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Properdin Factor B-Polymorphism in the Population of Hessen, Germany

P. Kühnl and W. Spielmann

Institut für Immunhämatologie der Universität Frankfurt/Main and Blutspendedienst Hessen des DRK, Sandhofstraße 1, D-6000 Frankfurt/Main, Federal Republic of Germany

Summary. The polymorphism of properdin factor B (Bf, C3 proactivator) in a population sample from Hessen, Germany has been investigated by agarose gel electrophoresis and immunofixation. In 522 unrelated individuals seven different phenotypes were observed and the following allele frequencies calculated: Bf^S = 0.7998, Bf^F = 0.1772, $Bf^{S0.7}$ = 0.0163 and Bf^{Fl} = 0.0077. Investigations of 100 families with 198 children and 30 mother-child combinations support the assumed autosomal codominant way of inheritance.

Key word: Properdin factor B, polymorphism

Zusammenfassung. Der Polymorphismus des Properdin-Faktor B (Bf, C3-Proaktivator) wurde an einer Bevölkerungsstichprobe aus Hessen mittels Agarosegelelektrophorese und Immunofixation untersucht. Bei 522 Personen wurden sieben verschiedene Phänotypen beobachtet und die folgenden Allelfrequenzen berechnet: Bf^S = 0,7998, Bf^F = 0,1772, $Bf^{S0,7}$ = 0,0163 und Bf^{Fl} = 0,0077. Untersuchungen an 100 Familien mit 198 Kindern und 30 Mutter-Kind-Kombinationen bestätigen den angenommenen autosomal kodominanten Vererbungsmodus.

Schlüsselwort: Blutgruppen, Properdinfaktor B, Polymorphismus

Properdin factor B (Bf, previously termed glycine-rich β-glycoprotein = GBG or C3 proactivator = C3 PA) has been shown to exhibit an extensive genetic polymorphism (Alper et al., 1972, Mauff et al., 1975, Kühnl, 1977). Two common alleles Bf^S and Bf^F give rise to three phenotypes S, FS and F. At least six additional rare alleles were described in Caucasoids, three further alleles in Negroid populations (Mauff et al., 1975, 1976, 1977), (Hauptmann et al. 1976, 1977_a).

A close immunogenetic linkage of Bf to the HLA-B locus of the major histocompatibility complex in man on chromosome 6 has been reported by Allen (1974) and confirmed among others by Rittner et al. (1975), Albert et al. (1975), Olaisen et al. (1975), and Kühnl et al. (1977). A linkage disequilibrium between Bf and HLA-B loci (Bf^F/Bw5, Bf^S/B8, $Bf^{S0.7}$/Bw21, Bf^{F1}/B18) has been described previously (Albert et al., 1975, Olaisen et al., 1975, Bender et al., 1977).

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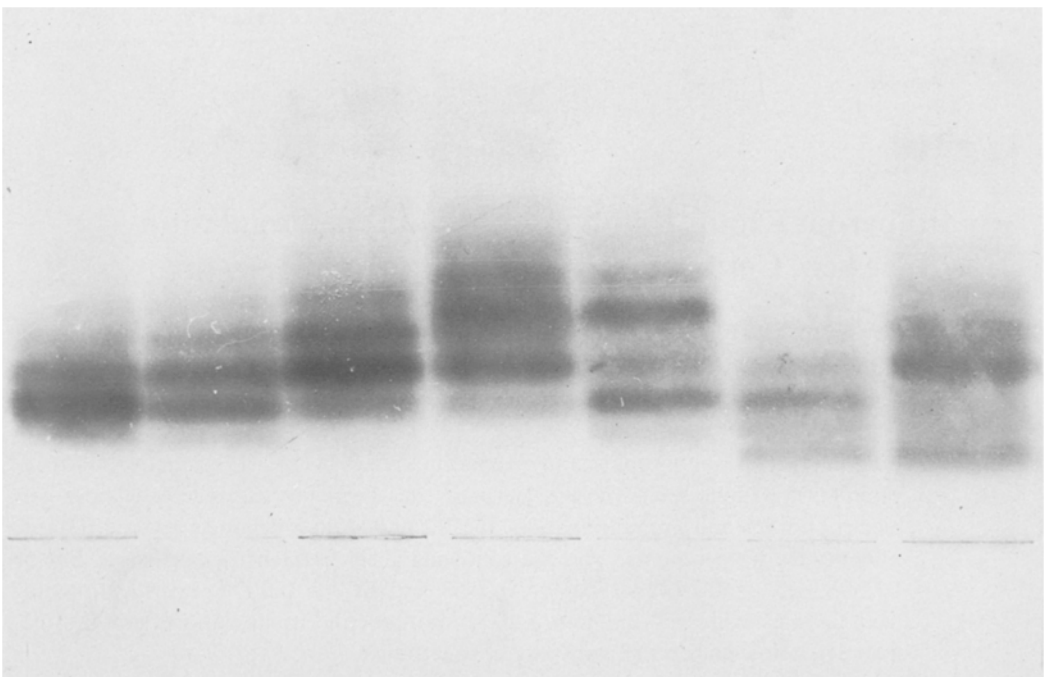

