Genetic variants of human platelet antigens in the Indian population from 1029 whole genomes

Mercy Rophina[1,2], Rahul C Bhoyar[1], Mohamed Imran[1,2], Vigneshwar Senthivel[1,2], Mohit Kumar Divakar[1,2], Anushree Mishra[1], Bani Jolly[1,2], Sridhar Sivasubbu[1,2], Vinod Scaria[1,2$]

[1] CSIR Institute of Genomics and Integrative Biology (CSIR-IGIB), Mathura Road, Delhi 110025, INDIA
[2]Academy of Scientific and Innovative Research (AcSIR), CSIR-HRDC Campus, Sector 19, Kamla Nehru Nagar, Ghaziabad, Uttar Pradesh 201002, INDIA

[$]Address for correspondence
Corresponding author Email:
Dr. Vinod Scaria - vinods@igib.in ; Tel: 91-11-29879 109

Running Title - HPA variants in Indian population

Author Contributions

MR performed the analysis of the data. RCB, MI, VS, MKD, AM and BJ were involved in the generation of the study data. VS and SSB conceived and designed the project. MR and VS wrote the manuscript. All authors have read and approved the final manuscript.

Abstract

Background
Genetic variants in human platelet antigens (HPAs) considered as allo- or auto antigens are associated with various disorders including neonatal alloimmune thrombocytopenia, platelet transfusion refractoriness and post-transfusion purpura. While global differences in genotype frequencies were observed, the distribution of HPA variants in the Indian population are largely unknown. This study aims to explore the landscape of HPA variants in India to provide a basis for risk assessment and management of related complications.

Materials and methods
Population specific frequencies of genetic variants associated with the 35 classes of HPAs (HPA-1 to HPA-35) were estimated by systematically analyzing genomic variations of 1029 healthy Indian individuals as well as from global population genome datasets..

Results
Allele frequencies of the most clinically relevant HPA systems in the Indian population were found as follows, HPA-1a - 0.89, HPA-1b - 0.15, HPA-2a - 0.94, HPA-2b - 0.05, HPA-3a - 0.66, HPA-3b - 0.36, HPA-4a - 1.00, HPA-4b - 0, HPA-5a - 0.92, HPA-5b - 0.08, HPA-6a - 1.00, HPA-6b - 0, HPA-15a - 0.58 and HPA-15b - 0.42. In addition, HPA-4b allele frequencies were found to be significantly higher in India in comparison to global populations.

Conclusion
This study provides the first comprehensive analysis of HPA allele and genotype frequencies using large scale representative whole genome sequencing data of the Indian population.

Keywords : Human Platelet Antigens, Indian population, allele frequency, genotype prevalence

Introduction

Platelets are small, anucleate, cells that have a key role in haemostasis. Recent studies have explored their functional roles in inflammation (Leslie 2010), innate and adaptive immunity (Pacheco et al. 2011) and key contributions to a range of disorders including cancer (Leslie 2010). Platelets function through ligand-receptor interactions involving cell surface glycoproteins. Genetic variations occurring in these glycoprotein genes collectively give rise to human platelet antigens (HPAs). HPAs can be recognized as allo- or auto antigens and lead to a range of immune platelet disorders like multitansfusion platelet refractoriness (MPR), fetal and neonatal alloimmune thrombocytopenia (FNAIT) and post transfusion purpura (PTP) (Bianchi et al. 2012), (Pacheco et al. 2011).

HPAs were first described as early as 1960s and about 41 antigens encoded by 8 different platelet glycoproteins namely GPIIIa, GPIbα, GPIIIb, GPIa, GPIIb, GPIbβ, CD109 and GPIX have been documented and approved by the International Platelet Immunology Nomenclature Committee of the International Society of Blood Transfusion (ISBT). This includes a total of 6 biallelic systems (HPA-1 , HPA-2, HPA-3, HPA-4, HPA-5 and HPA-15) and 29 monoallelic systems (HPA - 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 and 35) (Curtis and McFarland 2014). A vast majority of HPAs are expressed on GPAIIIa, making it the most immunogenic of the platelet glycoproteins (Rozman 2002).

