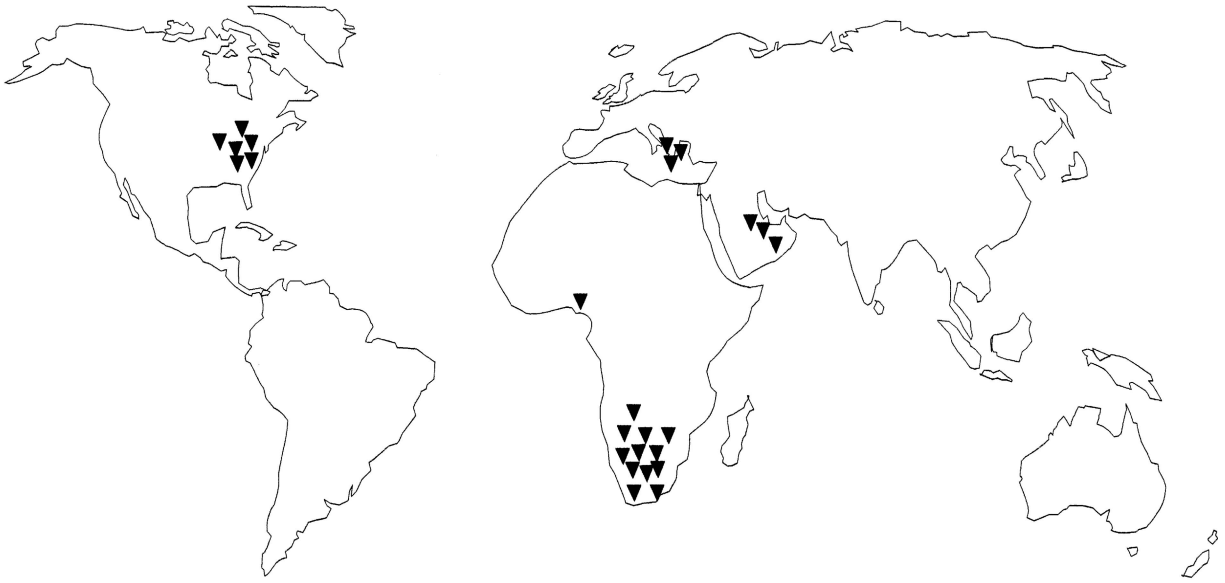

Figure 1 Geographic origins of 3120+1G→A–carrying individuals whose DNA samples were contributed to this study

heterozygotes for 3120+1G→A and for the major CF mutation, ΔF508. The extensively studied ΔF508 mutation has been shown to have a single origin in several investigated populations, with a common dimorphic marker haplotype (Kerem et al. 1989; Dörk et al. 1992; Claustres et al. 1996; Morral et al. 1996) and three major intragenic microsatellite haplotypes—23-31-13, 17-32-13, and 17-31-13—accounting for >85% of ΔF508 chromosomes (Zielenski et al. 1991; Morral et al. 1993, 1994; Claustres et al. 1996; Hughes et al. 1996). Under the assumption that the ΔF508 mutation has occurred only once and has been introduced into the African American population by ethnic admixture, we were able to use the known major ΔF508 haplotypes to deduce the most likely haplotypes for the 3120+1G→A allele in the three additional single African American patients. Within these limitations, all results obtained with the intragenic CFTR markers were consistent with an identical intragenic haplotype for all investigated 3120+1G→A alleles—with the exception of Greek haplotypes, which differed at a single microsatellite locus (IVS8CA) by one repeat unit (16 vs. 17 CA repeats). These two related intragenic haplotypes together account for <15% of non-CF alleles in the general Caucasian population (Morral et al. 1993, 1994, 1996; Russo et al. 1995; Claustres et al. 1996; Hughes et al. 1996), and we have observed these intragenic haplotypes only once in a preliminary study of 12 Arab and 10 African non-CF alleles. Thus, our analysis of intragenic markers indicates that the 3120+1G→A mutation in the four study populations most likely derives from a common ancestor. On the 5′ side, the shared haplotype extends beyond the CFTR gene in all populations, up to a point where a difference is again observed between the Greek and the Arab/African CF alleles—namely, distal to the marker CS.7, which is located >220 kb upstream of the CFTR gene. In previous studies, this region between KM.19 and XV-2c had been found to be prone to recombinations (Estivill et al. 1987; Dörk et al. 1992). On the 3′ side, at the extragenic locus pJ3.ll, which is located some 660 kb downstream of the CFTR gene, haplotypic variability is even seen within the Arab and native African patient groups. The 3120+1G→A chromosomes of the African American patients, however, carried the pJ3.11 *Msp*I allele 1 in every informative case.

