










Human Platelet Antigen Datasets for Malays, Chinese, and Indians in Peninsular Malaysia

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Dear Editor,

Human platelet antigens (HPAs) are genetically inherited polymorphic glycoproteins expressed on the platelet membrane [1]. HPAs are transfusion and gestation compatibility determinants, and HPA alloantibodies have been reported in post-transfusion purpura, platelet transfusion refractoriness, and neonatal alloimmune thrombocytopenia (NAIT) cases [2].

Previously, we reported HPA allele frequency data for Malay subethnic groups [3] and Orang Asli [4] in Peninsular Malaysia. These earlier studies have provided a valuable preliminary source of genetic information for health assessments and population genetics. However, a complete picture of the genetic structure in Peninsular Malaysia should also include data from Malays (i.e., Deutero-Malays), Chinese, and Indians, as they represent >75% of the total population [5]. There are some HPA data for Malays, Chinese, and Indians reported by Tan, *et al.* [6]; the present HPA data can be compared with those data.

We typed HPA-1 to -6 and HPA-15 loci in blood samples obtained with informed consent from a total of 222 individuals registered as voluntary, non-remunerated blood donors at the Hospital Universiti Sains Malaysia (Kelantan), Hospital Seberang

Jaya (Pulau Pinang), and Temerloh Hospital (Pahang) in Malaysia. The individuals were un-admixed with no history of intermarriage with other ethnic groups for three generations. The ethnicity classes of these samples were assigned as Malay (N=97), Chinese (N=77), and Indian (N=48) based on individual pedigree information. Our proposed study was reviewed and approved by the Human Ethical Committee, Universiti Sains Malaysia, Malaysia, and the Medical Research and Ethics Committee, Ministry of Health, Malaysia. The HPA typing and data analysis were performed as previously described by Wan Syafawati, *et al.* [3] and Syafawati *et al.* [4]. Briefly, isolated genomic DNA was amplified using polymerase chain reaction and sequence-specific primers (PCR-SSP) for HPA-1 to -6 and -15. Amplified products were then separated using agarose gel electrophoresis (2% agarose gels stained with ethidium bromide) and visualised using a UV photometer (Quantum ST4-1000/20M, VilberLourmat, Deutschland GmbH, Eberhardzell, Germany). The separated band patterns (amplified allele-specific HPA products and human growth hormone) were then compared with a 100 base pair DNA size standard (Bioline, London, UK). HPA allele frequencies were determined by dividing the allele count numbers

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Table 1. HPA allele frequency distribution in the present and previous studies

Population	(N)	1a	1b	2a	2b	3a	3b	4a	4b	5a	5b	6a	6b	15a	15b
Malays (present study)	97	0.985	0.015	0.969	0.031	0.510	0.490	1.000	0.000	0.990	0.010	0.990	0.010	0.479	0.521
Chinese (present study)	77	1.000	0.000	0.980	0.020	0.591	0.410	1.000	0.000	0.987	0.013	0.994	0.006	0.526	0.474
Indians (present study)	47	0.979	0.021	0.969	0.031	0.521	0.479	1.000	0.000	0.959	0.041	0.990	0.010	0.375	0.625
Banjar [3]	30	1.000	0.000	0.950	0.050	0.616	0.384	0.950	0.050	0.950	0.050	0.980	0.020	0.480	0.520
Bugis [3]	37	1.000	0.000	1.000	0.000	0.554	0.446	1.000	0.000	0.950	0.050	0.910	0.090	0.620	0.380
Champa [3]	51	0.980	0.020	0.970	0.030	0.677	0.323	1.000	0.000	0.990	0.010	0.980	0.090	0.480	0.520
Jawa [3]	39	1.000	0.000	1.000	0.000	0.628	0.372	1.000	0.000	0.960	0.040	1.000	0.000	0.450	0.550
Kelantan [3]	35	1.000	0.000	0.940	0.060	0.571	0.429	1.000	0.000	1.000	0.000	0.990	0.010	0.490	0.510
Orang Kanaq [4]	11	1.000	0.000	1.000	0.000	0.818	0.182	1.000	0.000	1.000	0.000	1.000	0.000	0.909	0.091
Batek [4]	27	1.000	0.000	1.000	0.000	0.500	0.500	1.000	0.000	0.852	0.148	1.000	0.000	0.000	1.000
Lanoh [4]	25	1.000	0.000	1.000	0.000	0.640	0.360	1.000	0.000	1.000	0.000	1.000	0.000	0.260	0.740
Kensiu [4]	36	0.958	0.042	1.000	0.000	0.875	0.125	1.000	0.000	0.847	0.153	1.000	0.000	0.361	0.639
Che Wong [4]	26	1.000	0.000	1.000	0.000	0.423	0.577	1.000	0.000	0.788	0.212	1.000	0.000	0.500	0.500
Semai [4]	40	0.988	0.012	1.000	0.000	0.671	0.329	1.000	0.000	0.890	0.110	1.000	0.000	0.524	0.476
Malays [6]	200	0.975	0.025	0.963	0.037	0.503	0.497	0.995	0.005	0.950	0.050	0.993	0.007	0.515	0.485
Chinese [6]	200	1.000	0.000	0.967	0.033	0.573	0.427	0.998	0.002	0.983	0.017	0.983	0.017	0.498	0.502
Indians [6]	200	0.885	0.115	0.960	0.040	0.620	0.380	0.995	0.005	0.940	0.060	0.995	0.005	0.408	0.592

