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A Study of Ten Red Cell Enzymatic Markers in the Naples' Population

Report of a New GPT Variant Phenotype

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Summary. A sample of the population of Naples has been examined for several red cell enzyme markers. About 2,000 newborn have been analyzed for ACP, GLO I, and UMPK; 1,000 of them were also analyzed for PepA and PepB, and 500 for PGM_1 and PGM_2. In addition about 400 school children have been typed for the PGD and PGP polymorphisms. The observed gene frequencies for the polymorphic systems are: $ACP^A = 0.293$, $ACP^B = 0.667$ and $ACP^C = 0.040$; $GLO^1 = 0.372$; $GPT^2 = 0.462$; $UMPK^2 = 0.029$; $PGM_1^2 = 0.279$; $PGD^C = 0.037$; $PGP^1 = 0.953$, $PGP^2 = 0.038$ and $PGP^3 = 0.009$. Moreover during the screening of PepA, PepB and GPT markers, some rare alleles have been encountered, one of which, at the GPT locus, has never been reported before. We propose for it the name GPT^{10}.

Key words: Red cell enzyme markers – Population of Naples – GPT, new phenotype

Zusammenfassung. Eine Stichprobe aus der Bevölkerung Neapels wurde auf verschiedene Enzymsysteme der roten Blutkörperchen untersucht. Ungefähr 2000 Neugeborene wurden auf ACP, GLO I, GPT und UMPK: davon 1000 auf PepA und PepB und 500 auf PGM_1 und PGM_2 analysiert. Weiterhin wurden bei ungefähr 400 Schülern die PGD- und PGP-Polymorphismen bestimmt. Die beobachteten Genhäufigkeiten in den polymorphen Systemen verteilen sich wie folgt: $ACP^A = 0{,}293$, $ACP^B = 0{,}667$ und $ACP^C = 0{,}040$; $GLO^1 = 0{,}372$; $GPT^2 = 0{,}462$; $UMPK^2 = 0{,}029$; $PGM_1^2 = 0{,}279$; $PGD^C = 0{,}037$; $PGP^1 = 0{,}953$, $PGP^2 = 0{,}038$ und $PGP^3 = 0{,}009$.

Darüber hinaus sind wir während des Screening von PepA-, PepB- und GPT-Mustern auf einige seltene Allele gestoßen, von denen eines, das sich auf dem GPT-Locus befindet, nie zuvor in der Literatur beschrieben worden ist. Für dieses Allel schlagen wir den Namen GPT^{10} vor.

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Introduction

In spite of the numerous population studies on red cell enzyme markers, data concerning Southern Italy are still scarce.

As a part of an extensive research programme on the genetics of the Southern Italian population[1], we performed the analysis of several enzyme systems on a sample of individuals living in Naples.

The following genetic markers were investigated: Acid phosphatase (ACP), Glyoxalase I (GLO I), Glutamic pyruvic transaminase (GPT), 6-Phospho gluconate dehydrogenase (PGD), Phosphoglucomutase-locus 1 and 2 (PGM_1 and PGM_2), Phosphoglycolate phosphatase (PGP), Uridin monophosphate kinase (UMPK) and Peptidases A and B (PepA and PepB). In the usual conditions of analysis, the ACP and PGP polymorphisms are characterized by three codominant alleles, [1, 2] the GLO I, GPT, PGD, PGM_1 and UMPK systems by two codominant alleles, [3, 4, 5, 6, 7] whereas PGM_2, PepA and PepB loci are monomorphic in almost all populations [8, 9].

Material and Methods

The sample was comprised of about 2,000 newborn and 400 school children (9–11 years old). The analysis of all the above mentioned enzymes was carried out on the first group with the exception of PGP and PGD, for the typing of which, the second group was utilized. Blood specimens (cord blood for newborn) were collected in EDTA and packed washed red cells were stored at – 20° C for 2 or 3 weeks until tested. Before analysis, hemolysates were prepared by repeatedly freezing and thawing packed red cells.

Electrophoretic and staining procedures were performed according to the methods described by Meera Khan and Doppert for GLO I [10], Chen and Giblett for GPT [4], Meera Khan for PGD [11], Spencer et al. for PGM [6], Barker and Hopkinson for PGP [2], Giblett et al. for UMPK [7], and Lewis and Harris for PepA and PepB [9]. As far as ACP is concerned the electrophoresis was performed as reported by Karp and Sutton [12] and the isozymes were visualized using 4-methyl umbelliferyl phosphate as substrate according to the method of Swallow et al. [13].