In recent years, with the advent of wider genomic analysis, a large diversity of HPA genotypes have come out of genomic analysis of human ethnic groups from a variety of geographical locations (Silva-Malta et al. 2018),(Jovanovic Srzentic et al. 2021),(Yan et al. 2006). Many of these studies have suggested significant differences in the frequencies between populations. For example, HPA-4b antigen was found to be very rare in Caucasians but more frequent in Asian populations. Anti-HPA-4a and anti-HPA-4b are common and implicated in alloimmune platelet disorders (Jovanovic Srzentic et al. 2021), (Yan et al. 2006), (Tan, Lian, and Nadarajan 2012). The recent availability of genomic data for Indian populations motivated us to analyze the allele and genotype frequencies of HPAs towards understanding frequent and rare alleles in the population .

Materials and methods

Datasets used in the study

A comprehensive catalogue of the human platelet antigens approved by the International Platelet Immunology Nomenclature Committee of the International Society of Blood Transfusion (ISBT) was retrieved from Human Platelet Antigen Database. **Table 1** The dataset provides the genomic coordinates and HGVS nomenclature of these reference variants. Genomic variations compiled from whole genome sequences of 1029 self declared healthy individuals from across India were used in the analysis (Jain et al. 2021). This dataset encompasses a total of 55,898,122 variants. Variants associated with HPAs were parsed in this dataset to systematically retrieve the genotype and allele frequencies using bespoke scripts.

Estimation and comparison of HPA frequencies

Frequencies and zygosity information of HPA variants were retrieved from the dataset of genetic variants compiled from the IndiGenomes resource (Jain et al. 2021). Expected number of genotypes were computed based on Hardy-Weinberg equilibrium calculations. Any deviation of the observed number of genotypes from the expected numbers was evaluated by Chi-square test (p-value < 0.05).

Results

Frequencies of HPA variants were analysed in a total of 1029 whole genome sequences. **Table 2** summarizes the observed frequencies of HPA variants along with the counts of samples in homozygous and heterozygous states. In the HPA-1 system, HPA-1a/a was observed as the most frequent genotype (79.04%) followed by HPA-1a/b (18.62%) and HPA-1b/b (2.34%). Similarly genotype frequencies observed in classes 2-5 and 15 are as follows, HPA-2a/a - 88.49%, HPA-2a/b - 11.22%, HPA-2b/b - 0.29%, HPA-3a/a - 43.63%, HPA-3a/b - 43.33%, HPA-3b/b - 13.04%, HPA-4a/a - 99.80%, HPA-4a/b - 0.20%, HPA-4b/b - 0%, HPA-5a/a - 85.13%, HPA-5a/b - 14.29%, HPA-5b/b- 0.59%, HPA-15a/a - 33.79%, HPA-15a/b - 48.83%, HPA-15b/b - 17.38%. Expected genotype frequencies were duly estimated for HPA-1, 2, 3, 4, 5 and 15 alleles based on Hardy-Weinberg equilibrium. Chi-square test was performed to evaluate significant differences between observed and expected frequencies. Distribution of HPA genotype frequencies in the Indian population tested for Hardy-Weinberg equilibrium is tabulated in **Table 3.** In accordance with the observed p-values, significant deviations of genotypes were seen in HPA-1 (p-val: 0.0094) and -4 (p-val: 0.0001) systems. **Supplementary Tables 1 and 2** elaborate the frequencies of HPA variants reported from various subpopulations of gnomAD (Karczewski et al. 2020) and 1000 genomes project (1000 Genomes Project Consortium et al. 2015). Distribution of HPA allele frequencies among various global populations is graphically depicted in **Figure 1.**

Discussion and Conclusion

Genotyping of human platelet antigens and establishment of population specific donor registries have been suggested to serve in donor selection and management of platelet-specific alloimmunization (Jovanovic Srzentic et al. 2021).

