Transferrin Polymorphism in Korean

Ⅰ. Phenotypic Distribution of Tf in Jeju-do Population

Moon-you Oh

韓國人에서의 Transferrin(Tf) Polymorphism에 관한 硏究

Ⅰ. 濟州島人 集團에서의 Tf의 表現型 分布에 대하여

吳 文 儒

Summary

Genetic Polymorphim of transferrin (Tf) in Jeju-do (Korea) population was studied by prolonged isoelectric focusing (PAGIF) of human sera on polyacrylamide gels. In these samples (n=364) three common phenotypes, TfC1, C2-1, and C2, were observed only, and the alles frequences were calculated as following; TfC1=0.7198, TfC2=0.2802. Heterogeneous rate was 0.4066.

Introduction

Transferrin(Tf or Tr) was discovered by Homberg and Laurell in 1945 and independently by Schade and Caroline in 1946(Putnam. 1975). The function of transferrin is transportation of iron from blood to tissues and is regulation and control of iron absorption and protects against iron intoxication. And transferrin is returned to the circulation after unloading its iron in the reticuloendothelial system. When saturated with iron, transferrin has a pinkish color. Since transferrin normally is only about 30% saturated with iron, serum changes from yellow to yellow-red on the addition of ferrous iron.

When it was discovered, the common form of transferrin was transferrin C because it was originally detected as the third component in the beta-globulin region in starch gel electrophpresis of human serum(Smithies 1957, 1958, Horsfall and Smithies 1958). When the first transferrin variant was discovered in the serum of Negroes and Australian Aborigines, it was named tranaferrin D because of its slower mobility.

Many authors have been reported the genetic polymorphism and geographic distribution of human transferrins. Sutton and Jamieson(1972) are the most recent to review the chemistry and physical properties of transferrins. Recently, Beckman et al(1980) presented the results of a study of the relatioship between transferrin C subtypes and spontaneous abortion.

A listing of human transferrin variants in order of decreasing mobility based on a summary by Giblett(1975) is given in Table 1(Plasma

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Proteins Vol. 1, p. 297).

Fig. 1, from Sutton and Jamieson(1972) gives a diagramatic representation of the mobilities in starch gel electrophoresis of 21 of the variants (Plasma Proteins. Vol. 1, p. 298).

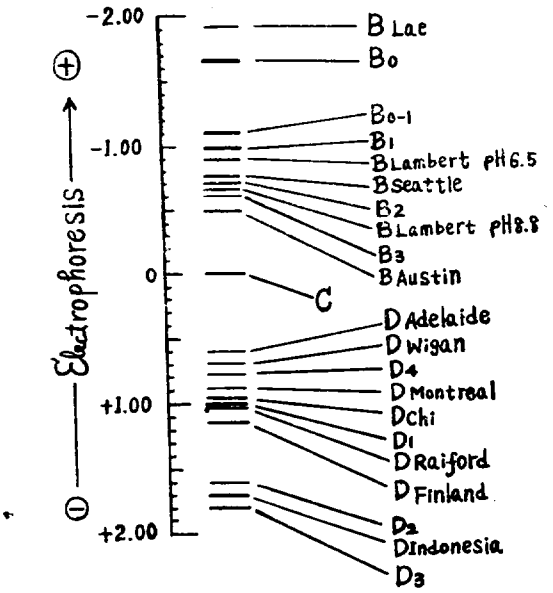

Fig. 1. A diagram showing the relative electrophoretic mobilites of the inherited variants of human transferrin (Reproduced from Putnam 1975).

Table 1. Genetic variants of human Transferrins**

Transferrin	Source of first sample
BLae	New Guinea native
BGoldsmith	India(Goldsmith population)
BO-1	Amercan White
BO-1	Navajo Indian
BAtlanti	Greek White
B1	English White
BLambert	American White
B1-2	Italo-African
BMadiga	India(Madiga population)
B2	Canadian White
B3	Japanese
C1	German White
C3	German White
C2	German White
DAdelaide	Australian White
Do	American Black
DWigan	English White
Do-1	English White
DMontreal	Canadian White
DChi	Chinese
D1	American Black
DFinn	Finnish White
D2	African Black
D3	American Black

** The transferrins are listed in order of increasing electrophoretic mobility(i.e., BLae has the fastest migration rate). (Modified from Table V. of Putnam, 1975)

And recently, two common subtypes of the Tf C allele were explained as Tf C1, C2 by Kuehnl and Spielmann(1978) after isoelectric focusing of sera on polyacrylamide gels. And in their study, the distribution of the phenotypes Tf C1, C2—1, and C2 provided a good fit to the Hardy-Weinberg Equation.

