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ORIGINAL ARTICLE

Allelic frequencies and heterozygosities of microsatellite markers covering the whole genome in the Korean

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Abstract Microsatellite markers are an essential tool for genetic linkage analysis because of their high polymorphism content. Four hundred commercially available markers covering the entire genome were genotyped from 578 sib individuals from 249 Korean families. Allelic frequencies and heterozygosities were determined for each marker loci and compared between Korean, Taiwanese, Japanese and Caucasian populations. In the three Asian populations, 10–13% of the markers had less than 0.6 heterozygosity, whereas in the Caucasian population, only 0.5% of the markers had less than 0.6 heterozygosity. Mean identical by descent (IBD) values were calculated for 578 sib individuals.Analysis of IBD values greater than 0.5 suggested that markers with low heterozygosity can also provide positive linkages, at least for the IBD sharing method of model-free linkage analysis. The data presented in this study will be a useful reference for genome-wide screens of Koreans and comparative studies with other ethnic populations.

Keywords Microsatellite marker · Allele frequency · Heterozygosity · Linkage · IBD · Korean

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Introduction

Microsatellite markers are widely used to search for disease-associated genes by linkage analysis and for diversity studies in human genetics (Schellenberg et al. 1992; Bowcock et al. 1994; Thomson et al. 1999). Because microsatellite markers typically have greater than ten alleles, they are more polymorphic and more informative than SNP markers, which are usually biallelic. For use in linkage analyses, a locus should be highly polymorphic so that the alleles inherited from each parent can be distinguished from one another. The use of multiallelic markers offers greater statistical power, allowing detection of linkage disequilibrium and genetic linkage by way of parametric analysis of large families or nonparametric analysis of sibling pairs (Ott and Rabinowitz 1997; Tan et al. 2002).

As the use of microsatellite markers for linkage mapping becomes more widespread, primer sets for genome-wide screening or chromosome-specific mapping have become commercially available. Markers have been optimized for multiplex PCR and fragment analysis, and technology for analyzing microsatellite polymorphisms has been automated for high-throughput screening. Genotype information, including allelic frequency and heterozygosity, is available through various databases, but these data have been derived primarily from Caucasian samples.

Microsatellite markers are generally selected based on their heterozygosity and recombination frequency in Caucasians and thus may not be suitable for genetic analyses of other ethnic groups. Indeed, significant differences have been identified in the allelic distribution of microsatellite markers in Caucasian and Asian populations (Yamane-Tanaka et al. 1998; Ikari et al. 2001; Mizutani et al. 2001; Tan et al. 2002; Lu et al. 2004). Because allelic information differs between ethnic groups and certainly influences the statistical analysis, it is problematic to use information from other populations to study disease susceptibility genes in the Korean population.

In the present study, we report heterozygosity and allelic information for 400 dinucleotide repeat markers in 578 Korean subjects. The data are less informative compared with data compiled for the Caucasian population, but the data should be useful for genetic linkage studies in Koreans and other populations.

Materials and methods

Subjects and DNA preparation

Blood samples were collected from 578 sibs in 249 Korean families. Of these, 171 families had type-2 diabetes and 78 families had hypertension. We obtained written informed consent from all subjects. DNA was isolated from blood samples using the QIAamp DNA blood kit (Qiagen, Valencia, CA) according to the manufacturer's instructions.

Microsatellite marker genotyping

Genotyping was performed using the ABI PRISM Linkage Mapping Set MD-10 (Applied Biosystems), which is comprised of 400 microsatellite markers. All markers were dinucleotide repeats. PCR amplification using a fluorescently labeled forward primer and tailing reverse primer for each marker (95°C for 2 min, then 35 cycles at 95°C for 20 s, 58°C for 40 s, 72°C for 30 s, and 72°C for 45 min) was performed in a 384-well format in a total of 5 μl. Electrophoresis was performed on ABI 3730 Automated Sequencers (Applied Biosystems) using a standard protocol. The use of GeneScan 500 Liz (Applied Biosystems) as the internal size standard assisted in polymorphic fragment length calling and allowed more accurate allele calling and unambiguous comparison of data across experimental conditions.

Genotypes were initially scored using GENEMAPPER 3.7 software (Applied Biosystems) and reviewed independently to confirm the accuracy of allele calling. All genotyped markers were checked for incompatibilities using MARKERINFO from the SAGE package (version 5.2) (Elston 1992). Genotypes of the CEPH standard 1347-02 were used for quality control.

Statistical analysis

Allelic frequencies for each marker were computed using RECODE (ftp://www.linkage.rockefeller.edu/softwair/linkage) and FREQ from the SAGE package. Heterozygosity of each marker was determined in 249 unrelated individuals and 578 sib individuals. Heterozygosity of markers was assessed by comparing the expected value against the observed number of heterozygotes using the Fisher exact test (SAS software). The polymorphism information content (PIC) was also calculated using SAS software. Marker information for Caucasians, Japanese and Taiwanese was obtained from the CEPH database (http://www.cephb.fr) and other published data (Ikari et al. 2001; Lu et al. 2004). GENIBD from the SAGE package was used to estimate the mean ratio of IBD alleles among sib pairs at each autosomal marker.