Among the tested HPA systems, HPA-1 and 4 showed significant disequilibrium in the population. Generally, in all HPA systems, “b” allele was observed to occur at much lower frequency in comparison to the “a” allele with the exception of the HPA-15 system where allele frequencies of HPA-15a and 15b were 0.582 and 0.418 respectively. In addition, HPA-4 was the only system with the presence of a “b” allele but absence of “bb” genotype, indicating the heterozygous nature of the allele. Such patterns have been commonly reported in many East-Asian populations (Kupatawintu et al. 2005), (Phuangtham et al. 2017), (Seo et al. 1998), (Asmarinah et al. 2013), (Tan, Lian, and Nadarajan 2012), (Pai et al. 2013).

In comparison to global allele frequencies, HPA-1a and 1b alleles were found similar in most South Asian populations {ref}. Interestingly, HPA-1b allele frequencies varied from very high in populations like Brazilian, Moroccan and Tunisian (0.22-0.25) to low in South East Asians including Malaysians, Thai, Indonesians, Vietnamese, Han Chinese, Taiwanese, Japanese and Koreans. This finding is concordant with previous reports suggesting an increased rate of

alloimmunization due to antibodies to the HPA-1a antigen in Caucasians. Allele frequencies of HPA-2a were found to occur in a similar range among all global populations (0.61-0.99) whereas the 2b allele was found at a slightly higher frequency in Africans.

In conclusion, this study provides the first comprehensive catalogue of HPA allele frequencies in the Indian population. Our analysis suggests similarities and differences in the allelic profiles of Indians with that of other global ethinic groups. Such efforts could potentially serve as valuable resources for clinical research and interventions in future.

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Conflicts of Interest

None declared

Figures and Tables

Figure 1. Heatmap illustrating the distribution of HPA allele frequencies among various global populations

Table 1. Precise summary of the list of approved HPA variants analysed in the study

Table 2. Tabulation of observed frequencies of HPA variants in the Indian population. For HPA systems that are not listed in the table no variants were found in the population.

Table 3. Estimation of Chi squared statistic and P-values using the observed and expected genotype frequencies of various classes of HPA observed in the Indian population

Table 4. Precise tabulation of allele frequencies of HPA-1,2,3,4,5 and 15 systems across multiple global populations.