In 1979, Kuehnl and Spielmann revealed further genetic heterogeneity of the transferrin system (Tf) by prolonged focusing(PAGIF) of human sera on polyacrylamide gels (pH 4-6.5), and one of the two common subtypes of Tf C, designated previously as Tf C1, was split into Tf C1 and the new subtype, Tf C3. The gene product of Tf C3 had an isoelectric point between C1 and C2.

In this work, the author report the result of the study on transferrin polymorphism in Jeju-do population by the method of isoelectric focusing of sera on the thin layered polyacrylamide gels (PAGIF) as recommended by LKB, Bromma, Sweden(LKB application note 75 supplied with the Multiphor apparatus) with some modifications.

Materials and Methods

The thin layered gels(1㎜) were prepared as followings; 3.75 ㎎ of sucrose were dissolved in 19.5㎖ of distilled water. 4.0㎖ of 29.1% acryl-

amide solution(Eastman), 4.0㎖ of 0.9% N, N'-methylene bisacrylamide solution(Eastman), and 0.4㎖ of Ampholine carrier ampholytes, pH 4~6, and of 1.1㎖ pH 5~7 were added to the mixture. The mixture was stirred and after addition of 0.01 ㎖ of N, N, N', N'-tetramethylethylene diamine (TEMED, Eastman) it was deaerated, and 1㎖ of 1% ammonium persulfate was added. The solution was filled into the gel mold with a plastic syringe. After complete polymerization which took approximately 60min. at room temperature(20~25℃), the gels were stored at 4℃ overnight and used next morning. Ammonium persulfate was made freshly, and the acrylamide and the bisacrylamide solutions were made freshly every two weeks.

Isoelectric focusing was made as following; one strip of filter paper(10×240㎜ Whatman No.17 Chromatography paper) soaked in 1N phosphoric acid was placed at the anodal electrode and four strips of filter paper soaked in 1N NaOH were used as cathodal electrode. The power supply was set at 1,000V and 50mA, prerun was performed for 90min. After the prerun, filter papers(6×10㎜ Schleider and Schull grade 270 paper)soaked in the serum samples were put on the middle of the gel, or at 3㎝ apart from the cathodal electrode filter paper, and the run was continued for 30min. The filter papers were removed and the main run was continued for 60min. at 1,000V, then the voltage was increased to 1,200 and the focusing was continued for 120min.

After the focusing, the gels were stained for 30min. with Coomassie brilliant blue solution prepared with 400㎖ of distilled water in which 72g of trichloracetic acid and 22g of sulfosalicylic acid and 100㎖ of methyl alcohol containing 0.6g of Coomassie brilliant blue(Sigma) were dissolved. During the stain the solution was kept at 60℃~65℃. Then the gels were destained in the solution containing of 750㎖ of ethyl alcohol, 240㎖ of glacial acetic acid, and 1950㎖ of distilled water. The destaining solution was changed for several times. Serum samples were collectel from 364 unrelated healthy individuals in Jeju-do, and were kept in −20℃.

Results and Discussion

After PAGIF pH range 3.5~9.5, three common subtypes of Tf C (Tf C1, Tf C1—C2, Tf C2)