Fig. 1. Bf phenotypes after prolonged agarose gel electrophoresis and immunofixation. The anode is at the top. From left to right Bf S, FS, F, F1F, F1S, SS0.7 and FS0.7

Table 1. Bf phenotypes and allele frequencies in a random sample from Hessen

Phenotype	η obs	η (exp)	Allele frequencies
S	334	333.92	$Bf^S = 0.7998$
FS	150	147.96	$Bf^F = 0.1772$
F	14	16.39	$Bf^{S0.7} = 0.0163$
SS0.7	11	13.60	$Bf^{F1} = 0.0077$
FS0.7	5	3.02	
F1S	6	6.40	$\Sigma \chi^2 = 0.3849$
F1F	2	1.42	$0.50 < P < 0.70$ (ldf)[a]
	522	521.71	

[a] All heterozygous carriers of the Bf^{F1} or $Bf^{S0.7}$ allele were combined for χ^2 calculation

The distribution of Bf alleles appears suitable for an application of this polymorphism in selected cases of disputed paternity (Mauff et al., 1975). The present communication reports results of a population study in West Germany; they are compared with those of other authors. For the classification of our material we have adopted a new nomenclature for Bf allotypes based on the relative electrophoretic mobilities of all phenotypes which are not common S or F, using the distance S-F1 as reference (Mauff et al., 1977).

Table 2. Comparison of Bf allele frequencies in Caucasoid populations

Authors	η	Bf^S	Bf^F	$Bf^{S0.7}$[a]	Bf^{F1}	$Bf^{F1.55}$[a]	$Bf^{F0.55}$
Alper et al. (1972) (USA)	158	0.709	0.278	0.013	-	-	-
Mauff et al. (1975) (Western Germany)	1245	0.8084	0.1743	0.0092	0.0077	0.0004	-
Olaisen and Teisberg (1975) (Norway)	172	0.814	0.174	0.006	0.006	-	-
Rittner et al. (1975) (Western Germany)	82	0.8264	0.1492	0.0122	0.0122	-	-
Allen et al. (1976) (USA)	199	0.731	0.239	0.025	0.005	-	-
Scherz et al. (1977) (Switzerland)	654	0.805	0.176	0.009	0.010	-	-
Hauptmann et al. (1977) (France)	469	0.821	0.157	0.013	0.008	-	0.001
Bender et al. (1977) (Southwestern Germany)	325	0.8138	0.1600	0.0200	0.0062	-	-
This Paper (1977) (Hessen)	522	0.7998	0.1772	0.0163	0.0077	-	-

[a] According to the new nomenclature proposed by Mauff et al. (1977) the designations $Bf^{S0.7}$ and $Bf^{F1.55}$ are used for Bf^{S1} and $Bf^{F1.6}$ respectively

Table 3. χ^2 test of various Caucasoid population samples[a] (3df; $P < 0.05$; $\Sigma\chi^2 > 7.815$)

	Alper et al. USA	Olaisen et al. Norway	Mauff et al. Western Germany	Scherz et al. Switzerland	This paper Hessen
Alper et al. USA	-	10.46	22.93	19.11	18.53
Olaisen et al. Norway		-	0.84	1.75	2.09
Mauff et al. Western Germany			-	0.90	1.60
Scherz et al. Switzerland				-	0.63
This paper Hessen					-

[a] A statistically significant difference ($P < 0.05$) for 3df exists if the $\Sigma\chi^2$ value obtained by comparison of the phenotypes of two population samples exceeds 7.815. All heterozygous carriers of the $Bf^{S0.7}$ or Bf^{F1} allele were combined for χ^2 calculation (cf. Race and Sanger, 1975)

Material and Methods

Serum samples were obtained from 522 unrelated blood donors and 100 families with 198 children from Hessen. Some of the families and 30 mother-child combinations were investigated in the course of paternity testing, the samples being kept at −30°C for up to three months. Only cases with a biostatistical W-value (Essen-Moeller) above 99 % were included in the family material.

Bf typing was carried out by immunofixation after prolonged agarose gel electrophoresis (Alper et al., 1972, Teisberg, 1970) with minor modifications as described by Mauff et al. (1975). We used anti-human properdin factor B serum (goat) from Atlantic Antibodies Inc., Westbrook Maine, USA, or anti-C3 activator serum (rabbit) from Behringwerke, Marburg, Germany. The staining was performed with Coomassie Blue R 250 (Serva, Heidelberg, Germany) which proved to be superior to Amidoschwarz 10 B (Merck, Darmstadt, Germany).