by the total numbers of chromosomes ($2n$) tested. Genetic differentiations between pairs of HPA population datasets were evaluated using Arlequin version 3.0 software [7] and were considered statistically significant at $P < 0.05$.

The present and previously reported HPA datasets of various population groups in Peninsular Malaysia are shown in Table 1 [3, 4, 6]. These HPA datasets reveal that Malays and Chinese differ significantly ($P < 0.05$) from Indians (Table 2). However, no significant differences were observed between the HPA datasets of Malays and Chinese. Importantly, Malays, Chinese, and Indians are the modern-day descendants of ancestrally unrelated ethnic groups in Peninsular Malaysia; the inability of the HPA datasets to differentiate between Malays and Chinese needs to be resolved using more informative genetic markers, including genome-wide single nucleotide polymorphisms and whole genome sequencing data [8]. In addition, some of the ancestral relationships might also be obscured by demographic processes such as natural selection and founder effects. Of these forces, natural selection is expected to have a greater effect on genes that are important in the medical field such as HPA, compared with other regions in the human genome [1]. For example, some differences observed between ancestrally related Proto-Malays (Orang Kanaq), Malay subethnic groups, and Malays could possibly be attributed to gene flow via admixture and historical events

at the population level (as mentioned earlier), rather than different origins (Table 2) [8].

In our view, HPA datasets for various population groups in Peninsular Malaysia (Tables 1 and 2) also have significant value for health and have been identified as genetic risk factors for many diseases [9]. The risk of HPA alloimmunization in Peninsular Malaysia might be expected to be most frequently associated with alloantibodies against HPA-3 and HPA-15 products, as these are the most polymorphic loci observed within and between population groups in Peninsular Malaysia (Tables 1 and 2). Our hypothesis regarding HPA alloimmunization risk is supported by the presence of HPA-1a, -3a, -5a, and -15b alloantibodies in most of the NAIT cases and multi-transfused thrombocytopenia patients in Malaysia [10]. Therefore, implementation of HPA typing could reduce the incidence of HPA alloimmunization cases in Malaysia.

In conclusion, to the best of our knowledge, our study is the first complete representative collection of HPA datasets for all population groups in Peninsular Malaysia. These datasets can be used for developing better healthcare services and as a reference standard for identifying genetic risk factors for many diseases associated with HPAs.

