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Duffy blood group system, phosphoglucomutase and glutamate-pyruvate transaminase in homo- and heterozygous cases of mucoviscidosis

By

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The phenotype and genotype distributions and the gene frequencies of the Duffy blood group system and the phosphoglucomutase and glutamate-pyruvate transaminase red blood cell enzyme systems were examined in mucoviscidosis homo- and heterozygotes, and the results were compared with the data for the average Hungarian population.

In view of the amylase defect in mucoviscidosis, a study was made of the variations in distribution of the protein products of adjacent gene loci (Duffy and phosphomucoglutase), and of the association of identical genotypes (Duffy and phosphoglucomutase homo- and homozygosity, or hetero- and heterozygosity). In the mucoviscidosis homo- and heterozygotes, the percentage values agreed with those for the average population, both for the phenotypes and genotypes of the individual blood groups and the above enzymes, and for the gene frequencies. No differences specific for mucoviscidosis were found for Duffy and phosphoglucomutase. No common genetic regulation could be found between the adjacent gene loci (amylase and Duffy or phosphoglucomutase).

In mucoviscidosis (MV) a marked decrease of pancreatic amylase activity must be reckoned with. The gene locus of amylase is situated on the long arm (q) of the autosomal chromosome 1. Neighbouring gene loci of the latter are those of the Duffy and Kidd blood group system genes, and also phosphoglucomutase (PGM) and peptidase C, an intralysosomal protein-degrading enzyme [1, 8]. Elevated glycoprotein concentrations of bronchial mucin, amniotic fluid and meconium have been demonstrated in MV homozygotes [3]. On the basis of thi fact, the intactness of PGM and peptidase C activities has been suggested in MV. Examinations in this respect have already been carried out with regard to arginine esterase activity [4, 8].

It therefore appeared interesting to investigate the products of the gene loci immediately adjacent to the amylase gene, the Duffy blood group system and the PGM system, in patients with MV.

Materials and Methods

Duffy (Fy) blood group antigen and PGM and glutamate-pyruvate transaminase (GPT) red blood cell enzyme system

examinations were performed in 15 MV homozygous children aged from 18 months to 8.5 years, and in 38 MV obligatory heterozygous parents, or children proved to be MV heterozygotes by the Szczepanski Br^- test. For technical reasons it was not possible to determine the Fy antigen in 1 member of the homozygote group and in 5 members of the heterozygote group. Hungarian data (10) were utilized as control values.

The PGM_1 red blood cell enzyme system and the GPT red blood cell enzyme system were studied by horizontal starch gel electrophoresis.

The Duffy blood group system was studied by Biotest and Molter test sera (incomplete-type, anti-human globulin sera reacting in the Coombs test) by the tube technique, with simultaneous application of appropriate homo- and heterozygote control blood samples. The material was evaluated after transfer to a slide.

Results

Results concerning Fy, PGM_1 and GPT in the MV homo- and heterozygotes are seen in Table I. In these individuals the distribution of Fy, PGM_1 and GPT exhibit an essential difference from that of the normal population.

The proportions of the associations between the Fy, PGM_1 and GPT genotypes in the individual groups examined are given in Table II. The data indicate that the genotype associations between the products of the individual adjacent gene loci were not characteristic of the groups, but rather pointed to a random association.

Table I

Red blood cell Fy, PGM and GPT blood group and isoenzyme genotypes and gene frequencies in homo- and heterozygotic mucoviscidosis patients

	Normal n (%)	MV homozygotes n (%)	MV heterozygotes n (%)
Fy aa.		3 (21%)	6 (15%)
Fy ab		7 (50%)	17 (44%)
Fy bb		4 (28%)	15 (39%)
Fy^a gene frequency	0.451	0.464	0.381
Fy^b gene frequency	0.549	0.535	0.618
PGM_1 1—1	112 (58%)	11 (73%)	27 (62%)
PGM_1 2—1	122 (36.9%)	4 (26%)	14 (32%)
PGM_1 2—2	16 (4.8%)	0	2 (5%)
PGM_1^1 gene frequency	0.766	0.866	0.790
PGM_1^2 gene frequency	0.234	0.133	0.209
GPT 1—1	82 (26.1%)	5 (33%)	12 (28%)
GPT 2—1	154 (49.0%)	9 (60%)	15 (35%)
GPT 2—2	78 (24.8%)	1 (6%)	16 (37%)
GPT^1 gene frequency	0.506	0.633	0.453
GPT^2 gene frequency	0.493	0.366	0.546