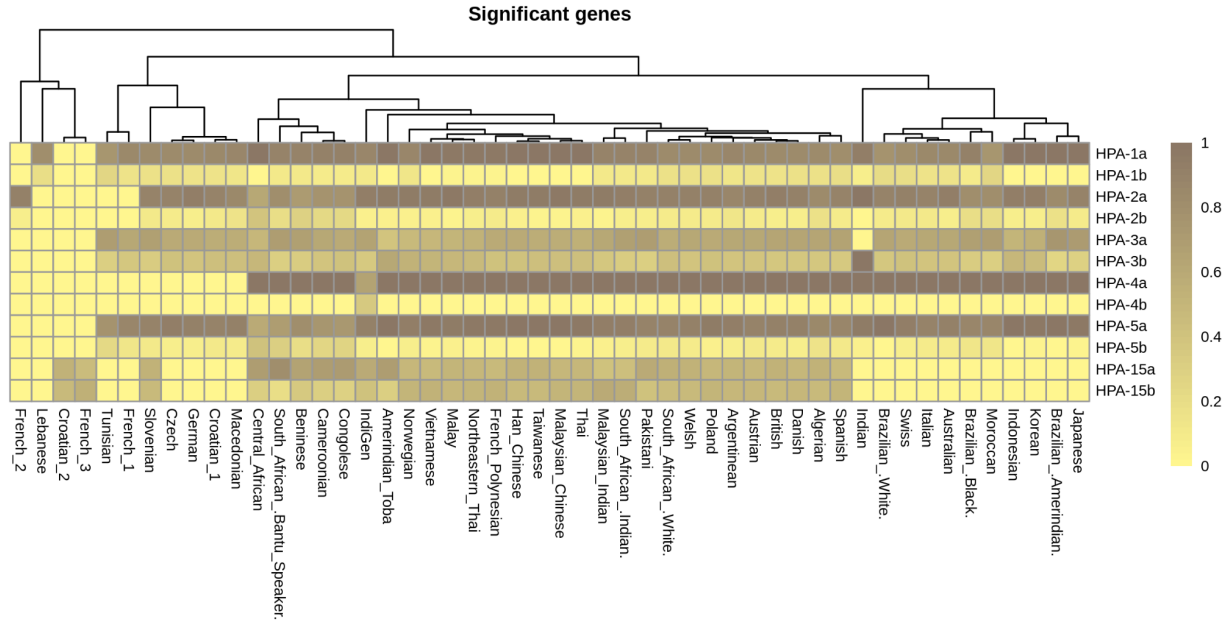

Figure 1. Heatmap illustrating the distribution of HPA allele frequencies among various global populations

HPA	HGNC Gene	Chromosome	Entrez Gene	Ref-Seq	Uni-Prot	dbSNP	Pos (Hg38)	Pos (Hg19)	Nucleotide Change	Precursor Protein	Mature Protein
HPA-1b	ITGB3	17	3690	NM 000212	ITB3 Human	rs5918	47283364	45360730	176T>C	L59P	L33P
HPA-2b	GP1BA	17	2811	NM_000173	GPBA_Human	rs6065	4933086	4836381	482C>T	T161M	T145M
HPA-3b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs5911	44375697	42453065	2621T>G	I874S	I843S
HPA-4b	ITGB3	17	3690	NM_000212	ITB3_Human	rs5917	47284587	45361953	506G>A	R169Q	R143Q
HPA-4	ITGB3	17	3690	NM_000212	ITB3_Human	rs5917	47284587	45361953	506G>A	R169Q	R143Q
HPA-5b	ITGA2	5	3673	NM_002203	ITA2_Human	rs1801106	53062927	52358757	1600G>A	E534K	E505K
HPA-5	ITGA2	5	3673	NM_002203	ITA2_Human	rs1801106	53062927	52358757	1600G>A	E534K	E505K
HPA-5	ITGA2	5	3673	NM_002203	ITA2_Human	rs1801106	53062927	52358757	1600G>A	E534K	E505K
HPA-6b	ITGB3	17	3690	NM_000212	ITB3_Human	rs13306487	47292422	45369788	1544G>A	R515Q	R489Q
HPA-7b	ITGB3	17	3690	NM_000212	ITB3_Human	rs121918448	47292175	45369541	1297C>G	P433A	P407A
HPA-8b	ITGB3	17	3690	NM_000212	ITB3_Human	rs151219882	47300548	45377914	1984C>T	R662C	R636C
HPA-9b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs74988902	44375716	42453084	2602G>A	V868M	V837M

