

Letter to the Editor

High Frequency of the Deafness-Associated 167delT Mutation in the Connexin 26 (*GJB2*) Gene in Israeli Ashkenazim

To the Editor:

In a study of an American Ashkenazi Jewish population (555 individuals), Morell et al. have reported a particularly high carrier rate (4.03%) of the 167delT mutation in the connexin 26 (*GJB2*) gene [Morell et al., 1998], which is associated with non-syndromic recessive deafness [Denoyelle et al., 1997; Kelsell et al., 1997]. We have now screened an Israeli Ashkenazi population (467 individuals) for mutations in connexin 26 and have determined a carrier rate of 2.78% of the 167delT mutation. Although the carrier rate for the 167delT mutation within our sample group was somewhat lower than that reported by Morell et al. [1998], it was within their reported 95% confidence interval (2.5–6.0%) and nonetheless quite high when considering the situation in general of disease-carrying alleles in a population. Although deafness has not been cited as a common condition in Ashkenazi Jews, this is certainly a high carrier rate, comparable to, for instance, Tay-Sachs disease (3–4%), Gaucher disease (4–6%), and Canavan disease (1–2%) [Motulsky, 1995], for which routine screening has been carried out for some years.

We have tested a representative Israeli Ashkenazi population for connexin 26 mutations (DNA samples from the Rabin Medical Center and from the National Laboratory for the Genetics of Israeli Populations, Tel-Aviv University; URL, <http://www.tau.ac.il/medicine/NLGIP/nlgip.htm>). First, we amplified the appropriate area of the connexin 26 gene in the DNA samples tested using PCR with a ³²P labeled primer. We electrophoresed the amplification products on standard sequencing (denaturing Urea-PAGE) gels to check for the presence of deletions by fragment length. All samples which showed deletions were sequenced to identify the specific deletions. Of 467 samples, a total of 14 carriers

(3.00%, range = 1.85–4.92% at 95% confidence) were found, comprising thirteen 167delT carriers (2.78%, range = 1.69–4.65% at 95% confidence) and one 30delG carrier (0.21%, range 0.20–1.04% at 95% confidence). We then typed markers flanking the *GJB2* gene on chromosome 13 in the carrier samples (Table I) in order to determine alleles associated with the 167delT mutation and compare them to those obtained by Morell et al. [1998].

Many data exist on the incidence of genetic disorders among Ashkenazi Jews. There are many reports on several specific diseases and mutations, which have been concentrated due to bottleneck effects and limited outbreeding when compared to other European populations [DellaPergola, 1992; Jorde, 1992]. High patient interest and compliance has facilitated studying and screening of various genetic diseases in the Ashkenazi population. Although some variability of carrier rates between different Ashkenazi sample groups has been seen, the general trends between the groups remain basically the same [Motulsky, 1995].

Our results on the 167delT mutation suggest the same 3/4 haplotype for the markers D13S141/D13S175 (Table I) and similar carrier frequency to that shown by Morell et al. [1998]. This supports a single origin among the Ashkenazim for this mutation. Although the incidence of inherited deafness is no higher in the Ashkenazi Jewish population than in other European populations, mutations in this particular gene may be responsible for most cases of non-syndromic inherited deafness in the Ashkenazi population [Brownstein et al., 1991; Feinmesser et al., 1990; Morell et al., 1998]. Both the 167delT mutation, with its higher prevalence in the Ashkenazi population, and the 30delG mutation, which has been shown to be common in Mediterranean populations [Zelante et al., 1997], can now be tested by relatively simple PCR/restriction endonuclease procedures [Storm et al., 1999] quickly and without the use of radioactivity.

We are currently testing non-Ashkenazi Jewish populations (North African, Turkish, etc.) for carrier frequencies of the 167delT and 30delG mutations. We hope to be able to further understand the population history and clarify relationships between these different populations. We agree with a recent editorial [Zlotogora, 1999] that a universal approach to identifi-

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TABLE I. Frequencies of Marker Alleles in the 167delT Carriers

	Number of chromosomes	Expectation for non-carriers ^a	χ^2 P value
D13S141 alleles			
1	0	0.2	0.00412 ^b 0.00011 ^c
2	7	15.08	
3	19	9.49	
4	0	1.09	
5	0	0.14	
D13S175 alleles			
1	1	0.95	0.04586 ^b 0.00008 ^d
2	0	0.68	
3	2	6.03	
4	20	10.22	
5	0	1.42	
6	1	2.77	
7	1	0.61	
8	1	2.91	
9	0	0.34	
10	0	0.07	
Two loci alleles			
3 & 4	13	5.19	0.00001 ^e
Others	0	7.81	

^aExpectation was based on allele frequencies in the Ashkenazi Jewish population published by Morell et al. [1998].

^bAllele frequencies in carriers versus non-carriers.

^cAllele 3 frequency in carriers versus non-carriers.

^dAllele 4 frequency in carriers versus non-carriers.

^eFrequency of individuals carrying both Alleles 3 and 4, 167delT carriers versus non-carriers.

cation of hearing defects in newborns, using either automated auditory brainstem responses or transiently evoked otoacoustic emissions, is most appropriate. However, in attempts to trace diversity among ethnic communities or to determine common origins of the 167delT or 30delG mutation in certain consanguineous lineages, it would be very useful to know which *GJB2* mutations are present. Standardization of these tests into a clinical kit format should be reasonably straightforward and would allow easy testing for families with a history of hereditary deafness who wish to have such testing performed.

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