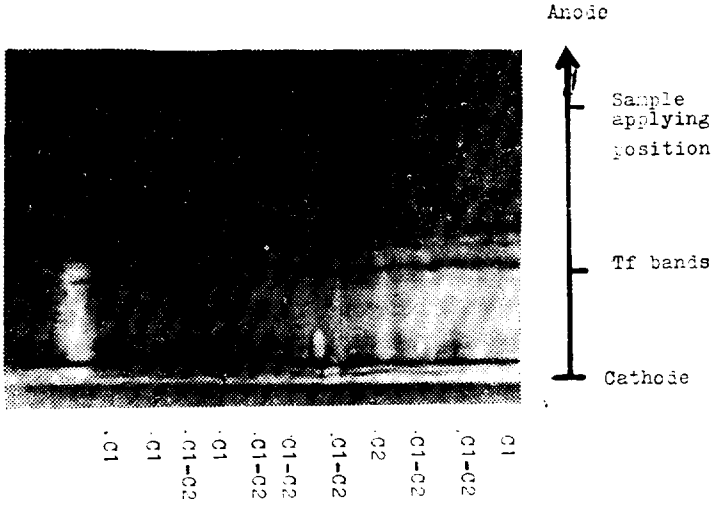

Fig. 2. Transferrin patterns obtained by the isoelectric focusing.

Table 2. Transferrin polymorphism

Countries or populations	Number total	Number C1	Number C1	Number C1 C2	Number C2	Variants	Allele Frequencies C1	Allele Frequencies C2	Allele Frequencies Variants	Author	Year
Korea	120		119			CD1;1				Shim	1964
〃	487		478			CBKoreal CBKorea2				Kirk et al	1978
〃	364	188		148	28		C1;0.7198 C2;0.2802			Oh	1980
Chinese	116		109			CDChinese;7			DChi;0.030	Parker et al	1961
Japanese	46		45			B3D;1				〃	〃
〃	240									Kirk et al	1978
〃	4,020		3,936			CDChi;47 CDHir 1;2 CDHir 2;2 CDHir 3;3 CDNGS 1;1 CB 3;9 CBHir 2;19 CBHir 4;1				Ferrell et al	1977
Congo(Pygmies)	99		93			CD1;6	C=0.939		CD1=0.061	Giblett et al	1966
〃 (Tsui, Hutu)	113		100			CD1=13	C=0.925		CD1=0.075	〃	〃
Liberia	333		308			CD1;25	C; 0.925		CD1; 0.069	〃	〃
Nigeria											
Fulani	111		104			CD1;7	C; 0.937		CD1; 0.063	〃	〃
〃	67		57			CD1;10	C; 0.838		CD1; 0.147	〃	〃
Habe	120		102			CD1;18	C; 0.850		CD1; 0.150	〃	〃
Ibo	70		61			CD1;9	C; 0.872		CD1; 0.128	〃	〃
Gambia	157		153			CD1;4	C; 0.975		CD1; 0.025	〃	〃
Uganda(Baganda)	165		160			CD1;5	C; 0.970		CD1; 0.030	〃	〃
(Misc. Bantu)	26		26				C; 1.0				
Tanganyika(Bondi)	60		55			CD1;5	C; 0.917		CD1; 0.083	〃	〃
Kenya(Masai)	50		50				C; 1.0				
South Africa, Zulu	116		113			CD1;3	C; 0.974		CD1; 0.026	〃	〃
〃 ,Hottentot	59		55			CD1;4	C; 0.933		CD1; 0.067	〃	〃
〃 ,Bushmen	113		99			CD1;14	C; 0.876		CD1; 0.124	〃	〃
〃 ,Colored	88		86			CD1;2	C; 0.977		CD1; 0.023	〃	〃
North Afrfca											
Negro	952		874			CD1;78	C; 0.919		CD1; 0.081	〃	〃

Greece	649		645			CDChi, CD1 CB1-2, CBAtlanti				Blumberg et al	1964
Germany	942	631		269	27	C1B2;10 C1B1-2;3 C2B2;1	0.8195	0.1720	B2;0.0064 B1-2;0.0016 D1;0.0005	Kuehnl et al	1978
		(1-1)		(2-1)	(2)	B2D1;1					
〃	515	17		139	356	3-1;1	Tf1;0.1689		Hpa3;0.0029	Kuehnl et al	1977
		(C1)	(C3-1)	(C3)	(C3-2)	3-2;2	Tf2;0.8282				
〃(Hessen)	252	158	17	1	2	C1B2;4	C1;0.795		B2;0.008	Kuehnl et al	1979
		(C2-1)		(C2)			C2;0.155				
		64		6			C3;0.042				
Danish	132	7		35	90		Tf1;0.18516 Tf2;0.8144			Thymann	1978
Belgium	253	160		81	12		C1;0.792	C2;0.208		Hoste	1979
U.S. White	149	99		40	7	C1B2;1 C2D2;1 C2B2;1	C1;0.802	C2;0.188	B2;0.007 D2;0.003	Kueppers et al	1979
U.S. Black	166	115		35	1	C1D1;15	C1;0.843	C2;0.111	D1;0.045	Kueppers et al	1979
South American Indians										Tanis et al	1973
Yanomama	982	982								〃	〃
Makiritare	186	186								〃	〃
Piaroa	146	146								〃	〃
Makushi	188	188								〃	〃
Wajana(Surinam)	279	279								Geerdink et al	1974
Trio (〃)	413	413								〃	〃
Canada Eskimo	67	67								Parker et al	1961
N·Y. Negro	99	89				CD1;9				〃	〃
						D1D1;1	C;0.944		D1;0.056	〃	〃
Sapelo Negro	38	28				CD1;10	C;0.868		D1;0.132	〃	〃