Results

Distribution of allele frequencies in Koreans

We genotyped 400 markers from 578 individuals. All markers could be amplified. Individuals with ambiguous genotypes were not included in the analysis. Hardy–Weinberg equilibrium was evaluated using the Fisher exact test; 23 of the 400 loci did not meet the criteria for Hardy–Weinberg equilibrium ($P < 0.01$).

The frequency was calculated for each autosomal and X chromosome marker using 249 unrelated individuals and 188 unrelated females, respectively. Table 1 summarizes the size range and number of each allele in Koreans. The number of alleles ranged from 4 (D4S1575) to 25 (D4S402). The average number of alleles was 11.26 (SD ± 3.21).

Heterozygosity varies between populations

Heterozygosities for the 400 marker loci in Koreans (this study), Taiwanese and Caucasians are summarized in Table 1. Heterozygosity ranged from 0.19 (D4S1575) to 0.93 (D15S205), with an average of 0.72 (SD ± 0.12), for Koreans and ranged from 0.21 (DXS8055) to 0.93 (D7S636), with an average of 0.73 (SD ± 0.12), for Taiwanese. Fifty-two markers (13%) had a heterozygosity of <0.6 in the Korean population, and 48 markers (12.03%) had a heterozygosity of <0.6 in the Taiwanese

Table 1 Allele information and heterozygosities for 400 microsatellite markers in the Korean population compared with Taiwanese and Caucasians

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
1	D1S486	192–214	11	0.72	0.81	0.76	0.7111	0.4579
	D1S214	123–145	9	0.66	0.70	0.78	0.6149	0.4481
	D1S450	315–349	14	0.88	0.80	0.81	0.8038	0.4373
	D1S2667	130–156	13	0.81	0.81	0.82	0.7694	0.4477
	D1S2697	285–299	6	0.37	0.46	0.70	0.3858	0.4735
	D1S199	98–122	13	0.79	0.80	0.83	0.7729	0.4856
	D1S234	264–284	11	0.82	0.82	0.81	0.8038	0.4829
	D1S255	91–103	8	0.37	0.34	0.75	0.3434	0.4879
	D1S2797	114–130	9	0.70	0.75	0.74	0.6817	0.4897
	D1S2890	210–232	12	0.72	0.71	0.81	0.7095	0.4949
	D1S230	148–166	10	0.57	0.59	0.78	0.5333	0.5041
	D1S2841	233–251	10	0.84	0.83	0.78	0.8185	0.5147
	D1S207	146–172	13	0.82	0.80	0.84	0.7812	0.5171
	D1S2868	201–221	10	0.59	0.65	0.76	0.5644	0.5091
	D1S206	210–226	9	0.77	0.80	0.82	0.7440	0.5030
	D1S2726	275–299	11	0.73	0.68	0.75	0.6843	0.4890
	D1S252	89–107	10	0.69	0.77	0.81	0.7655	0.4806
	D1S498	182–208	14	0.74	0.74	0.82	0.7235	0.4800
	D1S484	276–286	6	0.67	0.70	0.64	0.6380	0.5003
	D1S2878	148–176	10	0.81	0.80	0.84	0.7859	0.5198
	D1S196	319–331	6	0.62	0.58	0.74	0.5911	0.5214
	D1S218	269–289	11	0.81	0.82	0.83	0.7975	0.5194
	D1S238	296–320	11	0.78	0.80	0.86	0.7541	0.5120
	D1S413	249–267	10	0.68	0.68	0.76	0.6451	0.5047
	D1S249	163–187	13	0.73	0.70	0.87	0.7197	0.5013
	D1S425	340–358	8	0.53	0.54	0.81	0.4905	0.4880
	D1S213	104–130	14	0.79	0.84	0.86	0.8347	0.4890
	D1S2800	201–223	11	0.72	0.74	0.77	0.7327	0.4856
	D1S2785	171–189	11	0.85	0.86	0.76	0.8346	0.4980
	D1S2842	343–355	7	0.71	0.65	0.76	0.6543	0.5098
	D1S2836	233–257	12	0.71	0.71	0.79	0.7281	0.5068
2	D2S319	125–139	8	0.74	0.72	0.73	0.6663	0.4869
	D2S2211	241–261	11	0.55	0.68	0.74	0.5684	0.4875
	D2S162	118–144	12	0.85	0.81	0.75	0.8020	0.4720
	D2S168	158–178	11	0.71	0.75	0.82	0.7275	0.4723
	D2S305	314–336	9	0.79	0.78	0.72	0.7348	0.4764
	D2S165	143–173	16	0.85	0.86	0.85	0.8409	0.4695
	D2S367	308–340	15	0.88	0.87	0.86	0.8698	0.4624
	D2S2259	317–341	11	0.65	0.60	0.79	0.5850	0.4690
	D2S391	145–159	8	0.75	0.70	0.79	0.7196	0.4704
	D2S337	283–313	15	0.84	0.85	0.88	0.8069	0.4729
	D2S2368	90–116	14	0.85	0.84	0.83	0.8069	0.4752
	D2S286	87–103	9	0.80	0.80	0.66	0.7629	0.4702
	D2S2333	79–111	12	0.84	0.83	0.82	0.8156	0.4863
	D2S2216	209–225	9	0.71	0.65	0.76	0.6878	0.5004
	D2S160	202–220	9	0.71	0.74	0.78	0.6544	0.4978
	D2S347	230–298	12	0.62	0.68	0.80	0.5744	0.4915