Table 2A. Homogeneity between pairs of population groups in Peninsular Malaysia

	HPA-1																
	Malays [†]	Chinese [†]	Indians [†]	Banjjar [3]	Bugis [3]	Champa [3]	Jawa [3]	Kelantan [3]	O. K. [4]	Batek [4]	Lanoh [4]	Kensiu [4]	C. W. [4]	Semai [4]	Malays [6]	Chinese [6]	Indians [6]
Malays [†]	*	0.257	NA	NA	0.558	NA	0.557	0.568	NA	NA	NA	0.340	NA	NA	NA	NA	<0.000
Chinese [†]	0.088	*	0.145	NA	NA	0.158	NA	NA	NA	NA	NA	0.032	NA	0.344	NA	NA	<0.000
Indians [†]	1.000	0.294	*	0.520	0.501	NA	0.499	0.507	NA	0.534	0.544	0.650	0.538	NA	NA	NA	0.004
Banjjar [3]	0.441	0.063	0.669	*	NA	0.530	NA	NA	NA	NA	NA	0.241	NA	NA	NA	NA	0.003
Bugis [3]	0.184	1.000	0.254	0.085	*	0.508	NA	NA	NA	NA	NA	0.114	NA	NA	NA	NA	<0.000
Champa [3]	0.209	1.000	0.349	0.193	1.000	*	0.504	0.516	NA	0.539	NA	0.645	0.545	NA	NA	NA	0.003
Jawa [3]	0.183	1.000	0.249	0.076	NA	1.000	*	NA	NA	NA	NA	0.108	NA	NA	NA	NA	0.001
Kelantan [3]	0.453	0.034	0.450	1.000	0.052	0.160	0.046	*	NA	NA	NA	0.239	NA	NA	NA	NA	<0.000
O. K. [4]	1.000	1.000	1.000	0.551	NA	1.000	NA	0.557	*	NA	NA	NA	NA	NA	NA	NA	0.162
Batek [4]	0.340	1.000	0.546	0.239	NA	1.000	NA	0.127	NA	*	NA	0.252	NA	NA	NA	NA	0.004
Lanoh [4]	0.343	1.000	0.545	0.241	NA	1.000	NA	0.135	NA	NA	*	0.263	NA	NA	NA	NA	0.008
Kensiu [4]	0.190	1.000	0.255	0.088	NA	1.000	NA	0.052	NA	NA	NA	*	NA	NA	NA	NA	0.159
C.W [4]	0.338	1.000	0.255	0.242	NA	1.000	NA	0.131	NA	NA	NA	NA	*	NA	NA	NA	0.005
Semai [4]	0.178	1.000	0.249	0.076	NA	1.000	NA	0.043	NA	NA	NA	NA	NA	*	NA	NA	0.004
Malays [6]	0.812	0.035	1.000	0.713	NA	0.079	NA	0.498	0.623	0.223	0.386	0.139	0.230	0.086	*	NA	<0.000
Chinese [6]	0.857	0.200	0.782	0.492	0.343	0.272	0.352	0.360	0.705	0.439	0.660	0.662	0.350	0.543	0.857	*	<0.000
Indians [6]	1.000	0.106	1.000	0.542	0.269	0.196	0.280	0.426	0.641	0.459	0.438	0.271	0.459	0.277	1.000	0.836	*

HPA-2

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Table 2B. Continued

	HPA-3																	
	Malays [†]	Chinese [†]	Indians [†]	Banjar [3]	Bugis [3]	Champa [3]	Jawa [3]	Kelantan [3]	O. K. [4]	Batek [4]	Lanoh [4]	Kensiu [4]	C. W. [4]	Semai [4]	Malays [6]	Chinese [6]	Indians [6]	
Malays [†]	*	0.132	0.251	0.186	<0.001	0.002	0.116	0.600	0.016	0.871	0.038	<0.001	0.419	0.016	0.711	0.190	0.018	
Chinese [†]	NA	*	0.522	0.960	<0.001	0.263	0.899	0.891	0.192	0.193	0.467	<0.001	0.048	0.376	0.136	0.872	0.784	
Indians [†]	NA	NA	*	0.584	0.019	0.130	0.402	0.526	0.060	0.236	0.381	<0.001	0.139	0.376	0.434	0.388	0.297	
Banjar [3]	0.013	0.019	0.075	*	0.014	0.638	1.000	0.804	0.332	0.206	0.722	0.003	0.063	0.675	0.239	0.761	0.297	
Bugis [3]	NA	NA	NA	0.085	*	0.025	0.006	0.001	0.016	<0.001	0.160	<0.001	<0.001	0.002	<0.001	<0.001	0.955	
Champa [3]	NA	NA	NA	0.047	NA	*	0.602	0.186	0.572	0.014	0.900	0.012	0.003	0.590	0.001	0.060	0.009	
Jawa [3]	NA	NA	NA	0.077	NA	NA	*	0.700	0.346	0.15	0.661	0.002	0.038	0.743	0.105	0.658	0.099	
Kelantan [3]	NA	NA	NA	0.095	NA	NA	NA	*	0.105	0.605	0.337	<0.001	0.172	0.348	0.554	0.969	0.964	
O. K. [4]	NA	NA	NA	0.551	NA	NA	NA	NA	*	0.025	0.373	0.467	0.003	0.672	0.008	0.101	0.694	
Batek [4]	NA	NA	NA	0.238	NA	NA	NA	NA	NA	*	0.050	<0.001	0.667	0.048	0.630	0.280	0.216	
Lanoh [4]	NA	NA	NA	0.240	NA	NA	NA	NA	NA	NA	*	0.009	0.015	0.448	0.056	0.257	0.279	
Kensiu [4]	NA	NA	NA	0.089	NA	NA	NA	NA	NA	NA	NA	*	<0.001	0.020	<0.001	<0.001	<0.001	
C.W [4]	NA	NA	NA	0.242	NA	NA	NA	NA	NA	NA	NA	NA	*	0.006	0.341	0.069	0.009	
Semai [4]	NA	NA	NA	0.073	NA	NA	NA	NA	NA	NA	NA	NA	NA	*	0.008	0.184	0.523	
Malays [6]	NA	NA	NA	0.002	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	*	0.127	0.009	
Chinese [6]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	*	0.396	
Indians [6]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.368	*	0.368	*