The observed identity of extended CFTR haplotypes for the 3120+1G→A alleles in the Arab, African, and African American patients strongly suggests that this mutation has a common origin in these groups. This finding is not surprising in the case of Africans and African Americans, since the latter group has originated mostly from the western African coast and came to North America between the 16th and 19th centuries, which is too recent to allow origination of significant CFTR-mutation haplotype changes restricted to African Americans. It is not quite so simple to explain the presence of the 3120+1G→A mutation in African and Saudi Arab patients. Although recent ethnic admixture accounts for a few percent of Africans in Saudi Arabia, this is very unlikely to explain our findings, since none of the Saudi families had any anthropomorphological signs of an African descent. However, a continuous gene flow between Arab and African populations probably

Table 1

Intra- and Extragenic CFTR Marker Haplotypes of the 3120+1G→A Mutation in Diverse Populations

Group and Mutations	Haplotype[a]														
	MetH (*Msp*I)	XV2c (*Taq*I)	CS.7 (*Hha*I)	KM.19 (*Pst*I)	J44 (*Xba*I)	IVS8CA	TUB9 (*Mnl*I)	M470 (*Hph*I)	T854 (*Ava*II)	TUB15 (*Nsi*I)[b]	IVS17bTA	IVS17bCA	TUB18 (*Hin*fI)	Q1463 (*Tsp*509I)	J3.11 (*Msp*I)
CF families:															
African American:															
Bal236:															
3120+1G→A	1	1	2	2	1	17	(2)	1	2	(2)	7	17	(2)	2	1
ΔF508	1	1	2	2	1	17	(1)	1	1	(1)	31	13	(1)	1	1
Bal719:															
3120+1G→A	1	1	2	2	1	17	2	1	(2)	2	7	17	2	2	1
ΔF508	1	1	2	2	1	17	1	1	(1)	1	32	13	1	1	1
Bal962:															
3120+1G→A	1	(1)	(2)	(2)	(1)	17	2	1	2	(2)	(7)	(17)	(2)	(2)	…
405+3A→C	1	(2)	(1)	(1)	(2)	16	2	1	2	(1)	(31)	(13)	(1)	(1)	…
Bal963:															
3120+1G→A	(1)	1	2	2	1	(17)	(2)	1	(2)	(2)	(7)	(17)	(2)	(2)	…
ΔF508	(2)	1	2	2	1	(23)	(1)	1	(1)	(1)	(31)	(13)	(1)	(1)	…
Bal964:															
3120+1G→A	1	1	2	2	1	17	(2)	1	(2)	(2)	(7)	(17)	(2)	(2)	1
ΔF508	1	1	2	2	1	17	(1)	1	(1)	(1)	(31)	(13)	(1)	(1)	1
Bal965:															
3120+1G→A	1	1	2	2	1	(17)	(2)	1	(2)	(2)	(7)	(17)	(2)	(2)	…
ΔF508	1	1	2	2	1	(23)	(1)	1	(1)	(1)	(31)	(13)	(1)	(1)	…
Saudi Arabian:															
CF10:															
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	2
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	2
CF16:															
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
CF46:															
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1