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D2S112	71–85	8	0.61	0.71	0.71	0.6266	0.4867
	D2S151	234–254	10	0.78	0.79	0.82	0.7629	0.4862
	D2S142	235–249	8	0.67	0.71	0.76	0.6360	0.4788
	D2S2330	170–186	9	0.82	0.79	0.81	0.7907	0.4689
	D2S335	186–212	14	0.82	0.84	0.79	0.8274	0.4801
	D2S364	227–255	13	0.80	0.75	0.80	0.7634	0.4781
	D2S117	191–217	13	0.84	0.85	0.82	0.8531	0.4891
	D2S325	156–188	16	0.80	0.74	0.82	0.7646	0.4932
	D2S2382	305–337	17	0.49	0.47	0.81	0.4798	0.4845
	D2S126	121–145	12	0.79	0.82	0.82	0.7698	0.4782
	D2S396	226–252	13	0.78	0.89	0.83	0.8400	0.4773
	D2S206	126–160	12	0.83	0.82	0.80	0.7822	0.4762
	D2S338	274–298	13	0.83	0.85	0.81	0.8271	0.4496
	D2S125	87–113	14	0.83	0.83	0.82	0.7848	0.4494
3	D3S1297	349–365	9	0.75	0.74	0.82	0.7253	0.4654
	D3S1304	257–277	10	0.72	0.80	0.80	0.7526	0.4838
	D3S1263	185–217	15	0.86	0.89	0.86	0.8897	0.4613
	D3S2338	91–117	14	0.58	0.77	0.86	0.7037	0.4498
	D3S1266	294–306	7	0.69	0.71	0.73	0.6443	0.4631
	D3S1277	287–307	7	0.63	0.68	0.82	0.5926	0.4691
	D3S1289	202–220	10	0.82	0.80	0.81	0.7861	0.4750
	D3S1300	234–260	11	0.81	0.83	0.82	0.7862	0.4798
	D3S1285	237–247	6	0.62	0.74	0.73	0.6729	0.4613
	D3S1566	155–185	12	0.87	0.85	0.84	0.8359	0.4505
	D3S3681	124–164	14	0.80	0.81	0.83	0.7973	0.4453
	D3S1271	90–100	6	0.62	0.63	0.73	0.5479	0.4519
	D3S1278	229–257	15	0.73	0.77	0.87	0.7023	0.4658
	D3S1267	92–126	17	0.70	0.76	0.88	0.6934	0.4687
	D3S1292	120–146	14	0.91	0.89	0.85	0.8665	0.4759
	D3S1569	155–183	15	0.76	0.76	0.80	0.7243	0.4796
	D3S1279	265–283	10	0.76	0.76	0.85	0.7482	0.4878
	D3S1614	101–121	11	0.66	0.74	0.83	0.6163	0.4863
	D3S1565	176–192	9	0.76	0.76	0.64	0.7204	0.4879
	D3S1262	114–132	10	0.69	0.71	0.80	0.7159	0.4836
	D3S1580	217–249	17	0.80	0.81	0.84	0.7955	0.4846
	D3S1601	302–328	13	0.81	0.80	0.85	0.7454	0.4818
	D3S1311	137–159	11	0.77		0.83	0.7058	0.4803
4	D4S412	162–180	10	0.68	0.71	0.77	0.6099	0.4925
	D4S2935	83–107	11	0.68	0.64	0.62	0.6008	0.4843
	D4S403	170–186	9	0.52	0.61	0.77	0.5190	0.4734
	D4S419	225–289	10	0.66	0.65	0.77	0.6839	0.4597
	D4S391	147–175	13	0.78	0.81	0.85	0.7632	0.4734
	D4S405	286–304	10	0.79	0.73	0.86	0.7406	0.4789
	D4S1592	112–146	12	0.78	0.83	0.72	0.8071	0.4684
	D4S392	87–107	10	0.76	0.79	0.82	0.7588	0.4697
	D4S2964	123–143	8	0.65	0.73	0.76	0.6495	0.4689
	D4S1534	143–171	13	0.84	0.81	0.77	0.8130	0.4747
	D4S414	232–246	8	0.67	0.78	0.89	0.7212	0.4786