Results and Discussion

In a total of 522 blood donors from Hessen four of the eight known Bf alleles in Caucasoids were observed. Besides the three common phenotypes S, FS and F the two heterozygous carriers of the $Bf^{S0.7}$ and Bf^{F1} allele are presented in Fig. 1. For the designation of Bf allotypes was applied the classification proposed by Mauff et al. (1977) at the EMBO workshop on the genetics of the complement system in Cambridge, England. After the redesignation the three 'old' allotypes F1.6, S0.8 and S1 are identical with F1.55, S0.45 and S0.7, respectively.

Bf S and F exhibit one major band with one equidistant cathodal and two anodal minor bands each, the phenotype Bf FS reveals a composite pattern with two major bands of approximately equal intensity and the minor bands of the F and S allele. The identification of the S0.7 or F1 heterozygotes was also easy. We performed retyping of several samples and observed no discrepancy in the results obtained on different occasions. Our results were also ascertained in a reinvestigation of the rare

Table 4. Distribution of Bf phenotypes in 100 families with 198 children from Hessen

Matings			η obs	Phenotypes of the Children								df	χ^2
				S	FS	F	SS0.7	F1S	FS0.7	F1F	Total		
S	X	S	43	85	-	-	-	-	-	-	85		
FS	X	S	32	33 (35.0)	37 (35.0)	-	-	-	-	-	70	1	0.2286
FS	X	FS	9	6 (4.5)	9 (9.0)	3 (4.5)	-	-	-	-	18	2	1.0000
F	X	FS	2	-	2 (2.0)	2 (2.0)	-	-	-	-	4	1	-
F	X	S	4	-	6	-	-	-	-	-	6		
S	X	SS0.7	2	2 (1.5)	-	-	1 (1.5)	-	-	-	3	1	0.3333
FS	X	SS0.7	2	1 (0.5)	1 (0.5)	-	- (0.5)	-	- (0.5)	-	2	3	2.0000
S	X	FS0.7	3	-	3 (2.5)	-	2 (2.5)	-	-	-	5	1	0.2000
S	X	F1S	2	2 (2.0)	-	-	-	2 (2.0)	-	-	4	1	-
FS	X	F1S	1	1 (0.25)	- (0.25)	-	-	- (0.25)	-	- (0.25)	1	3	3.0000
Total			100	130	58	5	3	2	-	-	198		

η obs = number observed; expected values in brackets

phenotypes by Dr. G. Mauff, Cologne. There was no evidence for the occurrence of a very rare allele $Bf^{F1.55}$, $Bf^{F0.55}$, $Bf^{S0.25}$, or $Bf^{S0.45}$ hitherto described in Caucasoid populations or any other new allele. F1.55 was found only once in 1245 persons by Mauff et al. (1975), F0.55 in about 700 different unrelated adults, S0.45 was also found once in Caucasoids without referring to the number of individuals tested (Hauptmann et al., 1976, 1977_a). S0.25 was observed recently in a Swiss woman and three of her children (Mauff et al., 1977).

Our results for Bf phenotypes provide a satisfactory fit to the Hardy-Weinberg equation ($0.50 < P < 0.70$ at ldf). The allele frequencies listed in Table 1 are in good accordance with the results obtained by other authors in European countries (Table 2). The differences of Bf^F and Bf^S within the four German investigations are below 2 % with the exception of Rittner et al. (1975) whose sample size is very small.

There is, however, a statistically significant difference to one of the two samples from USA, when the phenotypes are compared by the χ^2 test (Table 3) according to Race and Sanger (1975). In the second sample from USA, an intermediate Bf^F frequency is reported by Allen (1976). The deviating results observed in US whites may be explained by an admixture of the negro genome or other non-German ethnic groups as the Bf frequencies differ markedly between the three racial groups: Bf^F frequencies were found to be significantly higher in USA negroes (0.512) by Alper et al. (1972) and South African Bantu populations (0.655) by Mauff et al. (1976). Scherz et al. (1977) calculated a Bf^F frequency of 0.25 in an Italian population, indicating considerable differences between the various ethnic groups of Caucasoids.

The results of our family investigations are summarized in Table 4. In 100 families with 198 children the segregation pattern supports the assumed way of autosomal codominant inheritance, observed and expected values of the children's phenotypes differ only by chance. In 30 mother-child combinations no contradiction to the formal hereditary rules was observed.

Mauff et al. (1975) discussed the application of the Bf system in cases of disputed paternity and calculated a single exclusion chance of 14.4 %. The localization of the Bf locus in the major histocompatibility complex and the allelic association between certain Bf and HLA-B alleles has to be considered in the calculation of biostatistical opinion (Mauff et al., 1975, Kühnl et al., 1977 and Walther, 1977).

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