Greek:															
CF17:															
3120+1G→A	2	2	2	2	1	16	2	1	2	2	7	17	2	2	1
1497delGG	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
CF541:															
3120+1G→A	2	2	(2)	(2)	(1)	16	2	(1)	(2)	(2)	7	(17)	(2)	(2)	1
711+3A→G	1	2	(1)	(1)	(2)	16	2	(2)	(1)	(1)	33	(13)	(1)	(1)	2
CF294:															
3120+1G→A	…	…	(2)	(2)	(1)	16	2	(1)	(2)	(2)	7	(17)	(2)	(2)	…
296+1G→C	…	…	(1)	(1)	(2)	16	2	(2)	(1)	(1)	31	(13)	(1)	(1)	…
Native African:															
IM:															
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
CL:															
3120+1G→A	1	1	2	2	1	17	2	1	2	2	7	17	2	2	1
G1249E	1	1	2	2	1	16	2	1	1	1	22	16	1	1	2
MC1:															
3120+1G→A	…	1	…	…	1	17	…	1	(2)	…	7	17	2	…	…
3196del54	…	1	…	…	1	16	…	1	(1)	…	7	17	2	…	…
MC2:															
3120+1G→A	…	1	…	2	1	17	…	1	(2)	…	7	17	(2)	…	…
2183delAA	…	2	…	2	2	16	…	1	(1)	…	21	16	(1)	…	…
M1115:															
3120+1G→A	1	1	…	2	1	17	…	1	2	2	7	17	2	…	…
ΔF508	1	1	…	2	1	23	…	1	1	1	34	14	1	…	…
African carriers:															
SABL1:															
3120+1G→A	1	…	(2)	(2)	(1)	(17)	2	1	2	(2)	(7)	(17)	(2)	(2)	…
Non-CF	1	…	(1)	(1)	(2)	(16)	2	1	2	(1)	(33)	(13)	(1)	(1)	…
SABL2:															
3120+1G→A	1	…	2	2	1	(17)	2	1	(2)	(2)	(7)	(17)	(2)	(2)	…
Non-CF	1	…	2	2	1	(16)	2	1	(1)	(1)	(34)	(13)	(1)	(1)	…

(*continued*)

Table 1 (continued)

Group and Mutations	Haplotype[a]														
	MetH (*Msp*I)	XV2c (*Taq*I)	CS.7 (*Hha*I)	KM.19 (*Pst*I)	J44 (*Xba*I)	IVS8CA	TUB9 (*Mnl*I)	M470 (*Hph*I)	T854 (*Ava*II)	TUB15 (*Nsi*I)[b]	IVS17bTA	IVS17bCA	TUB18 (*Hin*fI)	Q1463 (*Tsp*509I)	J3.11 (*Msp*I)
SABL3:															
3120+1G→A	1	…	2	2	1	(17)	(2)	1	(2)	(2)	(7)	(17)	(2)	2	…
Non-CF	1	…	2	2	1	(23)	(1)	1	(1)	(1)	(19)	(22)	(1)	2	…
SABL4:															
3120+1G→A	1	1	2	2	1	(17)	(2)	1	2	(2)	(7)	(17)	(2)	2	2
Non-CF	1	1	2	2	1	(19)	(1)	1	2	(1)	(20)	(16)	(1)	2	2
SABL5:															
3120+1G→A	1	…	2	2	1	(17)	(2)	1	(2)	(2)	(7)	(17)	(2)	(2)	1
Non-CF	1	…	2	2	1	(19)	(1)	1	(1)	(1)	(35)	(13)	(1)	(1)	1
SABL6:															
3120+1G→A	1	…	2	2	1	(17)	2	1	(2)	(2)	(7)	(17)	(2)	(2)	…
Non-CF	1	…	2	2	1	(16)	2	1	(1)	(1)	(30)	(13)	(1)	(1)	…
SABL7:															
3120+1G→A	1	…	2	2	(1)	17	(2)	1	(2)	(2)	(7)	(17)	(2)	2	…
Non-CF	1	…	2	2	(2)	17	(1)	1	(1)	(1)	(19)	(19)	(1)	2	…
SABL8:															
3120+1G→A	1	1	2	2	(1)	17	2	1	2	(2)	7	(17)	(2)	(2)	…
Non-CF	1	1	2	2	(2)	17	2	1	2	(1)	7	(18)	(1)	(1)	.....

Note.—Microsatellite analysis was perf40ormed as described (Morral et al. 1993), except that fluorescein-labeled forward primers were used and the products were analyzed on an ALF sequencer (Pharmacia).