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D4S1572	191–215	12	0.84	0.81	0.84	0.8147	0.4773
	D4S406	248–264	9	0.69	0.68	0.87	0.6508	0.4674
	D4S402	107–157	25	0.66	0.72	0.91	0.7823	0.4548
	D4S1575	296–302	4	0.19	0.28	0.65	0.2073	0.4678
	D4S424	194–214	11	0.66	0.66	0.83	0.6343	0.4713
	D4S413	283–331	18	0.60	0.60	0.85	0.5911	0.4805
	D4S1597	278–296	10	0.26	0.28	0.76	0.2528	0.4900
	D4S1539	310–324	6	0.40	0.41	0.68	0.3925	0.4991
	D4S415	258–300	16	0.79	0.75	0.80	0.7736	0.4982
	D4S1535	245–271	14	0.70	0.78	0.77	0.6977	0.4973
	D4S426	161–177	8	0.70	0.69	0.76	0.6563	0.4939
5	D5S1981	117–135	10	0.72	0.65	0.73	0.7026	0.4485
	D5S406	162–186	10	0.70	0.67	0.79	0.7314	0.4381
	D5S630	155–377	22	0.85	0.86	0.89	0.8703	0.4574
	D5S416	282–302	12	0.60	0.69	0.77	0.6469	0.4664
	D5S419	258–282	12	0.82	0.85	0.81	0.8342	0.4594
	D5S426	276–300	10	0.74	0.77	0.80	0.7173	0.4683
	D5S418	211–231	11	0.80	0.83	0.80	0.8013	0.4885
	D5S407	84–114	16	0.88	0.85	0.86	0.8469	0.4871
	D5S647	326–356	15	0.78	0.76	0.82	0.7807	0.4794
	D5S424	207–239	10	0.57	0.60	0.76	0.5527	0.4721
	D5S641	297–327	15	0.78	0.83	0.77	0.8097	0.4813
	D5S428	245–261	8	0.71	0.72	0.76	0.6547	0.4871
	D5S644	85–105	11	0.76	0.80	0.85	0.7920	0.4935
	D5S433	71–91	10	0.70	0.67	0.86	0.7081	0.4895
	D5S2027	186–204	8	0.61	0.60	0.78	0.5657	0.4878
	D5S471	238–256	12	0.71	0.73	0.76	0.6684	0.4800
	D5S2115	152–180	14	0.65	0.70	0.76	0.6685	0.4726
	D5S436	231–253	11	0.67	0.69	0.83	0.6939	0.4815
	D5S410	325–345	8	0.55	0.52	0.79	0.4992	0.4879
	D5S422	119–139	11	0.83	0.81	0.84	0.7855	0.4850
	D5S400	200–240	15	0.83	0.84	0.82	0.8543	0.4841
	D5S408	243–273	14	0.73	0.78	0.73	0.7136	0.4925
6	D6S1574	155–173	10	0.66	0.73	0.84	0.6541	0.4641
	D6S309	307–327	11	0.80	0.78	0.83	0.7428	0.4652
	D6S470	120–142	11	0.65	0.67	0.80	0.6365	0.4672
	D6S289	163–181	10	0.84	0.79	0.79	0.7797	0.4778
	D6S422	296–316	11	0.70	0.64	0.77	0.6461	0.4710
	D6S276	201–233	12	0.77	0.77	0.83	0.7148	0.4791
	D6S1610	196–212	9	0.73	0.78	0.84	0.7245	0.4872
	D6S257	163–191	14	0.85	0.86	0.87	0.8496	0.4890
	D6S460	278–300	11	0.78	0.80	0.81	0.7534	0.4711
	D6S462	103–117	8	0.54	0.52	0.68	0.5205	0.4485
	D6S434	200–230	14	0.84	0.75	0.86	0.7792	0.4357
	D6S287	117–137	10	0.61	0.63	0.85	0.5943	0.4380
	D6S262	170–190	11	0.68	0.77	0.82	0.6467	0.4399
	D6S292	152–180	15	0.75	0.83	0.83	0.7718	0.4345
	D6S308	335–347	7	0.68	0.64	0.75	0.6170	0.4434

