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PHOSPHOGLUCOMUTASE POLYMORPHISM IN AN ISOLATED COMMUNITY IN JAPAN[1]

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Summary The distribution of PGM phenotypes was determined among 171 individuals in an isolated community in Japan. There revealed a high frequency of the PGM_1^7 allele (=0.0380), compared with either that of neighbouring populations or that of other ethnic groups. In addition, one rare individual homozygous for the PGM_1^7 allele was detected among those in the community.

INTRODUCTION

Since it was shown by Spencer *et al.* (1964) that human red cell phosphoglucomutase [PGM: EC 2.7.5.1] exhibited genetic polymorphism with three common phenotypes, determined by two autosomal codominant alleles, PGM^1 and PGM^2, phosphoglucomutase as well as other red cell enzymes has been used as a genetic marker in the analysis of population structure.

Many authors have reported data on the allele frequencies for PGM_1 and PGM_2 in various populations and according to the report of Bhasin and Fuhrmann (1972), the allele frequency for PGM_1^2 generally ranges from 0.17 to 0.30 among most Europeans, from 0.01 to 0.28 among various Negro origins and from 0.08 to 0.35 among most Asiatic populations, except in certain isolated ethnic groups. In the Japanese, the allele frequency for PGM_1^2 ranges from 0.19 to 0.30, except in some isolates and among the Ainu (Ishimoto, 1975).

In addition to the two common alleles at the PGM_1 locus, several rare alleles have been detected in various populations: PGM_1^3, PGM_1^4, PGM_1^5, PGM_1^6, PGM_1^7, PGM_1^8, PGM_1^9 and a silent allele PGM_1^0 (Hopkinson and Harris, 1966; Hopkinson, 1968; Fiedler and Pettenkofer, 1968; Satoh *et al.*, 1977). Ishimoto (1975) pointed

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out that among the less common phenotypes the PGM_1^7 allele is the most frequently encountered in population studies.

In this paper, we report the distribution of the PGM_1 allele in an isolated community in Central Japan, where the PGM_1^7 allele frequency was found to be extremely high and is, in fact, presented in polymorphic proportions. In addition, one individual homozygous for the PGM_1^7 allele was detected in our electrophoretic survey of the inhabitants in this community.

MATERIALS AND METHODS

Blood samples from 171 adult individuals were collected in the course of a medical field survey in an isolated mountainous community, Tomiyama, Aichi prefecture in Central Japan.

The specimens, collected into ACD solution, were stored at −70°C with an equal volume of glycerol solution, after washing with physiological saline. Hemolysates for electrophoresis were prepared by the addition of an equal volume of distilled water. Electrophoretic separation was carried out according to a modified version of Spencer's method described by Blake and Omoto (1975). The bridge buffer was 0.1 M Tris-malate-EDTA, adjusted to pH 7.4 with sodium hydroxide. Thirteen percent starch gel was prepared using a 1 in 15 dilution of the bridge buffer. Horizontal starch gel electrophoresis was carried out at 8.5–9.0 V/cm for 18 hr at 5°C. The gel was sliced and the anodal portion was stained for the PGM system, according to the method described by Spencer *et al.* (1964).

The consanguinity rate and mean inbreeding coefficient in this community were calculated on the basis of information obtained through Koseki record checking.

RESULTS

Although electrophoretic separation was performed for both PGM_1 and PGM_2 phenotypes in the 171 samples, only the PGM_1 locus was polymorphic. The PGM_1 phenotype and allele frequency obtained in this survey are summarized in Table 1. The PGM_1^1 and PGM_1^2 allele frequencies were calculated to be 0.7047 and 0.2573, respectively. These values were somewhat different from those of some neighbouring populations reported by several other investigators (See Table 2).

