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Properdin Factor B-Polymorphism

An Indication for the Existence of a Bf^0-Allele

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Summary. The polymorphism of the properdin factor B (Bf, C3-proactivator, GBG = glycin-rich-β-glycoprotein) has been investigated by high voltage agarose gel immunofixation electrophoresis in 1115 unrelated persons from Southern Germany. Seven phenotypes were observed; the allele frequencies were calculated as $Bf^S = 0.8094$, $Bf^F = 0.1790$, $Bf^{S1} = 0.0094$, $Bf^{F1} = 0.0022$. A study of 94 parents with 98 children and 420 mother-child combinations showed no deviation from the assumed autosomal codominant mode of inheritance. In one additional family the findings suggested the existence of a silent allele at the Bf-locus.

Key words: Serum groups, properdin factor B, Bf-polymorphism, Bf^0-allele

Zusammenfassung. Unter Verwendung der Agarosegel-Hochspannungselektrophorese mit darauffolgender Immunofixation wurde der Polymorphismus des Properdin-Faktors B (Bf, C3-Proaktivator, GBG = Glyzin-reiches β-Glykoprotein) bei 1115 nicht verwandten Personen aus Süddeutschland untersucht. Sieben Phänotypen wurden beobachtet und folgende Allelfrequenzen berechnet: $Bf^S = 0{,}8094$, $Bf^F = 0{,}1790$, $Bf^{S1} = 0{,}0094$ und $Bf^{F1} = 0{,}0022$. Die Untersuchung von 94 Elternpaaren mit 98 Kindern und 420 Mutter-Kind-Verbindungen erbrachte keine Abweichungen vom angenommenen autosomal kodominanten Erbgang des Bf-Merkmals. In einer weiteren Familie ergab sich ein Hinweis für die Existenz eines stummen Allels auf dem Bf-Locus.

Schlüsselwörter: Serumgruppen, Properdin Faktor B, Bf-Polymorphismus, Bf^0-Allel

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The factor B of the properdin pathway for the human complement activation shows a genetically determined polymorphism (Alper et al., 1972). Three common phenotypes, Bf S, Bf FS, Bf F, and nine rare variants have been distinguished by the use of agarose gel electrophoresis (Alper et al., 1972; Mauff et al., 1975, 1976, 1978; Hauptmann et al., 1976, 1977).

Properdin factor B belongs to the immunogenetic linkage group which is localised on the short arm of human chromosome 6 (Allen, 1974). Allen (1974), Rittner et al. (1975), Albert et al. (1975), and Olaisen et al. (1975) have reported close linkage of the Bf locus to the HLA-B locus of the major histocompatibility gene complex. Further investigations (Albert et al., 1975; Olaisen et al., 1975; Bender et al., 1977) have shown the existence of a genetic linkage disequilibrium between Bf and certain HLA-B alleles (Bw5/Bf^F, B8/Bf^S, B18/Bf^{F1}, Bw21/Bf^{S1}). Up to now no information was available concerning the existence of a silent Bf-allele at the Bf-locus.

Material and Methods

Serum samples of 1115 unrelated persons from Southern Germany were obtained mainly from cases of disputed paternity. Samples were stored at −30° C for periods of up to one week prior to classification. Serum proteins were separated by high-voltage agarose gel electrophoresis (Teisberg, 1970). A Tris/barbital-buffer of pH 8.6 was used; the voltage was approximately 20 V/cm, the running time 3 h. The Bf-typing by immunofixation (Alper et al., 1969) with specific Bf-antiserum (goat) from Atlantic Antibodies Inc., Westbrook, Maine, USA was carried out subsequently. We used about 1 ml of antiserum for the investigation of 30 samples per plate. The electrophoretically separated Bf proteins were stained with Coomassie Brillant Blue R 250.

Results and Discussion

Table 1 shows the results of Bf-typing of 1115 unrelated persons from Southern Germany. There is good agreement between the observed and expected fre-

Table 1. Distribution of Bf-phenotypes and allele frequencies in Southern Germany

Phenotype		Observed		Expected		Allele frequencies	
		n	%	n	%		
Bf	S	735	65.92	730.44	65.52	Bf^S	0.8094
	FS	314	28.16	323.13	28.98	Bf^F	0.1790
	F	40	3.59	35.68	3.20	Bf^{S1}	0.0094
	SS1	18	1.61	16.94	1.52	Bf^{F1}	0.0022
	FS1	3	0.27	3.79	0.34		
	F1S	3	0.27	4.01	0.36	$Bf^{S1} \triangleq Bf^{S0.7}$	
	F1F	2	0.18	0.89	0.08		
Total		1115	100.00	1114.88	100.00		