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D6S441	162–196	14	0.82	0.80	0.86	0.7840	0.4517
	D6S1581	257–275	10	0.53	0.57	0.72	0.5360	0.4674
	D6S264	112–126	9	0.52	0.48	0.70	0.4703	0.4829
	D6S446	217–225	5	0.45	0.45	0.62	0.4504	0.4883
	D6S281	136–164	15	0.80	0.82	0.68	0.8150	0.4936
7	D7S531	281–295	8	0.74	0.72	0.77	0.6881	0.4729
	D7S517	245–263	10	0.76	0.78	0.83	0.7956	0.4679
	D7S513	170–204	17	0.86	0.91	0.83	0.8940	0.4560
	D7S507	81–111	14	0.81	0.86	0.89	0.8222	0.4634
	D7S493	201–241	19	0.71	0.68	0.88	0.6497	0.4760
	D7S516	312–326	8	0.76	0.74	0.76	0.7202	0.4833
	D7S484	103–117	8	0.80	0.78	0.74	0.7793	0.4824
	D7S510	75–103	13	0.79	0.75	0.77	0.7123	0.4711
	D7S519	259–277	10	0.76	0.73	0.81	0.7204	0.4703
	D7S502	289–317	15	0.88	0.87	0.84	0.8646	0.4828
	D7S669	177–197	11	0.83	0.85	0.80	0.8207	0.5037
	D7S630	330–358	13	0.73	0.77	0.73	0.7092	0.4899
	D7S657	243–269	11	0.83	0.83	0.81	0.8004	0.4877
	D7S515	137–189	13	0.74	0.75	0.82	0.7036	0.4817
	D7S486	224–238	8	0.77	0.78	0.81	0.7440	0.4792
	D7S530	100–124	12	0.66	0.66	0.78	0.6442	0.4741
	D7S640	106–148	19	0.87	0.88	0.85	0.8979	0.4797
	D7S684	345–361	9	0.83	0.84	0.81	0.7989	0.4577
	D7S661	307–329	12	0.79	0.82	0.75	0.8112	0.4498
	D7S636	129–173	23	0.90	0.93	0.90	0.9172	0.4524
	D7S798	71–91	11	0.78	0.75	0.84	0.7244	0.4469
	D7S2465	317–345	13	0.78	0.80	0.83	0.7704	0.4633
8	D8S264	141–163	12	0.81	0.85	0.83	0.8292	0.4888
	D8S277	151–185	15	0.82	0.81	0.73	0.7821	0.4802
	D8S550	192–220	14	0.80	0.75	0.87	0.7359	0.4874
	D8S549	76–86	5	0.52	0.49	0.63	0.4079	0.4914
	D8S258	148–158	6	0.69	0.68	0.70	0.6086	0.4823
	D8S1771	348–364	8	0.66	0.62	0.75	0.6047	0.4612
	D8S505	106–126	10	0.76	0.78	0.79	0.7381	0.4610
	D8S285	313–331	10	0.74	0.74	0.78	0.7108	0.4622
	D8S260	201–215	8	0.69	0.81	0.81	0.7917	0.4688
	D8S270	102–120	10	0.74	0.69	0.79	0.6850	0.4733
	D8S1784	281–295	8	0.73	0.72	0.67	0.6548	0.4644
	D8S514	216–230	8	0.73	0.70	0.77	0.6718	0.4847
	D8S284	272–316	19	0.89	0.83	0.83	0.8011	0.4947
	D8S272	238–264	11	0.78	0.80	0.81	0.7799	0.5021
9	D9S288	128–156	15	0.79	0.84	0.84	0.8347	0.5002
	D9S286	143–169	14	0.79	0.80	0.88	0.7265	0.4932
	D9S285	86–110	11	0.62	0.59	0.78	0.6086	0.4895
	D9S157	222–244	12	0.78	0.78	0.84	0.7792	0.4879
	D9S171	158–180	9	0.32	0.31	0.79	0.3000	0.4881
	D9S161	119–137	8	0.61	0.54	0.78	0.5184	0.4881
	D9S1817	275–315	17	0.85	0.82	0.88	0.8164	0.4924