Gene frequencies have been computed only on unrelated subjects for the sample of school children but on the total sample for the newborn, since the relationships within this group, if any, were unknown.

Results and Discussion

Table 1 shows the phenotype and gene frequencies for ACP, GLO I, GPT, PGD, PGM_1, PGP and UMPK polymorphisms. The results of the analysis of PGM_2, PepA and PepB markers are shown in Table 2.

1 This programme was organized by the Istituto Internazionale di Genetica e Biofisica of Naples. Blood specimens were collected in Naples at the S. S. Annunziata Hospital and at the elementary schools

ACP

The frequencies found for the ACP^A and ACP^B alleles are very similar to those reported for the Continental Italian populations whereas that of ACP^C (4%) lies near the lower limit of the range (3–8%) of variation (for a review see [14] and [15]).

Table 1. The phenotype and gene frequencies of the polymorphic systems analyzed in a sample of the Naples' population

Genetic markers	Phenotypes	Frequencies		Gene frequencies
		Observed	Expected	
ACP	A	185	181.67	$ACP^A = 0.293 \pm 0.007$
	BA	818	827.79	$ACP^B = 0.667 \pm 0.007$
	B	948	943.00	$ACP^C = 0.040 \pm 0.003$
	CA	53	49.76	
	CB	113	113.37	
	C	2	3.41	
	Total	2,119	2,119.00	$\chi^{2a}_{3df} = 0.27 \quad P > 0.80$
GLO I	1	260	275.45	$GLO^1 = 0.372$
	2-1	960	929.09	$GLO^2 = 0.628 \pm 0.008$
	2	768	783.46	
	Total	1,988[b]	1,988.00	$\chi^2_{1df} = 2.2 \quad P \sim 0.15$
GPT	1	591	567.81	$GPT^1 = 0.535 \pm 0.008$
	2-1	937	981.63	$GPT^2 = 0.462 \pm 0.008$
	2	446	424.27	$GPT^3 = 0.003 \pm 0.001$
	3-1	4	5.31	
	3-2	6	4.59	
	3	0	0.01	
	7-2	1		
	10-1	1		
	Total	1,986		$\chi^{2c}_{2df} = 4.85 \quad P \sim 0.10$
PGD	A	364	363.53	$PGD^A = 0.963$
	AC	27	27.93	$PGD^C = 0.037 \pm 0.007$
	C	1	0.54	
	Total	392	392.00	
PGM_1	1	249	250.56	$PGM_1^1 = 0.721$
	2-1	197	193.92	$PGM_1^2 = 0.279 \pm 0.014$
	2	36	37.52	
	Total	482	482.00	$\chi^2_{1df} = 0.12 \quad P > 0.70$

Table 1 (continued)

PGP	1	241	238.61	$PGP^1 = 0.953 \pm 0.009$
	2-1	17	19.04	$PGP^2 = 0.038 \pm 0.008$
	2	1	0.38	$PGP^3 = 0.009 \pm 0.004$
	3-1	2	4.76	
	3	1	0.02	
	3-2	1	0.19	
	Total	263	263.00	
UMPK	1	1578	1578.31	$UMPK^1 = 0.971$
	2-1	95	94.28	$UMPK^2 = 0.029 \pm 0.003$
	2	1	1.41	
	Total	1,674	1,674.00	

[a] For calculating χ^2 the CA and C phenotypes were pooled
[b] This figure includes 606 individuals previously analyzed [17]
[c] For calculating χ^2 the 3-1 and 3 phenotypes were pooled; 7-2 and 10-1 phenotypes were excluded

Table 2. Results of the analysis of PGM_2, PepA and PepB in a sample of the Naples' population

Genetic markers	Phenotypes	Frequencies	Gene frequencies
PGM_2	1	482	$PGM_2^1 = 1$
	Total	482	
PepA	1	962	$PepA^1 = 0.999$
	3-1	1	$PepA^3 = 0.001$
	Total	963	
PepB	1	961	$PepB^1 = 0.997$
	2-1	4	$PepB^2 = 0.002$
	3-1	1	$PepB^3 = 0.001$
	Total	966	

GLO I

The analysis of the GLO I polymorphism we previously carried out on about 30% of the present sample had shown that the incidence of the GLO^2 allele (61.1%) was one of the highest among Europeans (for a review see [16]) and significantly different ($P < 0.02$) from that (56.5%) found in an area of Northern Italy (province of Milan) [17]. The finding of a further, though slight, increase of this value in the present larger sample confirms the previous observations.

