

GENETIC POLYMORPHISMS OF OROSOMUCOID AND ALPHA-2-HS-GLYCOPROTEIN IN THAI, SRI LANKAN AND PARAGUAYAN POPULATIONS

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Summary The genetic polymorphism of orosomucoid (ORM) and alpha-2-HS-glycoprotein (AHSG) were studied in Thai, Sri Lankan and Paraguayan populations using isoelectric focusing. Gene frequencies in these populations were compared with those in other populations. Four new ORM variants were detected: *ORM1*15* in Thai, *ORM1*16* in Paraguayan, *ORM2*21* and *ORM2*22* in Sri Lankan.

Key Words polymorphism, serum type, ORM1, ORM2, AHSG

INTRODUCTION

Genetic polymorphism of human serum orosomucoid (ORM) was described by Johnson *et al.* (1969) using agarose gel electrophoresis followed by immunofixation. ORM polymorphisms have recently been studied using isoelectric focusing (IEF), and some variant alleles have been reported at two structural loci, ORM1 and ORM2 (Tsuge *et al.*, 1987; Weidinger *et al.*, 1987; Yuasa *et al.*, 1988; Umetsu *et al.*, 1989). In ORM1 locus, two duplicated alleles (*ORM1*2.1* and *ORM1*5.2*) have also been described (Yuasa *et al.*, 1987, 1988). The detection of the variant alleles are

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mainly due to the high resolving power of IEF in polyacrylamide gels containing Triton X-100 (Umetsu *et al.*, 1987).

Alpha-2-HS-glycoprotein (AHSG) polymorphism was first described by Anderson and Anderson (1977) using two-dimensional electrophoresis. Cox and Andrews (1983) and Umetsu *et al.* (1983) applied one-dimensional IEF to AHSG phenotyping and confirmed two common alleles (*AHSG*1* and *AHSG*2*). Since then, several variants have been identified, as summarized by Yuasa and Umetsu (1988).

The population studies of genetic polymorphisms of ORM and AHSG have been reported, and several alleles were known as specific genetic markers: *ORM1*3* and *AHSG*3* are for Caucasians, *ORM2*6* for Mongoloids, *AHSG*5* for Japanese, and *AHSG*10* for Blacks.

In the present work, we report distributions of ORM1, ORM2 and AHSG allele frequencies in Thai, Sri Lankan and Paraguayan populations and four new ORM variants were found in these populations.

MATERIALS AND METHODS

Serum samples of 709 unrelated individuals from three populations (369 from Thai, Chiang Rai; 140 from Sri Lankan, Peradeniya; 200 from Paraguayan, Asuncion) were tested for ORM and AHSG typing. The ORM typing was carried out by polyacrylamide gel IEF followed by immunoprinting (Yuasa *et al.*, 1986; Umetsu *et al.*, 1989). The AHSG typing was carried out by polyacrylamide gel IEF followed by immunoblotting (Yuasa and Umetsu, 1988).

RESULTS

ORM polymorphism

In 709 serum subjects ORM1 patterns were classified into nine known phenotypes (1, 2-1, 2, 3-1, 3-2, 2-1-1, 2-1-2, 5-2-1, 5-2-2) and two new rare phenotypes. Two new phenotypes were considered to be controlled by two rare ORM1 alleles, and these alleles were tentatively designated *ORM1*15* and *ORM1*16*, respectively. The ORM1 15 band appears between the ORM1 8 and ORM1 4 band, and ORM1 16 band migrates between the ORM1 7 and ORM1 10 band (Fig. 1). The results of ORM1 phenotyping and allele frequencies in Thai, Sri Lankan and Paraguayan populations are shown in Table 1. The distributions of ORM1 phenotypes were in a state of equilibrium based on the Hardy-Weinberg law in each of these populations (Thai, $\chi^2=0.1622$, $df=1$, $0.50 < p < 0.70$; Sri Lankan, $\chi^2=0.5227$, $df=1$, $0.30 < p < 0.50$; Paraguayan, $\chi^2=0.0500$, $df=1$, $0.70 < p < 0.80$).