As shown in Table 1, in addition to these common alleles, there were 12 individuals with the PGM_1^7 allele: the PGM_1 7-1 phenotype in ten, the PGM_1 7-2 in one and the PGM_1 7 in one among the 171 samples examined. The electrophoretic patterns for the three common phenotypes of PGM_1 as well as those for PGM_1 7-1, PGM_1 7-2 and PGM_1 7 phenotypes are shown in Fig. 1. In addition, various phenotypes involving the PGM_1^7 allele previously reported are illustrated diagrammatically in Fig. 2. It is apparent that the isoenzyme pattern attributable to PGM_1^7 allele consists of two distinguishable bands. With respect to the location of these

Table 1. Distribution of phenotypes and allele frequencies for PGM_1 in the community surveyed.

	PGM_1 phenotype						
	1	2-1	2	7-1	7-2	7	Total
Observed	83	65	11	10	1	1	171
Percentage	48.5	38.0	6.4	5.9	0.6	0.6	100.0
Expected	84.9	62.0	11.3	9.2	3.3	0.2	170.9
Allele frequency	PGM_1^1=0.7047		PGM_1^2=0.2573			PGM_1^7=0.0380	

χ^2=5.0682; 3 d.f.; 0.25>p>0.10

Table 2. Distribution of allele frequencies of PGM_1^1, PGM_1^2 and PGM_1^7 in various Japanese populations.

Population	No. tested	Allele frequency			Reference
		PGM_1^1	PGM_1^2	PGM_1^7	
Hokkaido	222	0.806	0.187	0.0068	Omoto and Harada (1972)
Ainu (Hokkaido)	191	0.822	0.178	—	Omoto and Harada (1972)
Tokyo	965	0.775	0.223	0.0016	Shinoda and Matsunaga (1970a)
Shizuoka	1,677	0.772	0.225	0.0015	Shinoda and Matsunaga (1970a)
Aichi	586	0.791	0.205	0.0017	Shinoda and Matsunaga (1970b)
Mie	983	0.780	0.217	0.0010	Ishimoto (1970)
Nara	757	0.761	0.235	0.0033	Ishimoto (1970)
Hiroshima	526	0.751	0.247	0.0019	Ishimoto *et al.* (1973)
	872	0.753	0.231	0.0155	Satoh *et al.* (1977)
Nagasaki	608	0.799	0.200	0.0016	Ishimoto and Kuwata (1973)
	1,023	0.758	0.222	0.0142	Satoh *et al.* (1977)
Okinawa	647	0.721	0.260	0.0147	Omoto *et al.* (1973)
Tomiyama (Aichi)	171	0.705	0.257	0.0380	Present study

two bands, one is located slightly cathodal to the 'c' band and anodal to the 'b' band, as well the other is located anodal to the 'd' band and cathodal to the 'e' band of PGM_2 locus under our electrophoretic condition. These bands exhibit unequal in staining intensity, with that of the latter being weaker than that of the former, a finding in agreement with that reported by Blake and Omoto (1975).

A careful family study of the PGM_1^7 homozygote was performed by means of Koseki record checking. However, unfortunately, this study did not provide us with any useful information about the source of this unusual finding, since neither parents were living and there were no immediate relatives available.

DISCUSSION

Tomiyama village, in which a clustering of the PGM_1^7 allele was found, is a mountainous community consisting of 243 inhabitants in 79 households, located in the central portion of Japan and completely isolated, geographically and socially,