TABLE II

Fy, PGM_1 and GPT genotype associations in normal individuals and in homo- and heterozygotic mucoviscidosis patients

	Normal n %	MV homozygotes n %	MV heterozygotes n %
Fy homoz.-PGM homoz.	175 (31.0%)	5 (35%)	15 (39%)
Fy heteroz.-PGM homoz.	172 (30.5%)	2 (14%)	11 (29%)
Fy homoz.-PGM heteroz.	124 (22.0%)	6 (42%)	6 (16%)
Fy heteroz.-PGM heteroz.	92 (16.3%)	1 (7%)	6 (16%)
Fy homoz.-GPT homoz.	75 (23.4%)	1 (7%)	13 (34%)
Fy heteroz.-GPT homoz.	76 (23.7%)	6 (43%)	12 (31%)
Fy heteroz.-GPT heteroz.	67 (20.9%)	3 (21%)	5 (13%)
Fy homoz.-GPT heteroz.	102 (31.8%)	4 (28%)	8 (21%)

DISCUSSION

The normal Fy gene frequencies in Hungary are $Fy^a = 0.451$, and $Fy^b = 0.549$ [10]. The occurrence of a silent Fy gene has not been observed.

In the MV homozygote and heterozygote groups, the Fy phenotype distribution and gene frequency did not differ appreciably from the values for the average population; in the MV homozygote group they were, $Fy^a = 0.464$, and $Fy^b = 0.535$; in the heterozygotes, $Fy^a = 0.381$, and $Fy^b = 0.618$, respectively.

As regards the Fy blood group, this being the neighbouring gene locus of amylase, it was investigated whether the MV homo- or heterozygosity varied together with the Fy homo- or heterozygosity. No close correlation was found, and thus the hypothesis of a common gene regulation was rejected.

The red blood cell PGM^1 catalyses the transformation of glucose-1-phosphate to glucose-6-phosphate. Its polymorphism was described by Spencer et al [9]. The three known phenotypes (PGM_1 1, PGM_1 2-1, and PGM_1 2) are determined by two autosomal codominant alleles [1, 5, 6].

In connection with forensic medical problems, Szabó and Somogyi [11] determined the frequency of the PGM_1 red blood cell enzyme system in the Hungarian population and calculated the gene frequency from the results. The distribution of PGM_1 phenotypes was as follows: $PGM_1 = 58.18\%$; PGM_1 2-1 $= 36.96\%$; PGM_1 2 $= 4.86\%$. The gene frequencies were: PGM_1 1 $= 0.766$; PGM_1 2 $= 0.234$. In our material the PGM phenotype distribution and gene frequency in the MV homo- and heterozygote groups agreed with the indices for the overall population.

No connection was observed in the occurrence of the Fy and PGM phenotype and genotype; i.e. we have indirectly confirmed the independent

functioning of the individual genes directing protein synthesis.

The genetically determined, inherited variants of red blood cell GPT were demonstrated by Chen and Giblett [2] in 1971, by starch gel electrophoresis. The enzyme catalyzes the reversible transformation of L-alanine and alpha-ketoglutaric acid to L-glutamate and pyruvate. The electrophoretic mobilities show the fast fraction to be the GPT 2, the slow one the GPT 1, and their combination the GPT 2-1, phenotype.

The inherited variants of the GPT system are determined by two autosomal, codominant alleles, GPT^1 and GPT^2. The gene loci of the latter are not known. Szabó and Somogyi [12] performed a study of the phenotype distribution of GPT in the Hungarian population. They found the frequencies GPT 1 = 26.11%; GPT 2-1 = = 49.05%; GPT 2 = 24.84%, and also a gene frequency of $GPT^1 = 0.506$; $GPT^2 = 0.493$. The percentage frequencies of the GPT types and the GPT^1 and GPT^2 gene frequencies in MV homo- and heterozygotes similarly agreed with the frequency data for the average Hungarian population. As regards the common gene correlation, the joint occurrence of GPT and Fy did not display a regularity; Mendel's law held for the mixture of the gene pools.

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