Population frequencies of three DNA alleles linked to the Duchenne muscular dystrophy gene

SUMMARY To enquire whether the known X linked probes linked to the Duchenne muscular dystrophy gene vary in their RFLP frequencies, three probes, 754, XJ1.1, and pERT87.8, were tested in European, Indian Muslim, and West African samples. Though the average heterozygosity for the three together is fairly similar in the three populations, significant differences in allele frequencies were evident.

Studies of nuclear and mitochondrial DNA polymorphisms have shown considerable variation in frequency from one race to another, and a race specific DNA marker has also been reported.^{1,2} In European populations the short arm X chromosome probes show no conclusive heterogeneity in allele frequency, except for the 5.3 kb allele identified by the RC8 (*DXS9*) probe, but for some of the probes different racial groups show much more variation.^{3–5} A recent study of DMD linked pERT probes in Japanese showed frequencies for pERT87.8 RFLPs significantly different from Europeans and Americans.^{5,6}

The diagnostic value of these DNA probes in various human populations will depend on the relative frequencies of their RFLPs. In Britain there are 3 million immigrants comprising several ethnic populations. There is as yet no information available on the distribution of DMD linked RFLPs in the ethnic groups of Britain, or in their parental populations. This paper presents data on DNA polymorphisms defined by three DMD linked probes (754, XJ1.1, and pERT87.8) in English, Indian Muslim, and Nigerian populations and comments on the usefulness of these probes for the prenatal diagnosis of DMD in families of ethnic minorities.

Material and methods

Blood samples from 101 unrelated subjects (71 females and 30 males) from north-east England were obtained and kept frozen at -80°C until DNA extraction. The samples from unrelated Indian Muslims and Nigerians were obtained as part of

previously described DNA studies still in progress.⁵ Forty DNA samples (22 females and 18 males) from Sunni Muslims living in Hyderabad, Andhra Pradesh, India and 14 females from Zaria, Nigeria were available for testing.

The DNA extraction procedure, the digestion with restriction endonucleases (*Pst*I and *Taq*I), electrophoresis of digested DNA, hybridisation, and autoradiography has already been described.⁵ The three probes (754, XJ1.1, and pERT87.8) were labelled by random priming to a specific activity of 10^8cpm/g DNA . The *Taq*I filter, after hybridisation with XJ1.1 and autoradiography, was washed and rehybridised with pERT87.8.

Results and discussion

The RFLPs identified by 754 are fragments of 12 kb (allele 1) and 9 kb (allele 2). Similarly, RFLPs for XJ1.1 are of 4.5 kb (allele 1) and 3.5 kb (allele 2) and for pERT87.8 of 3.8 kb (allele 1) and 1.1 and 2.7 kb (allele 2). These alleles were present in all three ethnic groups and no new allele was found. The phenotype numbers observed in females and males, the numbers expected in females, and the allele frequencies calculated from the total number of chromosomes tested in each population and for the three probes are given in the table. In all the female samples, there is agreement of the observed heterozygote numbers with those expected under Hardy-Weinberg equilibrium, except for the pERT87.8 probe in the female sample from north-east England, where there is a barely significant deficiency of observed heterozygotes ($\chi^2=6.9$, df 2, $p<0.03$); however, on account of the number of tests carried out in the same samples this may well be due to chance.

Received for publication 9 February 1988.

Revised version accepted for publication 28 November 1988.

TABLE Phenotypes and allele frequencies of DNA polymorphisms for 754, XJ1.1, and pERT87-8 in three different population groups.

Probe and size of allele fragment	Population and region	Sex	No tested	Phenotype			Allele frequency	
				1	2-1	2	*1	*2
754 (DX584)	English (North-east England)	F	71	26 (25-0)	34 (34-2)	11 (11-8)	0-593	0-407
		M	30	16		14		
*1 (12 kb) *2 (9 kb)	Muslim (Andhra Pradesh, India)	F	22	15 (14-3)	6 (6-9)	1 (0-8)	0-806	0-194
		M	18	14		4		
	African (Ibadan, Nigeria)	F	10	1 (1-0)	4 (4-3)	5 (4-7)	0-318	0-682
XJ1.1	English (North-east England)	F	64	3 (4-0)	26 (24-2)	35 (35-8)	0-252	0-748
		M	11	3		8		
*1 (4-5 kb) *2 (3-5 kb)	Muslim (Andhra Pradesh, India)	F	21	2 (2-4)	9 (9-4)	10 (9-2)	0-339	0-661
		M	11	5		6		
	African (Ibadan, Nigeria)	F	14	11 (10-3)	2 (3-4)	1 (0-3)	0-857	0-143
pERT87-8	English (North-east England)	F	64	10 (5-0)	19 (25-8)	35 (33-2)	0-280	0-720
		M	22	3		19		
*1 (3-8 kb) *2 (1-1 and 2-7 kb)	Muslim (Andhra Pradesh, India)	F	21	4 (3-7)	10 (10-3)	7 (7-0)	0-421	0-579
		M	15	6		9		
	African (Ibadan, Nigeria)	F	14	1 (0-6)	4 (4-8)	9 (8-6)	0-214	0-786

Expected numbers are given in parentheses.