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D9S273	202–220	9	0.59	0.61	0.74	0.6004	0.4889
	D9S175	260–288	15	0.69	0.72	0.85	0.6637	0.4979
	D9S167	306–334	12	0.78	0.82	0.87	0.7786	0.4989
	D9S283	90–106	8	0.70	0.70	0.80	0.6857	0.4985
	D9S287	297–309	6	0.62	0.67	0.67	0.5444	0.4811
	D9S1690	227–245	7	0.71	0.74	0.78	0.7216	0.4848
	D9S1677	223–255	15	0.89	0.88	0.81	0.8820	0.4722
	D9S1776	178–198	10	0.69	0.71	0.84	0.6852	0.4718
	D9S1682	151–159	5	0.66	0.63	0.68	0.5587	0.4675
	D9S290	243–259	9	0.67	0.69	0.83	0.6690	0.4787
	D9S164	81–101	11	0.84	0.82	0.80	0.8112	0.4828
	D9S1826	215–233	10	0.87	0.79	0.69	0.7892	0.4883
	D9S158	327–351	11	0.68	0.48	0.69	0.6426	0.4845
10	D10S249	117–139	12	0.79	0.77	0.74	0.7658	0.5061
	D10S591	318–340	9	0.58	0.57	0.71	0.5819	0.4955
	D10S189	185–195	6	0.76	0.75	0.72	0.6909	0.4916
	D10S547	236–260	13	0.52	0.49	0.74	0.4740	0.4826
	D10S1653	117–135	10	0.81	0.78	0.77	0.7428	0.4767
	D10S548	182–198	7	0.61	0.63	0.70	0.5232	0.4798
	D10S197	167–181	8	0.71	0.76	0.75	0.7146	0.4871
	D10S208	167–193	11	0.75	0.79	0.79	0.7482	0.4947
	D10S196	103–119	8	0.66	0.68	0.77	0.6184	0.4972
	D10S1652	272–296	12	0.69	0.66	0.78	0.6383	0.4891
	D10S537	147–165	10	0.78	0.79	0.83	0.7634	0.5003
	D10S1686	246–280	16	0.65	0.72	0.86	0.6401	0.5098
	D10S185	201–227	13	0.79	0.77	0.77	0.7576	0.5379
	D10S192	237–267	15	0.86	0.84	0.77	0.8256	0.5269
	D10S597	279–295	6	0.50	0.50	0.64	0.3924	0.5203
	D10S1693	209–229	10	0.78	0.76	0.80	0.7444	0.5130
	D10S587	88–116	13	0.80	0.80	0.80	0.7749	0.5120
	D10S217	97–117	11	0.82	0.84	0.81	0.8214	0.5099
	D10S1651	202–226	11	0.61	0.59	0.80	0.5549	0.4911
	D10S212	192–208	9	0.42	0.28	0.71	0.4006	0.4870
11	D11S4046	98–130	14	0.70	0.77	0.86	0.7679	0.4738
	D11S1338	258–270	8	0.64	0.71	0.74	0.6079	0.4652
	D11S902	148–172	13	0.79	0.81	0.80	0.7960	0.4591
	D11S904	185–207	11	0.72	0.74	0.83	0.6745	0.4770
	D11S935	193–215	11	0.82	0.73	0.73	0.7488	0.4904
	D11S905	270–296	14	0.46	0.79	0.75	0.7730	0.4701
	D11S4191	92–118	14	0.88	0.89	0.87	0.8744	0.4846
	D11S987	93–141	17	0.87	0.82	0.82	0.8076	0.4794
	D11S1314	92–112	11	0.78	0.82	0.78	0.7810	0.4965
	D11S937	144–180	16	0.76	0.83	0.88	0.7526	0.5095
	D11S901	316–330	7	0.66	0.66	0.82	0.6083	0.5120
	D11S4175	292–346	20	0.88	0.85	0.89	0.8334	0.5230
	D11S898	147–169	8	0.25	0.33	0.85	0.2515	0.5107
	D11S908	175–191	8	0.47	0.43	0.76	0.4115	0.4951
	D11S925	263–293	12	0.80	0.79	0.84	0.7752	0.4784

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D11S4151	330–346	9	0.38	0.53	0.79	0.4561	0.4825
	D11S1320	264–272	5	0.57	0.44	0.68	0.5063	0.4801
	D11S968	144–158	8	0.54	0.62	0.81	0.5796	0.4861
12	D12S352	157–175	10	0.69	0.78	0.73	0.6993	0.5021
	D12S99	261–303	16	0.84	0.83	0.83	0.7954	0.4993
	D12S336	107–127	11	0.67	0.74	0.82	0.6818	0.4936
	D12S364	292–336	19	0.82	0.84	0.87	0.8039	0.4908
	D12S310	244–256	7	0.62	0.63	0.69	0.5740	0.4910
	D12S1617	249–271	12	0.80	0.84	0.80	0.7917	0.4867
	D12S345	211–241	16	0.83	0.85	0.87	0.8175	0.4942
	D12S85	107–133	12	0.82	0.81	0.67	0.8050	0.4958
	D12S368	200–218	10	0.65	0.61	0.81	0.6005	0.4981
	D12S83	101–119	10	0.80	0.83	0.81	0.7261	0.4959
	D12S326	210–230	8	0.67	0.69	0.80	0.5990	0.4938
	D12S351	155–167	6	0.76	0.74	0.75	0.6963	0.4923
	D12S346	186–212	14	0.67	0.73	0.84	0.6538	0.4834
	D12S78	169–203	16	0.73	0.82	0.91	0.7389	0.4702
	D12S79	150–176	12	0.70	0.60	0.87	0.7693	0.4750
	D12S86	127–163	16	0.64	0.72	0.89	0.6605	0.4731
	D12S324	233–255	8	0.64	0.64	0.69	0.6137	0.4818
	D12S1659	304–324	6	0.50	0.52	0.78	0.4388	0.4830
	D12S1723	203–221	9	0.77	0.79	0.67	0.7418	0.4815
13	D13S175	103–113	6	0.68	0.71	0.76	0.6235	0.4938
	D13S217	246–266	12	0.72	0.78	0.68	0.7230	0.4976
	D13S171	177–199	11	0.63	0.64	0.73	0.5816	0.4998
	D13S218	143–161	7	0.72	0.64	0.66	0.5625	0.5095
	D13S263	147–177	14	0.80	0.78	0.84	0.7929	0.5056
	D13S153	85–115	15	0.90	0.90	0.81	0.8835	0.4930
	D13S156	277–295	10	0.80	0.78	0.80	0.7846	0.4923
	D13S170	139–167	16	0.85	0.85	0.90	0.8437	0.4987
	D13S265	105–119	7	0.67	0.61	0.70	0.6081	0.5033
	D13S159	158–194	17	0.81	0.77	0.90	0.7657	0.4961
	D13S158	113–139	12	0.38	0.76	0.82	0.6667	0.4750
	D13S173	238–250	7	0.74	0.74	0.82	0.6936	0.4843
	D13S1265	277–305	12	0.81	0.83	0.80	0.8022	0.4946
	D13S285	89–121	16	0.83	0.86	0.81	0.8427	0.4915
14	D14S261	273–301	9	0.68	0.64	0.75	0.6057	0.4907
	D14S283	129–157	14	0.80	0.78	0.81	0.7682	0.4869
	D14S275	149–161	7	0.47	0.53	0.70	0.4746	0.4864
	D14S70	102–110	5	0.71	0.74	0.75	0.6540	0.4881
	D14S288	184–214	16	0.86	0.88	0.83	0.8537	0.4969
	D14S276	232–254	11	0.78	0.76	0.76	0.7595	0.5039
	D14S63	177–203	12	0.78	0.73	0.76	0.7526	0.4930
	D14S258	196–212	9	0.60	0.65	0.79	0.6117	0.4930
	D14S74	298–316	10	0.80	0.75	0.79	0.7774	0.4826
	D14S68	319–335	9	0.57	0.79	0.91	0.7011	0.4843
	D14S280	240–252	8	0.64	0.71	0.68	0.5887	0.4781
	D14S65	128–156	11	0.76	0.76	0.79	0.7532	0.4627

