Incidence of the PLG*QO Allele in Human Populations.

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Knowledge about genetic variation at the plasminogen (PLG) locus has increased considerably since the independent discoveries of Hobart (1979) and Raum (1979) which described two common alleles. A recent publication by Skoda et al (1986), resulting from a 1984 symposium in Munich, West Germany, established a proposed nomenclature for the PLG system by recommending that the common alleles be called PLG A and PLG B. Eleven (11) additional variants identified by other contributing laboratories received a new name PLG*A1, A2, A3, M1, M2, M3, M4, M5, B1, B2 and B3.

Dysfunctional and fetal forms of PLG have been identified (Aoki et al, 1978; Aznar et al, 1980; Miyata, 1982; Dykes et al, 1984), but are generally associated with clinical abnormalities or, in the case of infants, transitional forms which disappear at 1-2 years of age (Dykes et al, 1984). After testing 11,071 white, 1156 black and 443 amerindian paternity cases we identified a null allele, PLG*QO, present only in whites and which generally appeared as maternal exclusions. This report documents the presence of the null allele by observations on apparent maternal and paternal exclusions, family data and quantitative testing.

MATERIALS AND METHODS

Bloods for paternity cases were drawn in ACD anticoagulant and stored at -20 until tested. Samples were tested with 14-16 genetic marker systems using a battery of RBC antigens and enzymes and serum proteins with a power of exclusion of P = 0.97 - 0.98. In selected cases HLA was also tested.

Routine PLG phenotyping was done using agarose gel isoelectric focusing (AGIF) at pH 5-8 (Pharmalyte) as described by Dykes et al (1983) without neuraminidase. Questionable samples on infants, unusual variants and maternal exclusions were also tested after treatment with neuraminidase.

Quantitation of PLG was done by immunological means using Plasminogen QUIPlates from Helena Laboratories. The radial immunodiffusion plates measured PLG in mg/dl. A control population of 49 healthy male and female blood donors was used to obtain normal ranges and mean PLG values.

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Calculations for the frequency of silent alleles used a formula provided by Dr. Henry Gershowitz, Department of Human Genetics, University of Michigan.

$$S = \frac{\text{frequency of parent-child incompatibility}}{\text{sum of heterozygotes}}$$

RESULTS AND DISCUSSION

Phenotype and gene frequency results are seen in table 1. The new variants PLG*M01 and A4 are further described by Dykes et al at this conference and focus slightly anodal to PLG B and A3 respectively.

TABLE 1. DISTRIBUTION OF PLG PHENOTYPES AND ALLELE FREQUENCIES IN MINNESOTA WHITES

PHENOTYPES	NO. OBSERVED	ALLELE FREQUENCIES
A	9664	A=0.6777
AA1	20	A1=0.0007
AA3	476	A3=0.0176
AA4	78	A4=0.0026
AB	7797	B=0.2860
AM01	101	M01=0.0035
AM1	13	M1=0.0004
AM5	323	M5=0.0115
A1B	11	* QO=0.0035
A3	13	
A3B	219	
A3M01	3	
A3M5	6	
A4	2	
A4B	22	
A4M1	2	
A4M5	2	
B	1824	
BM01	36	
BM5	143	
M1	2	
M1M5	1	
M5	1	
TOTAL	20759	

