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GENETIC POLYMORPHISM OF HUMAN FACTOR H (HF, β1H GLOBULIN) IN CHINESE HAN POPULATION IN NORTHEAST CHINA*

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Summary The distribution of human factor H of serum phenotypes were studied using ultrathin polyacrylamide gel isoelectric focusing (PAGIEF) and subsequent immunoblotting techniques in 203 Chinese of Han population in Liaoning Province of northeast China. The gene frequencies of HF*A and HF*B were 0.4828 and 0.5172, respectively. All the observed numbers of the phenotypes were in agreement with the expected numbers under the Hardy-Weinberg equilibrium. The gene frequencies among Chinese, Japanese, and Caucasian populations were compared.

Key Words polymorphism, human factor H, Chinese Han population

INTRODUCTION

Human factor H (HF, formerly β1H) is a cofactor in the complement system, which binds specifically C3b and promotes its cleavage by factor I. Factor H, a single polypeptide-chain plasma glycoprotein of M.W. 160,000, also displaces C3b from Bb, the major fragment of factor B, and regulates the decay of convertase C3bBb in the alternative pathway (Whaley and Ruddy, 1976; Pangburn *et al.*, 1977). Genetic polymorphism of human factor H was first detected after neuraminidase treatment and isoelectric focusing (IEF) under completely denaturing conditions. Three HF phenotypes, HF1, HF2, and HF3 were found, which have been postulated to be determined by autosomal codominant alleles (Rodriguez de

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Cordoba and Rubinstein, 1984).

In the present study, we report the distribution of phenotypes and gene frequencies of HF in Chinese Han population in Liaoning Province of northeast China. The excluding probability of paternity (E.P.P.) for forensic genetics was calculated based on gene frequencies of the present results. Some ethnic differences in the polymorphism of HF were also discussed.

MATERIALS AND METHODS

A total of 203 serum samples were obtained from unrelated healthy blood donors living in Liaoning Province of northeast China, and stored at −30°C until their use. The typing of HF was achieved by ultrathin polyacrylamide gel isoelectric focusing (PAGIEF), of which recipe was T=5%, C=3%, 8 mol/liter urea and 2.0% Ampholine pH range being 3.5–9.5 (Pharmacia, Sweden).

Electrode solutions of PAGIEF were 1 mol/liter H_3PO_4 for the anode and 1 mol/liter monoethanol-amine (MEA) for the cathode. Samples were applied 1.5 cm from the anodal end of a gel. Electrical running was carried out at a constant temperature of 6°C on a multiphor apparatus (LKB, Sweden) at a constant power of 3 W, maximum voltage of 2,000 V and current of 20 mA. Electric focusing was performed for 1 hr with sample strips, and continued for another 3 hr or more without the strips.

Immunoblotting procedures were in the similar manner as for C6 and C7 phenotyping (Tokunaga *et al.*, 1986). Focused proteins in the gel were transferred to a sheet of nitrocellulose membrane by pressing. Anti-human HF goat antiserum (ICN ImmunoBiologicals, USA) diluted 1:500 with 0.05% Tween 20 in Tris-NaCl buffered saline (TTBS, pH 7.5) was used as the first antibody and a peroxidase conjugated anti-goat immunoglobulin (Seikagaku Kogyo, Tokyo) diluted 1:1,000 with TTBS was used as the second antibody. Immune complexes formed on the nitrocellulose membrane were detected with 4-chloro-1-naphthol and H_2O_2.

RESULTS

After PAGIEF and subsequent immunoblotting, three HF phenotypes explained by the 2 alleles HF*A and HF*B were observed. No new rare variants were encountered in the present study. In Table 1 the results of the population study of HF in 203 unrelated Chinese Han blood donors living in Liaoning Province of northeast China are presented. All values of the observed and expected did not differ significantly each other on the assumption of a Hardy-Weinberg equilibrium.

Based on the gene frequencies of HF in the present study, the E.P.P. in Liaoning Han population was calculated as 0.1847.

Table 1. The distribution of phenotypes and gene frequencies of HF in Chinese Han population in Liaoning Province.

Phenotype	Observed		Expected		Gene frequency
	No.	%	No.	%	
HF A	53	26.11	47.32	23.31	HF*A=0.4838
HF B	60	29.56	54.30	26.75	HF*B=0.5172
HF AB	90	44.33	101.38	49.94	
Total	203	100.00	203.00	100.00	
		(χ^2=1.34, d.f.=2, 0.50<p<0.75)			

Table 2. The comparison of HF gene frequencies in various populations.

Population	Number	Gene frequency			Author
		HF*A	HF*B	Other	
Chinese	203	0.4828	0.5172	—	This paper
Japanese	536	0.4261	0.4895	0.0844	Nakamura *et al.*, 1990
Caucasian					
North American	81	0.691	0.302	0.006	Rodriguez de Cordoba S *et al.*, 1984
German	152	0.419	0.424	0.157	Luckenbach *et al.*, 1988

DISCUSSION

PAGIEF and subsequent immunoblotting has become a standard tool in the determination of a wide variety of serum types including HF, C6, C7, and $C8_1$. As to the nomenclature of HF, there are the numeric system (Rodriguez de Cordoba and Rubinstein, 1984) and the alpha-numeric system (Nakamura *et al.*, 1990). HFA (FH1), HFB (FH2), HFAB (FH1, 2), HFAM (FH1, 3) and HFBM (FH2, 3) are five common phenotypes which are encoded by three different co-dominant alleles, HF*A (FH*1), HF*B (FH*2), and HF*M (FH*3). Recently other rare phenotypes such as HFA1B, A1, A1A, and Q0 have been reported (Nakamura *et al.*, 1990). In the present study we have found three common phenotypes, *i.e.* HFA (FH1), HFB (FH2), and HFAB (FH1, 2), and no new rare variations of HF phenotypes were encountered.

According to the gene frequencies of HF in the present study, the E.P.P. in Liaoning Han population was found to be 0.1847. This value is similar to those of such serum types as C6 (0.2189), C7 (0.1608), and $C8_1$ (0.1859) *etc.* (Pang *et al.*, 1992). Since the E.P.P. value of HF has been reported as 0.131 in Japanese (Nakamura *et al.*, 1987), typing of HF in a paternity test is more significant in Chinese Han population than in Japanese.

The comparison of some reported gene frequencies of HF in Japanese (Nakamura *et al.*, 1990) and Caucasian (Rodriguez de Cordoba *et al.*, 1984; Luckenbach *et al.*, 1988) are listed in Table 2. It indicated that the present gene frequencies of HF are almost similar to those for Japanese and German ($p > 0.05$), while a marked difference is noted for North American population ($p < 0.05$).

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