On the other hand, ORM2 patterns were classified into three known phenotypes (1, 3-1, 6-1) and two new rare phenotypes. Two new phenotypes were considered to be controlled by two rare ORM2 alleles, and these alleles were tentatively designated *ORM2*21* and *ORM2*22*, respectively. The ORM2 21 band appears

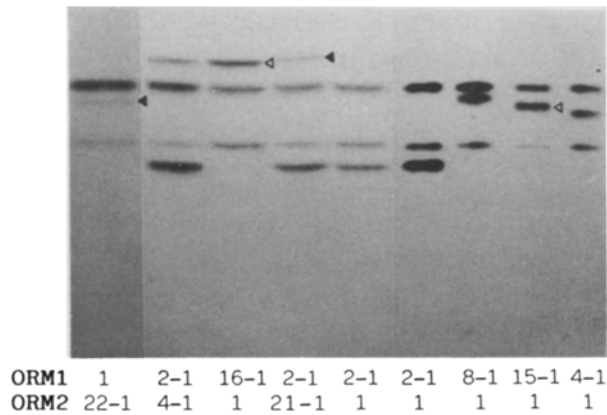


Fig. 1. Immunoprinted band patterns of several ORM types after isoelectric focusing. Anode at the top. Open and closed triangle indicate new ORM1 and ORM2 variant band, respectively.

Table 1. Distribution of ORM1 phenotypes and allele frequencies in Thai, Sri Lankan and Paraguayan populations.

Phenotypes	Thai		Sri Lankan		Paraguayan	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
1	242	244.5	68	68.5	83	83.2
2-1*	100	96.9	55	52.5	80	79.3
2	9	9.6	8	10.0	18	18.9
3-1	0	18.0	0	9.0	7	18.6
3-2	0		0		2	
2-1-1	16		4		4	
2-1-2	1		2		5	
5-2-1	0	18.0	1	9.0	0	18.6
5-2-2	0		2		0	
15-1	1		0		0	
16-1	0		0		1	
Others	0		0		0	
Total	369	369.0	140	140.0	200	200.0
Allele frequencies						
ORM1*1	0.8140		0.6996		0.6448	
ORM1*2	0.1610		0.2675		0.3073	
ORM1*3	0		0		0.0225	
ORM1*2-1	0.0236		0.0221		0.0230	
ORM1*5-2	0		0.0107		0	
ORM1*15	0.0014		0		0	
ORM1*16	0		0		0.0025	

Obs., observed; Exp., expected. *, including two ORM1 (2/1 and 2-1/2-1) genotypes.

between the ORM2 14 and ORM2 4 band, and ORM2 22 band migrates at a slightly cathodal position to ORM2 2 (Fig. 1). The distribution of ORM2 phenotypes and allele frequencies are shown in Table 2.

AHSG polymorphism

In 709 serum subjects, three common phenotypes, AHSG 1, 2-1 and 2, and four variant phenotypes, 3-1, 3-2, 10-1 and 10-2, were identified, which have been described previously (Yuasa and Umetsu, 1988). The distribution of AHSG phenotypes and allele frequencies in Thai, Sri Lankan and Paraguayan populations are shown in Table 3. The observed and the expected values provide a good fit to

Table 2. Distribution of ORM2 phenotypes and allele frequencies in Thai, Sri Lankan and Paraguayan populations.

Populations	n	Phenotypes				
		1	3-1	6-1	21-1	22-1
Thai	369	363	0	6 ^a	0	0
Sri Lankan	140	136	1 ^b	0	1 ^c	2 ^d
Paraguayan	200	200	0	0	0	0

Allele frequencies: Thai, $ORM2*1=0.9919$, $ORM2*6=0.0081$; Sri Lankan, $ORM2*1=0.9857$, $ORM2*3=0.0036$, $ORM2*21=0.0036$, $ORM2*22=0.0071$; Paraguayan, $ORM2*1=1.0000$.

^a ORM1 2-1(3), ORM1 2(3); ^b ORM1 1; ^c ORM1 2-1; ^d ORM1 1.