could be distinguished (Kuehnl and Spielmann 1978). The more anodal set was called Tf C2, when both sets (two bands) were present, the phenotype was called Tf C1—C2. In this study the same patterns were appeared. The transferrin patterns obtained by isoelectricfocusing are shown in Fig. 2.

The allele freuqencces Tf C1=0.7198, Tf C2= 0.2802 (Table 3). As in Table 3 Hardy-Weinberg equilibrium was quite fit. Comparing with other populations (Table 2), the allele frequency of Tf C1 was the lowest(0.7198) among them(Germany; 0.7995~0.8195, Belgium; 0.792, U. S. White; 0.802, U. S. Black; 0.843), while the allele frequency of Tf C2 was the highest (0.2802) (Germany; 0.155~0.1720, Belgium; 0.208. U. S. White; 0.188, U. S. Black; 0.111). I was regreted that I couldn't compare this result with other Asian populations because of the shortage of references.

Table 3. Allele frequencies of transferrin of Jeju-do population.

	Total	C1	C1C2	C2
Percent	100.00	51.65	40.66	7.69
Obs.	364	188	148	28
Exp.	364	188.59	146.83	28.58

$X^2=0.02294$ $0.95<P<0.99$

Gene frequencies: C1=0.7198
C2=0.2802

Heterogeneous rate; 0.4066

Acording to the study of Kuehnl and Spielmann (1979), they could detect seven phenotypes; Tf C1, C2-1, C2, C3-1, C3-2, C3 and C1B2, by prolonged isoelectric focusing and increased voltage (4.5 hr, 1.800V).

In this study the focusing was prologed for 5hr. but maximum voltage was 1,200 (for last 2hr). I couldn't detect any other variants besides 3 common phenotypes; Tf C1, C1-C2, and C2.

The highest frequencies of the C2 gene were found in Japanese (0.26) and Chinese (0.20), and the lowest in Africans(0.05) (Beckman et al 1980). In the frequency of the Tf C2 gene, Japanese population (0.26) and Jeju-do population (0.28) are quite near. The author found the similar result in the study on Gc (Group-Specific Component), too. It would be possible to explain that Jeju-do population and Japanese population are similar to each other.

Shin(1964) reported an example of D1 variant in Korean population from the analysis of 120 serum samples by means of starch gel electrophoresis. But I couldn't detect any other variants, besides common Tf phenotypes from 364 serum samples of individuals in Jeju-do population. Further studies are needed to detect variants from this population.

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〈國文抄錄〉

韓國人에서의 Transferrin(Tf) Polymorphism에 관한 硏究

濟州島人 集團에서 Polyacrylamide gel isoelectric focusing 方法을 利用하여 Serum中의 Transferrin polymorphism에 관한 硏究에서 다음과 같은 結果를 얻었다.

1. 濟州島人 集團에서의 (n=364) Transferrin subtype은 TfC1, C2-1, C2의 3가지이었다.
2. 各 Subtype의 分布는 TfC1; 188명(51.65%), C2-1;148명(40.66%), C2;28명(7.69%)의 순서를 나타내었다.
3. Allele frequency는 TfC1=0.7198, TfC2=0.2802로서 他集團에 비해서 TfC1은 낮은 反面 TfC2는 높았다.
4. Heterogeneous rate는 0.4066이었다.