HPA-4

(Continued to the next page)

Table 2C. Continued

	HPA-5																
	Malays [†]	Chinese [†]	Indians [†]	Banjar [3]	Bugis [3]	Champa [3]	Jawa [3]	Kelantan [3]	O. K. [4]	Batek [4]	Lanoh [4]	Kensiu [4]	C. W. [4]	Semai [4]	Malays [6]	Chinese [6]	Indians [6]
Malays [†]	*	1.000	0.093	1.000	0.049	1.000	0.142	1.000	1.000	< 0.001	< 0.001	1.000	< 0.001	1.000	0.723	0.723	0.008
Chinese [†]	1.000	*	0.200	1.000	0.088	1.000	0.333	1.000	1.000	< 0.001	< 0.001	1.000	< 0.001	0.546	1.000	1.000	0.038
Indians [†]	1.000	1.000	*	0.154	0.723	0.193	1.000	0.134	1.000	0.023	0.010	0.292	0.003	0.125	0.233	0.229	0.834
Banjar [3]	0.556	0.484	1.000	*	0.122	1.000	0.254	NA	NA	0.001	< 0.001	NA	< 0.001	NA	0.596	0.598	0.203
Bugis [3]	0.001	0.001	0.018	0.068	*	0.158	0.709	0.116	0.559	0.099	0.045	0.140	0.012	0.049	0.071	0.071	1.000
Champa [3]	1.000	1.000	1.000	1.000	0.009	*	0.318	1.000	1.000	< 0.001	< 0.001	1.000	< 0.001	1.000	1.000	1.000	0.098
Jawa [3]	0.143	0.109	0.321	0.628	0.190	0.312	*	0.241	1.000	0.042	0.018	0.271	0.004	0.115	0.214	0.212	0.813
Kelantan [3]	1.000	1.000	1.000	0.459	0.011	1.000	0.240	*	NA	< 0.001	< 0.001	NA	< 0.001	NA	0.597	0.595	0.093
O. K. [4]	1.000	1.000	1.000	1.000	0.177	1.000	1.000	NA	*	0.074	NA	0.046	0.018	NA	1.000	1.000	0.635
Batek [4]	1.000	1.000	1.000	1.000	0.016	1.000	0.267	NA	NA	*	0.004	1.000	0.568	< 0.001	< 0.001	< 0.000	0.028
Lanoh [4]	1.000	1.000	1.000	1.000	0.036	1.000	0.275	NA	NA	NA	*	0.001	< 0.001	NA	1.000	1.000	0.242
Kensiu [4]	1.000	1.000	1.000	0.455	0.010	1.000	0.241	NA	NA	NA	NA	*	0.589	< 0.001	< 0.001	< 0.000	0.013
C.W [4]	1.000	1.000	1.000	1.000	0.035	1.000	0.265	NA	NA	NA	NA	NA	*	< 0.001	< 0.001	< 0.000	0.002
Semai [4]	1.000	1.000	1.000	0.428	0.004	1.000	0.113	NA	NA	NA	NA	NA	NA	*	0.604	0.601	0.295
Malays [6]	0.722	0.448	1.000	1.000	0.002	1.000	0.211	NA	NA	NA	NA	NA	NA	NA	*	1.000	0.003
Chinese [6]	0.724	0.450	1.000	1.000	0.002	1.000	0.210	NA	NA	NA	NA	NA	NA	NA	1.000	*	0.003
Indians [6]	0.602	1.000	0.474	0.344	< 0.001	0.492	0.032	NA	NA	NA	NA	NA	NA	NA	0.169	0.175	*