Table 3. Distribution of AHSG phenotypes and allele frequencies in Thai, Sri Lankan and Paraguayan populations.

Phenotypes	Thai		Sri Lankan		Paraguayan	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
1	154	151.0	95	93.7	61	62.7
2-1	164	169.2	38	40.9	98	94.6
2	51	47.9	6	4.5	34	35.7
3-1	0	0.0	0	1.0	2	6.9
3-2	0		0		1	
10-1	0		1		2	
10-2	0		0		2	
Others	0		0		0	
Total	369	369.1	140	140.1	200	199.9
Allele frequencies						
AHSG*1	0.6396		0.8179		0.5600	
AHSG*2	0.3604		0.1786		0.4225	
AHSG*3	0		0		0.0075	
AHSG*10	0		0.0036		0.0100	

the Hardy-Weinberg equilibrium in each of these populations (Thai, $\chi^2=0.4200$, $df=1$, $0.50 < p < 0.70$; Sri Lankan, $\chi^2=0.7237$, $df=1$, $0.30 < p < 0.50$; Paraguayan, $\chi^2=0.2507$, $df=1$, $0.70 < p < 0.80$).

DISCUSSION

Tables 4 and 5 summarize ORM1 and ORM2 allele frequencies in various populations, respectively. The frequency of duplicated allele, *ORM1*2.1*, in the Japanese populations is around 0.16 (Yuasa *et al.*, 1988). In contrast with Japanese, the *ORM1*2.1* allele frequencies in Thai, Sri Lankan, and Paraguayan are fairly low as those in Filipino (Umetsu *et al.*, 1988b), Libyan (Sebetan and Sagisaka, 1988) and German populations (Umetsu *et al.*, 1989). The *ORM2*6* allele frequency in Thai population was 0.008. It was much less than those in Japanese (Yuasa *et al.*, 1988) and Taiwanese (Umetsu *et al.*, 1988a). The higher frequency of *ORM1*2.1* and *ORM2*6* are likely to be characteristic of northern part of Mongoloid populations. It is very interesting that the *ORM1*5.2* and the *ORM2*3* alleles in the Sri Lankan population were indistinguishable from those observed in the Taiwanese and Japanese populations (Umetsu *et al.*, 1988a; Yuasa *et al.*, 1988).

In the ORM polymorphisms in Thai, Sri Lankan and Paraguayan, several rare ORM variants were detected, four of which were newly found and named ORM1 15, ORM1 16, ORM2 21 and ORM2 22. Future studies are needed to clarify the geographical origins and distributions of these variants.

Table 4 ORM1 allele frequencies in different populations.

Population (n)	Allele frequencies					References
	<i>ORM1*1</i>	<i>ORM1*2</i>	<i>ORM1*3</i>	<i>ORM1*2.1</i>	Others	
Japanese (200)	0.6800	0.1525	0	0.1550	0.0125	Yuasa <i>et al.</i> (1988)
Taiwanese (200)	0.7255	0.1805	0	0.0641	0.0300	Umetsu <i>et al.</i> (1988a)
Filipino (115)	0.7904	0.1687	0	0.0409	0	Umetsu <i>et al.</i> (1988b)
Thai (369)	0.8140	0.1610	0	0.0236	0.0014	The present study
Sri Lankan (140)	0.6996	0.2675	0	0.0221	0.0107	The present study
Nepalese (141)	0.6738	0.3121	0.0142	—	0	Yuasa <i>et al.</i> (1986)
Libyan (110)	0.6500	0.3091	0.0091	0.0318	0	Sebetan and Sagisaka (1988)
German (168)	0.5625	0.3929	0.0298	0.0119	0.0030	Umetsu <i>et al.</i> (1989)
Dane (215)	0.5810	0.3860	0.0330	—	0	Thymann and Eiberg (1986)
French (112)	0.5625	0.3884	0.0491	—	0	Yuasa <i>et al.</i> (1986)
Galician (218)	0.555	0.422	0.023	—	0	Montiel <i>et al.</i> (1988)
Paraguayan (200)	0.6448	0.3072	0.0225	0.0230	0.0025	The present study
USA Black (181)	0.6160	0.3840	—	—	0	Escallon <i>et al.</i> (1987b)

—, the allele which was not taken into consideration.