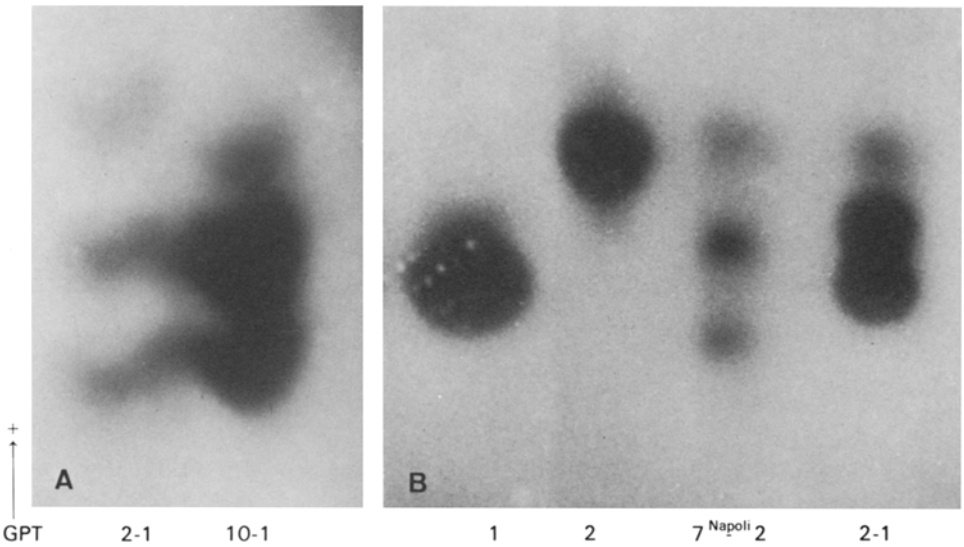

Fig. 1. Starch gel electrophoretic GPT phenotypes

GPT

The GPT^1 and GPT^2 alleles showed almost the same frequency in agreement with the data concerning Caucasians in general (for a review see [18]) and the few other Continental Italian populations so far examined (for a review see [19]).

During this study, in addition to the three common phenotypes, some variant patterns were also encountered, one of which has never been reported before (Fig. 1 a).

This last pattern can, even in the absence of family studies, be interpreted as the heterozygous combination of the common GPT^1 allele and a new allele (we have named it GPT^{10}), the product of which bands between the common GPT 2 and the rare GPT 4 [20] isozymes. The other anomalous patterns are due to the occurrence of the variant GPT^3 allele [20] and of a GPT^7 like allele (for the latter see Fig. 1 b). Since we have not been able to compare our variant with the only other described GPT^7 allele found in Norwegians [18, 21], we propose for it the name $GPT^{7\,Napoli}$.

PGD

The results of this study are in line with those reported by Corbo et al. [22] for L'Aquila (Central Italy) ($PGD^C = 3\%$) and by Brinkmann et al. [23] for a sample of people predominantly from Southern and Central Italy ($PGD^C = 3.1\%$). They differ significantly, however, ($P \sim 0.01$) from those reported by Carfagna et al. [24] in another sample from Naples ($PGD^C = 1.8\%$).

PGM_1

The incidence of the PGM_1^2 allele is very similar to those observed in other parts of Continental Italy [15, 25–27] and lies near the upper end of the European range of variation (18–30%) [28].

PGP

The only data available for Italy concern a group from the Po delta [29]. The frequencies found in that sample ($PGP^1 = 91.9\%$; $PGP^2 = 6.9\%$; $PGP^3 = 1.2\%$) are quite different from those reported by Barker and Hopkinson [2] for a "random European population" ($PGP^1 = 82.6\%$; $PGP^2 = 12.9\%$; $PGP^3 = 4.5\%$) and by Amorim et al. [30] for Germans ($PGP^1 = 87\%$; $PGP^2 = 10\%$; $PGP^3 = 3\%$), in that a lower incidence of PGP^2 and PGP^3 alleles was observed ($P \ll 0.0001$ vs. "random European population"; $P < 0.001$ vs. Germans). These differences have been confirmed by the present study in which an even lower frequency (3.8%) of the PGP^2 allele has been found.

UMPK

The results of this analysis are almost the same as those observed in Milan and Rome [31]. For this polymorphism therefore the Continental Italian population seems to be rather homogeneous ($UMPK^2$ mean frequency = $2.88\% \pm 0.2$) and can be differentiated from the other two Caucasian groups so far examined [7, 32] for a significantly lower frequency of the $UPMK^2$ allele ($P < 0.02$ vs. white North American population; $P < 0.002$ vs. Germans).

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