[a] Dimorphic markers were typed as described elsewhere (Estivill et al. 1987; Williams et al. 1988; Dörk et al. 1992; Morral et al. 1996). Markers located within the CFTR gene are underlined. Combined haplotypes were constructed from the analysis of homozygous patients (3 Arabs and 1 African) and from the analysis of parental samples (2 African Americans, 2 Greeks, and 4 Africans). The common haplotypes of the 3120+1G→A alleles are within boxes. In those cases in which the phase could not be established on the basis of family analysis, numbers shown in parentheses indicate the most likely haplotypes that have been inferred on the basis of the known haplotypes of the ΔF508 mutation (Dörk et al. 1992; Morral et al. 1994) and with consideration of the strong linkage disequilibrium between single markers (Dörk et al. 1992; Cuppens et al. 1994; Morral et al. 1996).

[b] Nucleotide substitution 3041-92G/A in intron 15, located 173 bp upstream of mutation 3120+1G→A and amplifiable together with the mutation in the same PCR product.

has persisted for many centuries, in association with trading and with the spread of the Islamic religion. Thus far, the Greeks are the only Caucasian population in which the 3120+1G→A mutation has been identified. A recurrent mutational event seems to be unlikely, because the Greek haplotype differs from the others in only two minor respects: there is a difference of one dinucleotide unit at the intragenic IVS8CA repeat, a difference that could result from a single slippage mutation; and the Greek alleles carry a different extragenic Met-XV2c haplotype that probably is due to a single recombination event. Similar events at these two marker loci also account for much of the haplotypic variability associated with the ΔF508 mutation, which has been shown to have a single origin (Morral et al. 1994). Greek and Arab/African haplotypes of the 3120+1G→A mutation thus may have diverged from a common ancestor and then evolved separately in the respective populations. In this context, it is interesting to note that there are other rare mutations shared by Saudi Arabs and Greeks, such as a polyadenylation-signal mutation in the α-globin gene of Saudi and Greek thalassemia patients (Traeger-Synodinos et al. 1993). Historical contacts—for example, under Alexander the Great or during the ancient Minoan civilization—may provide an explanation for the common ancestry of disease mutations in these ethnically diverse populations.

Current theories of a heterozygote advantage for CF carriers of frequent CFTR mutations include increased survival from diarrheal diseases, genetic drift, and hitchhiking (Romeo et al. 1989; Sereth et al. 1993; Gabriel et al. 1994; Macek et al. 1997*a*). The presence of a common ancient CF mutation in African, Saudi Arab, and Greek populations suggests that this mutation too may have been selected. This study demonstrates that the 3120+1G→A mutation shares the same extragenic CS.7-KM.19 "risk" haplotype with the other frequent and ancient CF mutations—ΔF508, N1303K, and G542X (Dörk et al. 1992; Morral et al. 1993)—but that it differs from these latter mutations with respect to intragenic CFTR markers. The extragenic CS.7-KM.19 "risk" haplotype recently has been associated with a selective advantage to the postnatal survival of female carriers without a family history of CF (Macek et al. 1997*a*). In summary, our present analysis provides the first evidence for a common origin of CF among African, Arab, Greek, and African American populations. The shared extra- and intragenic 3120+1G→A–associated haplotype is most easily explained by the assumption of a single origin for this mutation. 3120+1G→A appears to be an ancient mutation that may be more common than previously thought, in populations of the tropical and subtropical belt, where CF probably is an underdiagnosed disorder.

Acknowledgments

Part of this work was supported by an Alexander von Humboldt Foundation grant (to E.-H.A.E.-H.); by IGA MZ CR grants 2899-5, 3526-3, and 4124-3, GA CR grant 301/66/1606; and Barrande grant 970157 (all to M.M.).