HPA-10b	ITGB3	17	3690	NM_000212	ITB3_Human	rs200358667	47283451	45360817	263G>A	R88Q	R62Q
HPA-11b	ITGB3	17	3690	NM_000212	ITB3_Human	rs377302275	47300540	45377906	1976G>A	R659H	R633H
HPA-12b	GP1BB	22	2812	NM_000407	GPBB_Human	rs375285857	19723962	19711485	119G>A	G40E	G15E
HPA-13b	ITGA2	5	3673	NM_002203	ITA2_Human	rs79932422	53073171	52369001	2483C>T	T828M	T799M
HPA-14b	ITGB3	17	3690	NM_000212	ITB3_Human				1909_1911delAAG	K637del	K611del
HPA-15b	CD109	8	135228	NM_133493	Q8TDJ3	rs10455097	73783709	74493432	2108C>A	S703Y	S682Y
HPA-16b	ITGB3	17	3690	NM_000212	ITB3_Human	rs74708909	47284578	45361944	497C>T	T166I	T140I
HPA-17b	ITGB3	17	3690	NM_000212	ITB3_Human	rs770992614	47286307	45363673	662C>T	T221M	T195M
HPA-18b	ITGA2	5	3673	NM_002203	ITA2_Human	rs267606593	53070260	52366090	2235G>T	Q745H	Q716H
HPA-19b	ITGB3	17	3690	NM_000212	ITB3_Human	rs80115510	47284568	45361934	487A>C	K163Q	K137Q
HPA-20b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs78299130	44378507	42455875	1949C>T	T650M	T619M
HPA-21b	ITGB3	17	3690	NM_000212	ITB3_Human	rs70940817	47300524	45377890	1960G>A	E654K	E628K
HPA-22b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs142811900	44385326	42462694	584A>C	K195T	K164T
HPA-23b	ITGB3	17	3690	NM_000212	ITB3_Human	rs139166528	47300506	45377872	1942C>T	R648W	R622W
HPA-24b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs281864910	44380422	42457790	1508G>A	S503N	S472N
HPA-25b	ITGA2	5	3673	NM_002203	ITA2_Human	rs771035051	53087040	52382870	3347C>T	T1116M	T1087M
HPA-26b	ITGB3	17	3690	NM_000212	ITB3_Human	rs1156382155	47299435	45376801	1818G>T	K606N	K580N
HPA-27b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs149468422	44375704	42453072	2614C>A	L872M	L841M
HPA-28b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs368953599	44376345	424537 13	2311G>T	V771L	V740L
HPA-29b	ITGB3	17	3690	NM_000212	ITB3_Human	rs544276300	47274437	45351803	98C>T	T33M	T7M
HPA-30b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs377753373	44375923	42453291	2511G>C	Q837H	Q806H
HPA-31b	GP9	3	2815	NM_000174	GPIX_Human	rs202229101	12906207	12878095 0	368C>T	P123L	P107L
HPI-32b	ITGB3	17	3690	NM_000212	ITB3_Human	rs879083862	47284602	45361968	521A>G	D174S	D148S

HPA-33b	ITGB3	17	3690	NM_000212	ITB3_Human	rs1555572829	47292251	45369617	1373A>G	D458G	D432G
HPA-34b	ITGB3	17	3690	NM_000212	ITB3_Human	rs777748046	47283537	45360903	349C>T	R117W	R91W
HPA-35b	ITGB3	17	3690	NM_000212	ITB3_Human	rs779974422	47292392	45369758	1514A>G	R505H	R479H

Table 1. Precise summary of the list of approved HPA variants analysed in the study

HPA	HGNC Gene	Chromosome	Entrez Gene	Ref-Seq	Uni-Prot	dbSNP	Nucleotide Change	Precursor Protein	Mature Protein	Indigen AC	Indigen AN	Indigen AF	Homozygous	Heterozygous	Hom Proportion	Het Proportion	Hom %	Het %
HPA-1b	ITGB3	17	3690	NM_000212	ITB3_Human	rs5918	176T>C	L59P	L33P	239	2052	0.1165	24	191	0.023	0.186	2.34	18.62
HPA-2b	GP1BA	17	2811	NM_000173	GPBA_Human	rs6065	482C>T	T161M	T145M	121	2050	0.059	3	115	0.003	0.112	0.29	11.22
HPA-3b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs5911	2621T>G	I874S	I843S	708	2040	0.3471	133	442	0.130	0.433	13.04	43.33
HPA-4b	ITGB3	17	3690	NM_000212	ITB3_Human	rs5917	506G>A	R169Q	R143Q	708	2040	0.3471	0	2	0.000	0.002	0.00	0.20
HPA-5b	ITGA2	5	3673	NM_002203	ITA2_Human	rs1801106	1600G>A	E534K	E505K	158	2044	0.0773	6	146	0.006	0.143	0.59	14.29
HPA-6b	ITGB3	17	3690	NM_000212	ITB3_Human	rs1330487	1544G>A	R515Q	R489Q	4	2052	0.0019	0	4	0.000	0.004	0.00	0.39
HPA-12b	GP1BB	22	2812	NM_000407	GPBB_Human	rs37528585 7	119G>A	G40E	G15E	3	2030	0.0015	0	3	0.000	0.003	0.00	0.30
HPA-15b	CD109	8	135228	NM_133493	Q8TDJ3	rs10455097	2108C>A	S703Y	S682Y	856	2048	0.418	178	500	0.174	0.488	17.38	48.83
HPA-29b	ITGB3	17	3690	NM_000212	ITB3_Human	rs54427630	98C>T	T33M	T7M	1	2052	0.0005	0	1	0.000	0.001	0.00	0.10