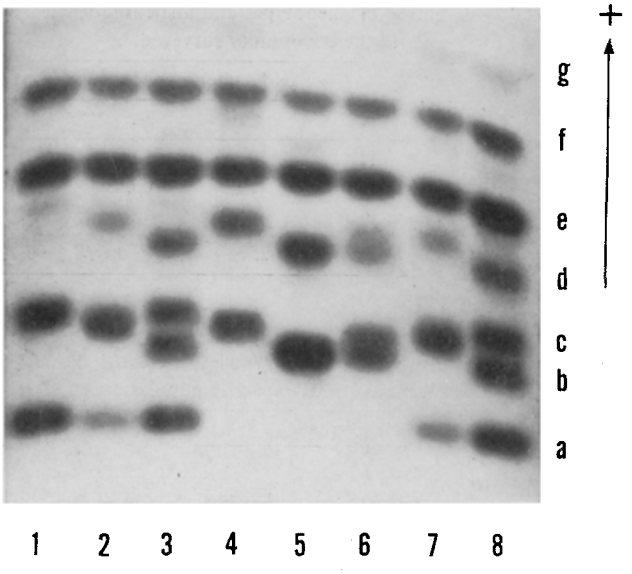

Fig. 1. Electrophoretic patterns of PGM_1 phenotypes. Well 1, $PGM_1 1$; 2, $PGM_1 7\text{-}1$; 3, PGM_1 2-1; 4, PGM_1 7; 5, PGM_1 2; 6, PGM_1 7-2; 7, PGM_1 7-1; 8, PGM_1 2-1.

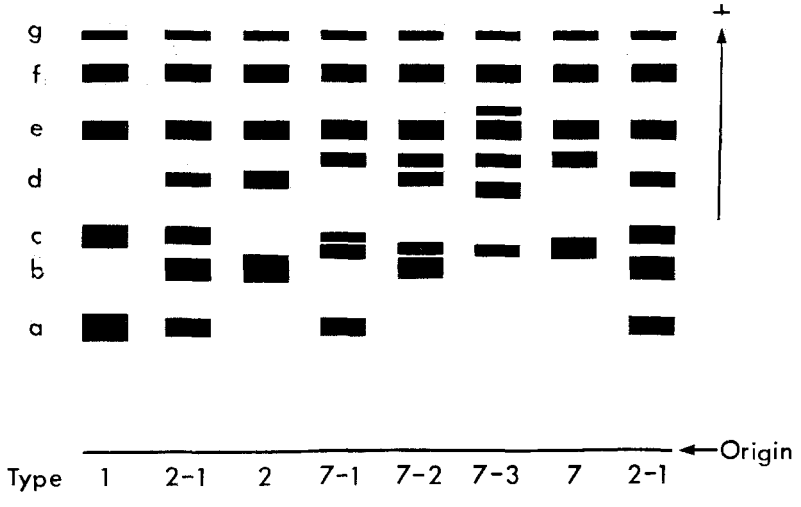

Fig. 2. Diagram showing PGM_1 common and rare phenotypes, detected so far, with PGM_1^7 allele.

from neighbouring populations. A detailed report on consanguinity in the community will be reported elsewhere, in order to accurately describe the genetic constitution of this isolate. We have obtained the remarkably high values of 39.2% in consanguineous marrige rate and 0.015564 in mean inbreeding coefficient. This

kind of isolated community, with a higher consanguinity rate, may be expected to provide us with very useful data on unusual variants.

The distribution of PGM_1^1 and PGM_1^2 allele frequencies in other populations in Japan is presented in Table 2. The values obtained in this community were found to be somewhat different, in comparison with data obtained from other populations.

The rare PGM_1^7 allele was first reported by Hopkinson and Harris (1966). So far, the allele frequency for PGM_1^7 exhibited very low values for the great majority of various ethnic groups, but a very high frequency of 0.0589 was found in the Western Caroline Islanders among 382 individuals examined (Blake *et al.*, 1973). As shown in Table 2, among the Japanese the allele frequency for PGM_1^7 falls between 0.0010 and 0.0068 in various different groups, except for 0.0147 in a population of Okinawa. However, it is interesting to note in a recent report by Satoh *et al.* (1977) that among 1,892 residents in Nagasaki and in Hiroshima the PGM_1^7 allele frequency was much higher, lying between 0.0142 and 0.0155, most likely as a result of modified electrophoretic conditions which detect the rare variants more accurately. As shown in Table 2, these values are approximately ten times higher than those reported previously in various Japanese populations.

In this survey we have obtained 0.0380 for the frequency of the PGM_1^7 allele, polymorphic and remarkably very high, compared with the incidence among various ethnic populations.

The electrophoretic pattern for one individual was interpreted as being consistent with the PGM_1 7 phenotype. This rare homozygote was first found in three persons among the Western Caroline Islanders. Authors suggest that the exsistence of this homozygote is most likely attributable to the special genetic structure of this isolated community, with an elevated consanguinity rate.

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