Thilo Dörk,[1] El-Harith A. El-Harith,[1,2] Manfred Stuhrmann,[2] Milan Macek, Jr.,[3] Michelle Egan,[4] Garry R. Cutting,[4] Maria Tzetis,[5] Emmanuel Kanavakis,[5] Soukeyna Carles,[6] Mireille Claustres,[6] Carolyn Padoa,[7] Michèle Ramsay,[7] and Jörg Schmidtke[1]

[1]*Institute of Human Genetics, Medical School Hannover, Hannover;* [2]*College of Health Sciences, Dammam, Saudi Arabia;* [3]*Department of Medical Genetics II, University Hospital Prague-Motol, Prague;* [4]*Center for Medical Genetics, Johns Hopkins Hospital, Baltimore;* [5]*First Department of Pediatrics, Athens University, Athens; Laboratoire de Biochimie Genetique, Institut de Biologie, Centre Hospitalier Universitaire, Montpellier, France; and* [7]*Department of Human Genetics, South African Institute for Medical Research and School of Pathology, University of the Witwatersrand, Johannesburg*

References

Carles S, Desgeorges M, Goldman A, Thiart R, Guittard C, Kitazos CA, de Ravel TJL, et al (1996) First report of CFTR mutations in black cystic fibrosis patients of southern African origin. J Med Genet 33:802–804

Claustres M, Desgeorges M, Moine P, Morral N, Estivill X (1996) *CFTR* haplotypic variability for normal and mutant genes in cystic fibrosis families from southern France. Hum Genet 98:336–344

Cuppens H, Teng H, Raeymaekers P, DeBoeck C, Cassiman JJ (1994) CFTR haplotype backgrounds on normal and mutant CFTR genes. Hum Mol Genet 3:607–614

Dörk T, Mekus F, Schmidt K, Boßhammer J, Fislage R, Heuer T, Dziadek V, et al (1994) Detection of more than 50 different CFTR mutations in a large group of cystic fibrosis patients. Hum Genet 94:533–542

Dörk T, Neumann T, Wulbrand U, Wulf B, Kalin N, Maass G, Krawczak M, et al (1992) Intra- and extragenic marker haplotypes of CFTR mutations in cystic fibrosis. Hum Genet 88:417–425

El-Harith EA, Dörk T, Stuhrmann M, Abu-Srair H, Al-Shahri A, Keller K-M, Lentze MJ, et al (1997) Novel and characteristic CFTR mutations in Saudi Arab children with severe presentation of cystic fibrosis. J Med Genet 34:996–999

Estivill X, Scambler PJ, Wainwright BJ, Hawley K, Frederick P, Schwartz M, Baiget M, et al (1987) Patterns of polymorphism and linkage disequilibrium for cystic fibrosis. Genomics 1:257–263

Gabriel SE, Brigman KN, Koller BH, Boucher RC, Stutts MJ (1994) Cystic fibrosis heterozygote resistance to cholera toxin in the cystic fibrosis mouse model. Science 266: 107–109

Hughes D, Wallace A, Taylor J, Tassabehji M, McMahon R, Hill A, Nevin N, et al (1996) Fluorescent multiplex micro-

satellites used to define haplotypes associated with 75 CFTR mutations from the UK on 437 CF chromosomes. Hum Mutat 8:229–235

Kerem B, Rommens JM, Buchanan JA, Markiewicz D, Cox TK, Chakravarti A, Buchwald M, et al (1989) Identification of the cystic fibrosis gene: genetic analysis. Science 245: 1073–1080

Macek M Jr, Macek M Sr, Krebsová A, Nash E, Hamosh A, Reis A, Varon-Mateeva R, et al (1997*a*) Possible association of the allele status of the CS.7/*Hha*I polymorphism 5′ of the *CFTR* gene with postnatal female survival. Hum Genet 99: 565–572

Macek M Jr, Mackova A, Hamosh A, Hilman BC, Selden RF40, Lucotte G, Friedman KJ, et al (1997*b*) Identification of common cystic fibrosis mutations in African-Americans with cystic fibrosis increases the detection rate to 75%. Am J Hum Genet 60:1122–1127

Morral N, Bertranpetit J, Estivill X, Nunes V, Casals T, Giménez J, Reis A, et al (1994) The origin of the major cystic fibrosis mutation (delta F508) in European populations. Nat Genet 7:169–175