						0												
HPA-30b	ITGA2B	17	3674	NM_000419	ITAB_Human	rs37775337 3	2511 G>C	Q837H	Q806H	30	2054	0.0146	1	28	0.001	0.027	0.10	2.73

Table 2. Tabulation of observed frequencies of HPA variants in the Indian population. For HPA systems that are not listed in the table no variants were found in the population.

HPA Genotype	Observed number	Observed Genotype Freq%	Observed Genotype Freq	Expected number	Expected Genotype Freq%	Expected Genotype Freq	Chi square	P value
HPA-1aa	814	0.790	79.04	803.2	0.781	78.06		
HPA-1ab	191	0.186	18.62	211.8	0.206	20.59		
HPA-1bb	24	0.023	2.34	14.0	0.014	1.36	9.331	0.0094
HPA-2aa	911	0.885	88.49	911.2	0.885	88.55		
HPA-2ab	115	0.112	11.22	114.3	0.111	11.10		
HPA-2bb	3	0.003	0.29	3.6	0.003	0.35	0.099	0.9515
HPA-3aa	454	0.436	43.63	438.6	0.426	42.63		
HPA-3ab	442	0.433	43.33	466.4	0.453	45.32		
HPA-3bb	133	0.130	13.04	124.0	0.120	12.05	2.47	0.2908
HPA-4aa	1027	0.998	99.80	438.6	0.426	42.63		
HPA-4ab	2	0.002	0.20	466.4	0.453	45.32		
HPA-4bb	0	0.000	0.00	124.0	0.120	12.05	1375.55	0.0001
HPA-5aa	877	0.851	85.13	876.1	0.851	85.14		
HPA-5ab	146	0.143	14.29	146.8	0.143	14.26		
HPA-5bb	6	0.006	0.59	6.1	0.006	0.60	0.009	0.9956
HPA-6aa	1025	0.996	99.61	1025.1	0.996	99.62		
HPA-6ab	4	0.004	0.39	3.9	0.004	0.38		
HPA-6bb	0	0.000	0.00	0.0	0.000	0.00	0.006	0.9969
HPA-12aa	1026	0.997	99.70	1025.9	0.997	99.70		
HPA-12ab	3	0.003	0.30	3.1	0.003	0.30		
HPA-12bb	0	0.000	0.00	0.0	0.000	0.00	0.005	0.9977
HPA-15aa	351	0.338	33.79	348.5	0.339	33.87		
HPA-15ab	500	0.488	48.83	500.7	0.487	48.66		
HPA-15bb	178	0.174	17.38	179.8	0.175	17.47	0.036	0.9822
HPA-29aa	1028	0.999	99.90	1028.0	0.999	99.90		
HPA-29ab	1	0.001	0.10	1.0	0.001	0.10		
HPA-29bb	0	0.000	0.00	0.0	0.000	0.00	0.001	0.9995

HPA-30aa	1000	0.972	97.18	999.2	0.971	97.10		
HPA-30ab	28	0.027	2.73	29.6	0.029	2.88		
HPA-30bb	1	0.001	0.10	0.2	0.000	0.02	2.866	0.2385

Table 3. Estimation of Chi squared statistic and P-values using the observed and expected genotype frequencies of various classes of HPA observed in the Indian population