$\Sigma\chi^2 = 0.8054$,
$df = 3$, $P > 0.20$

Table 2. Distribution of Bf-phenotypes in 420 mother-child combinations

Mothers		Children							
		BfS	FS	F	SS1	FS1	F1S	F1F	Total
Bf	S	214 (220.12)	51 (48.63)	—	5 (4.68)	—	2 (1.10)	—	272
	FS	45 (48.63)	62 (59.35)	8 (10.71)	1 (1.50)	—	1 (0.22)	—	117
	F	—	20 (10.71)	1 (2.35)	—	—	—	—	21
	SS1	3 (4.68)	1 (1.50)	—	4 (2.15)	1 (0.58)	—	—	9
	FS1	—	—	—	—	—	—	—	—
	F1S	—	—	—	—	—	—	1 (0.14)	1
	F1F	—	—	—	—	—	—	—	—
Total		262	134	9	10	1	3	1	420

In brackets are the expected values corresponding to the Hardy-Weinberg equilibrium

Table 3. Distribution of Bf-phenotypes in 94 parents with a total of 98 children

Parents		Children							Total
		BfS	FS	F	SS1	FS1	F1S	F1F	
S×S	37 (40.3)	37 (37)	—	—	—	—	—	—	37
S×FS	31 (37.9)	16 (17)	18 (17)	—	—	—	—	—	34
S×F	5 (4.5)	—	5 (5)	—	—	—	—	—	5
FS×FS	14 (8.9)	3 (3.75)	10 (7.5)	2 (3.75)	—	—	—	—	15
S×SS1	2 (1.6)	—	—	—	2	—	—	—	2
S×FS1	1 (0.4)	—	—	—	1	—	—	—	1
S×F1S	1 (0.6)	—	—	—	—	—	1	—	1
FS×SS1	1 (0.4)	1	—	—	—	—	—	—	1
FS×F1F	1 (<0.1)	—	—	—	—	—	1	—	1
F×SS1	1 (<0.1)	—	—	—	—	—	1	—	1
Total	94	57	33	2	3	0	3	0	98

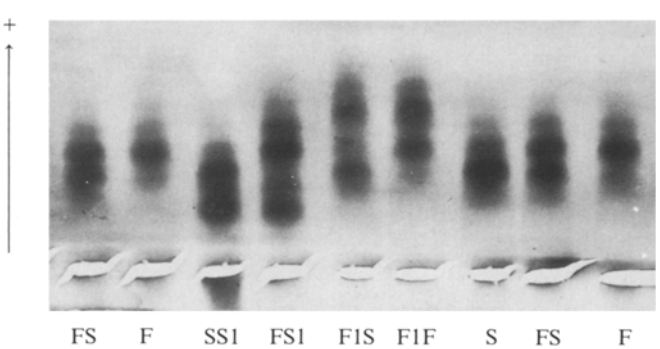

Fig. 1. Observed Bf-phenotypes after agarose gel immunofixation electrophoresis

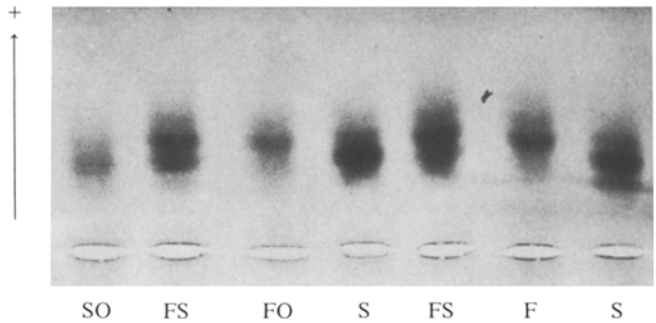

Fig. 2. Bf-phenotypes of the family St. From left to right: daughter B. Bf SO, son Ch. Bf FS, father Bf FO and mother Bf S. The three normal Bf types FS, F and S are shown for comparison

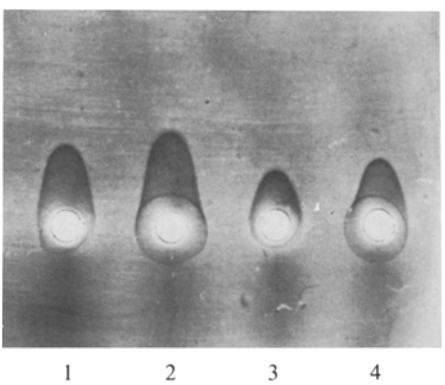

Fig. 3. Semiquantitative determination of properdin factor B by rocket immunoelectrophoresis. From left to right: mother H.St. (1), son Ch. (2), daughter B. (3) and father A.St. (4)