Table 6 lists the frequencies of the AHSB alleles in various populations, which have been reported thus far. In the Asian populations the frequencies of *AHSB*1* tends to decrease from Japan to Thai (Umetsu *et al.*, 1984; Yuasa and Umetsu, 1988; Umetsu *et al.*, 1988b). The frequencies of *AHSB*1* in Sri Lankans are sim-

Table 5. ORM2 allele frequencies in different populations.

Population (n)	Allele frequencies				References
	<i>ORM2*1</i>	<i>ORM2*3</i>	<i>ORM2*6</i>	Others	
Japanese (498)	0.9678	0.0050	0.0231	0.0040	Yuasa <i>et al.</i> (1988)
Japanese (400)	0.9637	0.0025	0.0326	0.0013	Umetsu <i>et al.</i> (1988a)
Taiwanese (200)	0.9475	0.0050	0.0450	0.0025	Umetsu <i>et al.</i> (1988a)
Filipino (115)	1.0000	0	0	0	Umetsu <i>et al.</i> (1988b)
Thai (369)	0.9919	0	0.0081	0	The present study
Sri Lankan (140)	0.9857	0.0036	0	0.0107	The present study
Libyan (110)	0.9816	0	0	0.0184	Sebetan and Sagisaka (1988)
German (272)	0.9963	0	0	0.0037	Weidinger <i>et al.</i> (1987)
German (168)	0.9970	0	0	0.0030	Umetsu <i>et al.</i> (1989)
Paraguayan (200)	1.0000	0	0	0	The present study

Table 6. AHSB allele frequencies in different populations.

Population (n)		Allele frequencies					References
		<i>AHSG*1</i>	<i>AHSG*2</i>	<i>AHSG*3</i>	<i>AHSG*10</i>	Others	
Japanese	(2,050)	0.7356	0.2639	0	0	0.0005	Umetsu <i>et al.</i> (1984)
Taiwanese	(199)	0.7286	0.2714	0	0	0	Yuasa and Umetsu (1988)
Filipino	(115)	0.6870	0.3130	0	0	0	Umetsu <i>et al.</i> (1988b)
Thai	(369)	0.6396	0.3604	0	0	0	The present study
Sri Lankan	(140)	0.8179	0.1786	0	0.0036	0	The present study
Nepalese	(140)	0.7571	0.2429	0	0	0	Yuasa <i>et al.</i> (1985)
Indian/Pakistani	(205)	0.8073	0.1878	0.0049	0	0	Westwood <i>et al.</i> (1987a)
Libyan	(110)	0.8364	0.1636	0	0	0	Sebetan and Heshmat (1988)
German	(344)	0.6642	0.3208	0.0058	0.0020	0.0072	Weidinger (1986)
French	(240)	0.7167	0.2750	0.0042	0	0.0042	Robinet-Lévy <i>et al.</i> (1988)
Canadian	(215)	0.6419	0.3535	0.0046	0	0	Cox <i>et al.</i> (1986)
Paraguayan	(200)	0.5600	0.4225	0.0075	0.0100	0	The present study
Afro-Caribbean	(119)	0.6597	0.2353	0	0.0966	0.0084	Westwood <i>et al.</i> (1987)

ilar to those in Libyan (Sebetan and Heshmat, 1988) and Indian-Pakistani (Westwood *et al.*, 1987a). These populations show the highest frequency for AHS₂G*1 in all the populations studied thus far. The Paraguayan population was characterized by the especially low AHS₂G*1 frequency as compared with all other population studied thus far. The AHS₂G*5 was not detected in the present study, while this allele was not infrequent in the Japanese (Yuasa and Umetsu, 1988). AHS₂G*5 may be a genetic marker specific for Japanese. The AHS₂G*10 in the Paraguayan is suggestive of some Black influence (Cox *et al.*, 1986; Westwood *et al.*, 1987b).

It appears from the above that the data on ORM and AHS₂G in various populations may contribute significantly to an understanding of the genetic structure of the populations.

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