Population	1a	1b	2a	2b	3a	3b	4a	4b	5a	5b	6a	6b	15a	15b	n
Malay	0.975	0.025	0.9625	0.0375	0.5025	0.4975	0.995	0.005	0.95	0.05	0.9925	0.0075	0.515	0.485	200
Malaysian_Chinese	1	0	0.9675	0.0325	0.5725	0.4275	0.9975	0.0025	0.9825	0.0175	0.9825	0.0175	0.4975	0.5025	200
Malaysian_Indian	0.885	0.115	0.96	0.04	0.62	0.38	0.9975	0.0025	0.94	0.06	0.995	0.005	0.4075	0.5925	200
Argentinean	0.878	0.122	0.875	0.125	0.612	0.388	1	0	0.927	0.073	1	0	0.511	0.489	192
Amerindian_Toba	1	0	0.944	0.056	0.389	0.611	1	0	1	0	1	0	0.685	0.315	27
Brazilian_(White)	0.78	0.22	0.9	0.1	0.63	0.37	1	0	1	0	0	0	0	0	400
Brazilian_(Black)	0.903	0.097	0.81	0.19	0.666	0.334	1	0	0.876	0.124	0	0	0	0	150
Brazilian_(Amerindian)	1	0	0.821	0.179	0.757	0.243	1	0	1	0	0	0	0	0	70
Algerian	0.8347	0.1653	0.8347	0.1653	0.6296	0.3704	1	0	0.8431	0.1569	0	0	0.53	0.47	485
Beninese	0.896	0.104	0.708	0.292	0.679	0.321	1	0	0.818	0.182	1	0	0.646	0.354	154
Cameroonian	0.907	0.093	0.763	0.237	0.614	0.386	1	0	0.746	0.254	1	0	0.691	0.309	118
Congolese	0.904	0.096	0.776	0.224	0.596	0.404	1	0	0.732	0.268	1	0	0.701	0.299	125
Central_African	1	0	0.607	0.393	0.5	0.5	1	0	0.595	0.405	1	0	0.698	0.302	110
Moroccan	0.748	0.252	0.818	0.182	0.682	0.318	1	0	0.861	0.139	1	0	0	0	
South_African_(Bantu_Speaker)	0.8905	0.1095	0.8135	0.1865	0.6995	0.3005	1	0	0.6835	0.3165	0	0	0.8075	0.1925	150
South_African_(Indian)	0.893	0.107	0.9305	0.0695	0.6695	0.3305	1	0	0.937	0.063	0	0	0.4395	0.5605	150
South_African_(White)	0.8205	0.1795	0.9005	0.0995	0.5735	0.4265	1	0	0.887	0.113	0	0	0.5405	0.4595	150
Tunisian	0.75	0.25	0	0	0.694	0.306	0	0	0.779	0.221	0	0	0	0	90