PROBE 754

For European populations the frequency reported for allele *2 ranges from 34% in Germans to 46% in the French. The present frequency of 41% is compatible with the previous report from Britain of 39%. In Indian Muslims this allele is infrequent (19%) whereas in Nigerians it is the highest so far reported (68%). The significance of the differences in allele count among the three ethnic groups was tested by Fisher's exact probability test, and proved highly significant (English ν Indian Muslim $p=0.0065$, Indian Muslim ν Nigerian $p=9.3 \times 10^{-5}$, and Nigerian ν English $p=0.0097$).

PROBE XJ1.1

The allele *2 is the common allele in the English population (75%) and in Indian Muslims (66%). The difference between the two populations is not significant ($p=0.285$). In the Nigerian sample the situation is reversed, allele *1 (86%) being more frequent than allele *2. The frequency difference in the Indian Muslim and English samples is highly significant ($p=1.5 \times 10^{-5}$ and $p=2.8 \times 10^{-9}$ respectively).

pERT87-8

The allele *2 frequency in the present English sample (72%) is very similar to that already reported

for Europeans.⁶ The allele frequencies in the Nigerian sample are very similar to the English population ($p=0.237$). The slight diminution of allele *2 frequency (58%) in the Indian Muslim sample is barely significant compared to Nigerian samples ($p=0.05$) and not significant compared to the English ($p=0.099$). The frequency in the Japanese is lower than in the Europeans and Negroes and is similar to the present sample of Indian Muslims.⁶

Since the allele frequencies differ, the expected heterozygosity differs and it ranges in the English from 30 to 48%, Indian Muslims 31 to 49%, and Nigerians 25 to 43%. But the average heterozygosity (H) for the three probes is quite similar in the English and Indian Muslim samples (39 and 42% respectively) and slightly lower in Nigerians (34%). While the three probes used together are likely to be almost equally useful in each of the three populations, in the English the most informative is likely to be 754 and in Muslims it will be pERT87-8. XJ1.1 is likely to be of limited value in Nigerian families. However, the situation within a family will, of course, depend on the zygosity status of each relevant subject.

To conclude, different populations may differ greatly in their frequencies of various RFLPs and it is important, therefore, to establish for various ethnic groups which probes are likely to be most

informative so that the most appropriate RFLPs can be used when an urgent prenatal diagnosis is required.

S S PAPIHA*, D F ROBERTS*, A CLARKE*, J BURN*,
D GARDNER-MEDWIN†, AND S S BHATTACHARYA*

*Department of Human Genetics,
University of Newcastle upon Tyne; and
†Neurological Centre, Newcastle General Hospital,
Newcastle upon Tyne.

References

- ¹ Bonne-Tamir B, Johnson MJ, Natali A, Wallace DC, Cavalli-Sforza LL. Human mitochondrial DNA types in two Israeli populations—a comparable study at the DNA level. *Am J Hum Genet* 1986;**38**:341–51.

- ² Wainscoat JS, Kulozik AE, Ramsay M, Falusi AG, Weatherall A. Taq 1γ-globin DNA polymorphism: an African-specific marker. *Hum Genet* 1986;**74**:90–2.
- ³ Schurmann M, Warneke R, Schwinger E. Four DNA polymorphisms on the short arm of X chromosome: allele frequencies in a German and in a Turkish population. *Hum Hered* 1987;**37**:329–33.
- ⁴ Summers KM. DNA polymorphism in human population studies: a review. *Ann Hum Biol* 1987;**14**:203–17.
- ⁵ Papiha SS, Bhattacharya SS, Roberts DF. DNA polymorphism identified by an X-chromosome short arm probe L1·28 (DXS7) in different racial groups. *Hum Hered* 1988;**38**:72–5.
- ⁶ Akita Y, Ohno S, Goto J, *et al.* Diagnosis of Duchenne and Becker muscular dystrophies by DNA polymorphism. *Jpn J Hum Genet* 1987;**32**:71–82.

Correspondence to Dr S S Papiha, Department of Human Genetics, 19 Claremont Place, Newcastle upon Tyne NE2 4AA.