Morral N, Dörk T, Llevadot R, Dziadek V, Mercier B, Ferec C, Costes B, et al (1996) Haplotype analysis of 94 cystic fibrosis mutations with seven polymorphic CFTR DNA markers. Hum Mutat 8:149–159

Morral N, Estivill X (1992) Multiplex PCR amplification of three microsatellites within the CFTR gene. Genomics 13: 1362–1364

Morral N, Nunes V, Casals T, Chillón M, Giménez J, Bertranpetit J, Estivill X (1993) Microsatellite haplotypes for cystic fibrosis: mutation frameworks and evolutionary tracers. Hum Mol Genet 2:1015–1022

Ramsay M, Williamson R, Estivill X, Wainwright BJ, Ho M, Halford S, Kere J, et al (1993) Haplotype analysis to determine the position of a mutation among closely linked DNA markers. Hum Mol Genet 2:1007–1014

Romeo G, Devoto M, Galietta LJV (1989) Why is the cystic fibrosis gene so frequent? Hum Genet 84:1–5

Russo MP, Romeo G, Devoto M, Barbujani G, Cabrini G, Giunta A, D'Alcamo E, et al (1995) Analysis of linkage disequilibrium between different cystic fibrosis mutations and three intragenic microsatellites in the Italian population. Hum Mutat 5:23–27

Sereth H, Shoshani T, Bashan N, Kerem B (1993) Extended haplotype analysis of cystic fibrosis mutations and its implications for the selective advantage hypothesis. Hum Genet 92:289–295

Traeger-Synodinos J, Kanavakis E, Tzetis M, Kattamis A, Kattamis C (1993) Characterization of nondeletion α-thalassemia mutations in the Greek population. Am J Hematol 44:162–167

Tzetis M, Kanavakis E, Antoniadi T, Adam G, Kattamis C (1997) Characterization of more than 85% of cystic fibrosis alleles in the Greek population, including five novel mutations. Hum Genet 99:121–125

Welsh MJ, Tsui LC, Boat TF, Beaudet A (1995) Cystic fibrosis. In: Scriver CR, Beaudet AL, Sly WS, Valle D (eds) The metabolic and molecular bases of inherited disease, 7th ed. McGraw-Hill, New York, pp 3799–3876

Williams C, Williamson R, Coutelle C, Loeffler F, Smith J, Ivinson A (1988) Same-day, first-trimester antenatal diagnosis for cystic fibrosis by gene amplification. Lancet 2: 102–103

Zielenski J, Markiewicz D, Rininsland F, Rommens J, Tsui L-C (1991) A cluster of highly polymorphic dinucleotide repeats in intron 17b of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Am J Hum Genet 49: 1256–1262

Address for correspondence and reprints: Dr. Thilo Dörk, Institute of Human Genetics, Medical School Hannover, D-30625 Hannover, Germany. E-mail: doerk.thilo@mh-hannover.de

0002-9297/98/6302-0043$02.00

Am. J. Hum. Genet. 63:662–663, 1998

Media Portrayals of Genetics

To the Editor:

The article by Condit et al. (1998) demonstrates some of the limitations of quantitative analysis. The authors select from *Reader's Guide* articles listed under "heredity" in various time periods. Not surprisingly, such articles consistently attribute characteristics to genes. When the 50 articles selected from the eugenic period attribute human characteristics to heredity at almost the same rate as those selected from the 1990s, the authors conclude that nothing has changed. Predictably, they find that the "degree of determinism" (which they calculate to the fifth decimal) is consistent over 90 years of profound scientific and social change.

The paper is an example of the problem of trying to quantitate what is most compellingly understood in qualitative terms. Our study of the gene in popular culture (Nelkin and Lindee 1995), a target of Condit et al.'s paper, was not a quantitative study for the precise reason that the counting of such ambiguous and heterogeneous materials provides little insight into the public meaning of science. We focused on qualitative changes in a much broader literature, to suggest that the gene has acquired new powers as a guide to social policy. In the 1990s, the cultural meanings attached to the gene are shaping employment practices, educational policies, and decisions in the courts. The serious issues raised by the high-profile gene deserve more serious analysis.

Dorothy Nelkin and M. Susan Lindee
Department of Sociology
New York University
New York