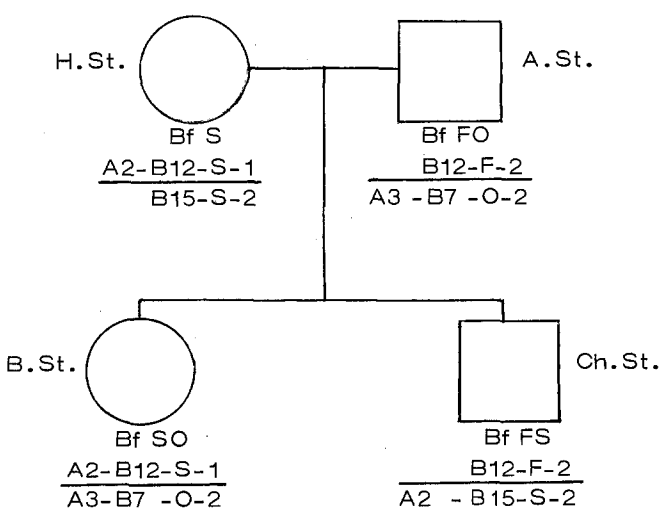

Fig. 4. Haplotypes (HLA-A, HLA-B, Bf, GLO) of the family St. on chromosome 6

quencies of phenotypes assuming Hardy-Weinberg equilibrium. The allelic frequencies are similar to those observed by other authors in Europeans (Mauff et al., 1975; Teisberg and Olaisen, 1977; Scherz et al., 1977; Kühnl and Spielmann, 1978). Figure 1 shows the seven phenotypes as observed by agarose gel electrophoresis and immunofixation. The allelomorphic bands are of nearly equal density, and the distance between components is always about the same. Even the distance F1→S is similar to the distance F→S1.

Tables 2 and 3 show the results of the examination of 420 mother-child combinations and of 94 parents with a total of 98 children. The mother-child combinations and the data of the families did not show any deviations from the expected distribution of phenotypes assuming an autosomal codominant mode of inheritance of the Bf-alleles. Mother-child exclusions as an indication for the existence of a silent gene have not been found.

In one family St. from the genetic counseling service unusual findings were obtained. The patient, a girl with Vitamin-D resistant rachitis, was examined together with her healthy parents and her unaffected brother. The girl had retarded growth, hypophosphatemia, and hyperphosphaturia. The findings suggested the existence of a Bf°-allele at the Bf-locus. Figure 2 shows the phenotypes of the parents and their two children together with the three normal Bf-types. The examined sera samples had the same age and were treated in the same way. Equal quantities of sera were applied on filter paper (Whatman Nr. 3). The father (apparent type Bf F) would have to be excluded as biological father of his daughter who apparently has the type Bf S. In the immunofixation agarose gel electrophoresis pattern the Bf-bands of both persons, however, were weaker than in normal phenotypes. This observation was confirmed in several repeat runs. Also semiquantitative estimation by rocket immunoelectrophoresis indicated low levels of Bf-components in the father as well as in the daughter (Fig. 3). The properdin factor B level in the serum of the father appears to be reduced to 70% of normal, in the daughter to 60% of normal. Figure 4 shows the haplotypes (HLA-A, HLA-B, Bf, GLO) of the family St. Twenty-three further blood, serum, and enzyme systems were tested in this family which routinely are examined in cases of disputed paternity. In none of the systems exclusion of parenthood was observed. The probability of the examined father for being indeed the biological father was calculated to be 99.5%. It is, therefore, very probable that he is, in fact, the father. Extension of the investigation to further family members of the father was not possible. The findings were interpreted as being due to a silent allele Bf° at the Bf locus. A relation between the findings in the Bf-system and the Vitamin D-resistant rickets with retarded growth present in the daughter appears most unlikely, since the father is unaffected and of normal height.

We applied classification of Bf-types in a total of 192 cases of disputed paternity; 17 exclusions were noted.

This result corresponds to an exclusion rate of 8.8%, while the theoretically expected exclusion rate is 13.5%.

The Bf-system is thus informative, the method of determination is practicable and classification results are highly reproducible. Bf phenotypes are, furthermore, fully expressed at birth. The system appears to be useful for analyses of cases of disputed paternity. The existence of a rare silent allele Bf°—which is suggested by our findings—would, however, limit its usefulness.

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