* Not used in calculating other gene frequencies

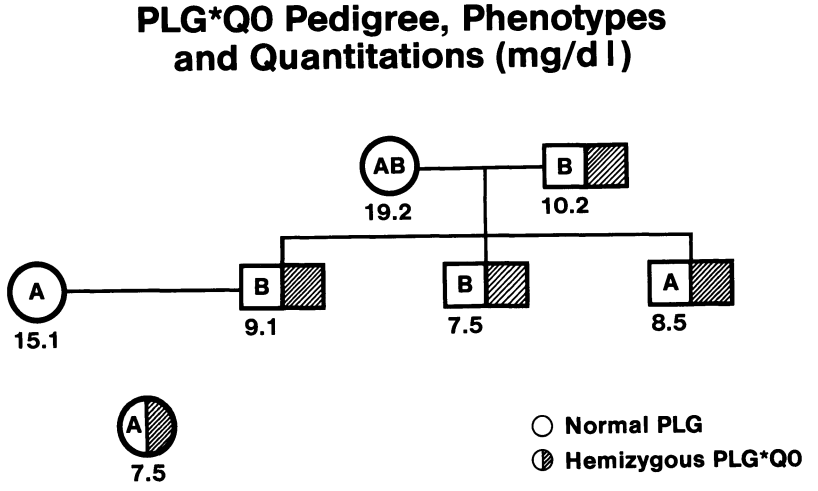
The paternity cases in this study demonstrated as of December 1986 a total of 32 apparent maternal exclusions, table 2. In all cases PLG was the only incompatibility. Based upon these results and the number of heterozygotes observed in the population the frequency of PLG*Q0=0.0035.

TABLE 2. MATERNAL EXCLUSIONS OBSERVED

PHENOTYPES		
CHILD	MOTHER	NO. OBSERVED
A	B	13
A	A3	1
B	A	18
	TOTAL	32

Single indirect paternal exclusions had been noted in 20 cases, most of which had high residual probabilities of paternity when the PLG exclusion was not considered. In those cases in which HLA testing was subsequently done no additional exclusions were observed and the residual probability increased. In one such case a family was obtained and appeared to demonstrate inheritance of the PLG*Q0 allele, figure 1. Testing of the family showed that the child in question, the alleged father and sibs and his mother all had depressed PLG levels. PLG levels of the suspected carriers ranged from 7.5- 10.2 mg/dl compared to a mean of 13.1 mg/dl in our control population of 49 donors (range 9.8 - 17.5, s.d. 1.75).

FIGURE 1.



CONCLUSION

The results indicate that PLG*QO is an inheritable allele. It is apparently population specific, since it has only been identified in whites. Individuals with PLG*QO have depressed PLG levels identified in fresh samples when tested by conventional radial immunodiffusion methods. Because the gene (PLG*QO) has a frequency of 0.0035 single indirect exclusion in cases of disputed parentage should be further investigated with additional genetic markers, quantitation and pedigree analysis.

REFERENCES

Hobart, MJ: Genetic polymorphism of human plasminogen. Ann. Hum. Genet. 42: 419-423 (1979).

Raum D:, Marcus D, Alper CA: Genetic polymorphism of human plasminogen. Am J Hum Genet 32: 681-689 (1980).

Skoda U, Bertrams J, Dykes D, Eiberg H, Hobart M, Hummel K, Kuhnl P, Mauff G, Nakamura S, Nishimukai H, Raum D, Tokunaga K, and Weidinger S: Proposal for the nomenclature of human plasminogen (PLG) polymorphism. Vox Sang 51: 244-248 (1986).

Aoki N, Moroi M, Sakata Y, and Yoshida N: Abnormal plasminogen: A hereditary molecular abnormality found in a patient with recurrent thrombosis. J. Clin. Invest. 61: 1186-1195 (1978).

Azner A, Gilabert J, Parrilla J: Dysfunctional plasminogen in full term newborn. Pediatr. Res. 14: 1180-1185 (1980).

Miyata T, Iwanaga S, Sakata Y and Aoki N: Plasminogen Tochigi: Inactive plasmin resulting from replacement of alanine-600 by threonine in the active site. Proc. Nat'l Acad. Sci. USA. 79: 6132-6136 (1982).

Dykes D, Mount M and Polesky H: Parentage testing using the serum protein plasminogen. Am. J. Clin. Path. 82: 722-725 (1984).

Dykes D, Nelson M and Polesky H: Distribution of plasminogen allotypes in eight populations of the western hemisphere. Electrophoresis 4: 417-420 (1983).

III. Monoclonal Antibodies