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D14S985	242–260	10	0.74	0.73	0.76	0.7068	0.4701
	D14S292	84–100	9	0.72	0.72	0.73	0.6626	0.4834
15	D15S128	197–219	12	0.84	0.80	0.78	0.8206	0.4733
	D15S1002	107–131	13	0.78	0.78	0.78	0.7640	0.4962
	D15S165	187–213	10	0.24	0.31	0.79	0.2353	0.4928
	D15S1007	78–110	16	0.83	0.82	0.86	0.8091	0.4868
	D15S1012	92–110	10	0.60	0.58	0.72	0.5636	0.4788
	D15S994	300–318	10	0.70	0.70	0.73	0.6339	0.4666
	D15S978	185–211	14	0.77	0.83	0.83	0.7630	0.4754
	D15S117	323–343	11	0.67	0.71	0.78	0.6510	0.4770
	D15S153	253–275	12	0.80	0.81	0.87	0.7926	0.4780
	D15S131	241–275	18	0.74	0.77	0.83	0.7304	0.4865
	D15S205	151–179	15	0.93	0.87	0.88	0.8523	0.4966
	D15S127	118–162	23	0.83	0.80	0.86	0.8260	0.4846
	D15S130	284–306	12	0.74	0.77	0.66	0.7354	0.4760
	D15S120	155–181	11	0.72	0.75	0.73	0.7515	0.4823
16	D16S423	136–158	11	0.80	0.84	0.73	0.8200	0.4833
	D16S404	273–285	7	0.73	0.75	0.80	0.6533	0.4846
	D16S3075	74–94	10	0.73	0.82	0.79	0.7912	0.4911
	D16S3103	317–337	11	0.46	0.44	0.81	0.4231	0.4902
	D16S3046	82–118	11	0.71	0.74	0.74	0.7138	0.4841
	D16S3068	221–241	10	0.72	0.71	0.77	0.6788	0.4847
	D16S3136	171–191	11	0.64	0.59	0.69	0.6157	0.4862
	D16S415	214–236	11	0.69	0.70	0.72	0.6261	0.4728
	D16S503	294–314	11	0.66	0.56	0.81	0.6615	0.4427
	D16S515	328–356	15	0.80	0.85	0.80	0.8153	0.4406
	D16S516	246–260	8	0.63	0.60	0.73	0.5961	0.4644
	D16S3091	164–196	15	0.83	0.83	0.73	0.8483	0.4711
	D16S520	150–166	9	0.79	0.80	0.84	0.7727	0.4845
17	D17S849	257–265	5	0.73	0.75	0.67	0.7061	0.4602
	D17S831	107–131	13	0.88	0.87	0.82	0.8495	0.4504
	D17S938	235–257	12	0.83	0.84	0.76	0.8197	0.4693
	D17S1852	284–314	13	0.83	0.81	0.87	0.8040	0.4773
	D17S799	193–207	9	0.64	0.68	0.68	0.6239	0.4414
	D17S921	200–212	7	0.71	0.67	0.72	0.6239	0.4414
	D17S1857	160–176	9	0.45	0.44	0.64	0.4356	0.4450
	D17S798	298–316	5	0.60	0.55	0.80	0.4308	0.4524
	D17S1868	254–268	8	0.80	0.82	0.73	0.7650	0.4651
	D17S787	143–173	11	0.82	0.80	0.81	0.7724	0.4878
	D17S944	319–333	9	0.43	0.42	0.75	0.4400	0.5016
	D17S949	214–232	10	0.78	0.80	0.80	0.7530	0.5154
	D17S785	165–193	13	0.65	0.74	0.83	0.6719	0.5147
	D17S784	227–247	11	0.55	0.63	0.77	0.5422	0.5097
	D17S928	70–104	18	0.83	0.83	0.76	0.8119	0.5016
18	D18S59	153–173	12	0.78	0.81	0.81	0.7829	0.5035
	D18S63	73–109	16	0.75	0.68	0.79	0.7036	0.5013
	D18S452	125–151	13	0.75	0.79	0.83	0.7696	0.4932
	D18S464	300–312	6	0.56	0.59	0.65	0.5087	0.4866