Austrian	0.852	0.148	0.918	0.082	0.612	0.388	1	0	0.892	0.108	1	0	0.5	0.5	
British	0.84	0.16	0.925	0.075	0.627	0.373	1	0	0.914	0.086	1	0	0.524	0.476	134
Croatian_1	0.854	0.146	0.89	0.11	0.575	0.425	0	0	0.895	0.105	0	0	0	0	219
Croatian_2	0	0	0	0	0	0	0	0	0	0	0	0	0.53	0.47	558
Czech	0.83	0.17	0.9	0.1	0.59	0.41	0	0	0.93	0.07	0	0	0	0	235
Danish	0.83	0.17	0.92	0.08	0.63	0.37	1	0	0.92	0.08	1	0	0.5	0.5	
French_1	0.848	0.152	0	0	0.62	0.38	0	0	0.874	0.126	0	0	0	0	6192
French_2	0	0	0.92	0.08	0	0	0	0	0	0	0	0	0	0	525
French_3	0	0	0	0	0	0	0	0	0	0	0	0	0.455	0.545	1242
German	0.84	0.16	0.93	0.07	0.6	0.4	0	0	0.92	0.08	0	0	0	0	
Italian	0.85	0.15	0.89	0.11	0.61	0.39	1	0	0.9	0.1	1	0	0	0	144
Lebanese	0.81	0.19	0	0	0	0	0	0	0	0	0	0	0	0	205
Macedonian	0.865	0.135	0.852	0.148	0.578	0.422	0	0	0.909	0.091	0	0	0	0	
Norwegian	0.867	0.133	0.943	0.057	0.471	0.529	1	0	0.929	0.071	0	0	0.495	0.505	105
Poland	0.824	0.176	0.901	0.099	0.582	0.418	1	0	0.944	0.056	0	0	0.485	0.515	
Slovenian	0.832	0.168	0.899	0.101	0.667	0.333	0	0	0.892	0.108	0	0	0.527	0.463	
Spanish	0.81	0.19	0.9	0.1	0.65	0.35	1	0	0.88	0.108	1	0	0.474	0.52	
Swiss	0.809	0.191	0.918	0.109	0.591	0.407	0.997	0.003	0.934	0.066	0	0	0	0	500
Welsh	0.8253	0.1747	0.9018	0.0982	0.6071	0.3929	1	0	0.9027	0.0973	1	0	0.5241	0.4759	
Indian	0.9244	0.0756	0.9979	0.0021	0.01	0.99	0.9953	0.0047	0.9562	0.0438	0.9923	0.0077	0	0	1164
Pakistani	0.885	0.115	0.92	0.08	0.69	0.31	1	0	0.9	0.1	0	0	0.59	0.41	593
Northeastern_Thai	0.972	0.028	0.938	0.062	0.533	0.467	1	0	0.963	0.037	0.985	0.015	0.495	0.505	300
Thai	0.985	0.015	0.952	0.048	0.56	0.44	1	0	0.968	0.032	0.986	0.014	0.491	0.509	500
Indonesian	0.991	0.009	0.939	0.061	0.505	0.495	1	0	0.995	0.005	0.967	0.033	0	0	107
Vietnamese	0.986	0.014	0.953	0.047	0.486	0.514	1	0	0.972	0.028	0.986	0.014	0.477	0.523	120
Han_Chinese	0.994	0.006	0.9515	0.0485	0.5945	0.4055	0.9955	0.0045	0.986	0.014	0.9865	0.0135	0.532	0.468	1,000
Taiwanese	0.9967	0.0033	0.96	0.04	0.575	0.425	0.9983	0.0017	0.985	0.015	0.9633	0.0367	0.538	0.462	300
Japanese	0.998	0.002	0.9	0.1	0.718	0.282	0.989	0.011	0.973	0.027	0.973	0.027	0	0	73
Korean	0.988	0.012	0.923	0.077	0.555	0.445	0.99	0.01	0.978	0.022	0.98	0.02	0	0	200
French_Polynesian	0.975	0.025	0.913	0.087	0.599	0.401	1	0	0.975	0.025	0.932	0.068	0.463	0.537	81
Australian	0.858	0.142	0.927	0.073	0.619	0.381	1	0	0.905	0.095	0	0	0	0	185

IndiGen	0.89	0.15	0.94	0.05	0.66	0.36	1.00	0.00	0.92	0.08	1.00	0.00	0.58	0.42	1029

Table 4. Precise tabulation of allele frequencies of HPA-1,2,3,4,5 and 15 systems across multiple global populations.

Supplementary Datasets

Supplementary Table 1. Frequencies of HPA alleles observed in various subpopulations of the gnomAD dataset

Supplementary Table 2. Frequencies of HPA alleles observed in various subpopulations of 1000 Genomes dataset

Website references

1. Human Platelet Antigen Database - https://www.versiti.org/medical-professionals/precision-medicine-expertise/platelet-antigen-database
2. IndiGenomes - https://clingen.igib.res.in/indigen/

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