HPA-6

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Table 2D. Continued

	HPA-15																
	Malays [†]	Chinese [†]	Indians [†]	Banjar [3]	Bugis [3]	Champa [3]	Jawa [3]	Kelantan [3]	O. K. [4]	Batek [4]	Lanoh [4]	Kensiu [4]	C. W. [4]	Semai [4]	Malays [6]	Chinese [6]	Indians [6]
Malays [†]	*	0.503	0.217	0.087	0.049	0.407	0.732	0.007	< 0.001	< 0.001	0.019	0.144	0.013	0.255	0.687	0.904	0.176
Chinese [†]	*	*	0.033	0.022	0.065	0.127	0.521	0.001	< 0.001	< 0.001	0.002	0.047	0.070	0.091	0.723	0.638	0.012
Indians [†]	*	*	*	0.120	0.007	0.308	0.375	0.029	< 0.001	< 0.001	0.443	0.606	0.003	0.147	0.041	0.070	0.866
Banjar [3]	*	*	*	*	0.300	0.626	0.046	0.862	0.013	< 0.001	0.080	0.020	< 0.001	0.794	0.050	0.049	0.109
Bugis [3]	*	*	*	*	*	0.260	0.031	0.116	0.080	< 0.001	0.002	0.003	< 0.001	0.475	0.077	0.045	0.004
Champa [3]	*	*	*	*	*	*	0.247	0.227	0.002	< 0.001	0.063	0.082	< 0.001	0.862	0.240	0.257	0.340
Jawa [3]	*	*	*	*	*	*	*	0.006	< 0.001	< 0.001	0.057	0.541	0.089	0.110	0.448	0.603	0.309
Kelantan [3]	*	*	*	*	*	*	*	*	0.013	< 0.001	0.031	0.003	< 0.001	0.428	0.002	0.603	0.011
O. K. [4]	*	*	*	*	*	*	*	*	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Batek [4]	*	*	*	*	*	*	*	*	*	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Lanoh [4]	*	*	*	*	*	*	*	*	*	*	*	0.352	< 0.001	0.033	0.002	0.003	0.183
Kensiu [4]	*	*	*	*	*	*	*	*	*	*	*	*	0.026	0.030	0.037	0.066	0.323
C. W. [4]	*	*	*	*	*	*	*	*	*	*	*	*	*	< 0.001	0.010	0.009	0.001
Semai [4]	*	*	*	*	*	*	*	*	*	*	*	*	*	*	0.188	0.172	0.136
Malays [6]	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	0.875	0.006
Chinese [6]	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	0.014
Indians [6]	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

Pairs of HPA datasets are considered significantly different if their $P < 0.05$ and are bold.

[†]Data from the present study; reference HPA datasets were obtained from Syafawati, et al. [3], Syafawati, et al. [4], and Tan, et al. [6]. Abbreviations: HPA, human platelet antigen; NA, not applicable; *, no value; O.K, Orang Kanaq; C.W, Che Wong.

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AUTHOR CONTRIBUTIONS

CGNH designed and performed the research, collected the data, analyzed the data, and wrote the manuscript; ZZ helped design the study, managed sample collection, and obtained our ethics permit from the Ministry of Health, Malaysia; NSMR and THTM helped with study design, sampling, and data collection; MNH, AMD, GEG, and GKC designed the study, advised on statistics, and edited the manuscript; and HAE designed and directed the study, advised on statistics, edited the manuscript, funded the research, managed the study, and obtained ethical approval from Human Ethics Committee, Universiti Sains Malaysia.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this paper were reported.

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