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
	D18S53	153–183	13	0.80	0.80	0.79	0.7828	0.4810
	D18S478	242–256	7	0.58	0.61	0.64	0.5298	0.4725
	D18S1102	82–104	11	0.68	0.76	0.79	0.6377	0.4663
	D18S474	121–147	14	0.73	0.80	0.82	0.8074	0.4644
	D18S64	322–342	11	0.82	0.80	0.74	0.8022	0.4938
	D18S68	270–292	12	0.79	0.81	0.68	0.7675	0.5053
	D18S61	209–239	13	0.79	0.82	0.87	0.7836	0.4913
	D18S1161	226–246	11	0.71	0.75	0.82	0.7224	0.4712
	D18S462	299–317	10	0.77	0.69	0.70	0.7029	0.4571
	D18S70	106–128	11	0.70	0.81	0.83	0.7083	0.4648
19	D19S209	239–259	10	0.82	0.80	0.77	0.7676	0.4899
	D19S216	258–272	8	0.68	0.59	0.76	0.5829	0.4825
	D19S884	93–117	13	0.81	0.82	0.86	0.7959	0.4736
	D19S221	88–112	12	0.63	0.83	0.86	0.7539	0.4569
	D19S226	233–257	13	0.83	0.87	0.85	0.8295	0.4640
	D19S414	168–196	11	0.52	0.61	0.78	0.4663	0.4623
	D19S220	269–299	16	0.83	0.87	0.84	0.8618	0.4735
	D19S420	99–117	10	0.79	0.76	0.79	0.7580	0.4794
	D19S902	240–262	12	0.85	0.84	0.79	0.8070	0.4833
	D19S571	286–324	12	0.42	0.42	0.81	0.4647	0.4868
	D19S418	89–107	10	0.61	0.55	0.66	0.6069	0.4876
	D19S210	172–190	8	0.62	0.62	0.74	0.5952	0.4889
20	D20S117	150–188	15	0.86	0.85	0.84	0.8723	0.4948
	D20S889	86–118	15	0.71	0.77	0.83	0.7701	0.4878
	D20S115	236–246	6	0.59	0.52	0.66	0.5314	0.4743
	D20S186	116–142	13	0.92	0.86	0.86	0.8556	0.4725
	D20S112	210–232	11	0.73	0.73	0.81	0.7032	0.4755
	D20S195	128–154	12	0.71	0.76	0.81	0.7173	0.4795
	D20S107	204–222	10	0.76	0.77	0.80	0.7090	0.4867
	D20S119	105–121	9	0.79	0.76	0.82	0.7358	0.4756
	D20S178	179–195	9	0.56	0.75	0.83	0.6914	0.4698
	D20S196	262–294	16	0.81	0.87	0.81	0.8498	0.4740
	D20S100	214–230	10	0.70	0.75	0.76	0.6817	0.4634
	D20S171	128–154	11	0.69	0.78	0.78	0.7237	0.4625
	D20S173	126–184	11	0.74	0.65	0.67	0.6747	0.4669
21	D21S1256	98–120	12	0.38	0.63	0.65	0.7361	0.4650
	D21S1914	257–279	12	0.73	0.80	0.86	0.7885	0.4635
	D21S263	198–234	13	0.78	0.83	0.75	0.8155	0.4686
	D21S1252	152–178	14	0.85	0.79	0.80	0.8069	0.4726
	D21S266	157–181	14	0.79	0.84	0.59	0.7748	0.4851
22	D22S420	150–166	9	0.72	0.73	0.77	0.7023	0.4843
	D22S539	201–217	8	0.51	0.56	0.58	0.5030	0.4867
	D22S315	183–207	11	0.73	0.81	0.78	0.7416	0.4838
	D22S280	210–228	10	0.83	0.77	0.82	0.7768	0.4828
	D22S283	129–159	17	0.76	0.82	0.89	0.8027	0.4803
	D22S423	280–312	16	0.84	0.81	0.82	0.7716	0.4784
	D22S274	273–299	11	0.81	0.79	0.77	0.7874	0.4788

Table 1 continued

Chr	Marker	Allele size range	Allele no.	Korean het	Taiwanese het	Caucacians het	Korean PIC	Mean IBD value
X	DXS1060	240–260	11	0.86	0.85	0.84	0.8310	
	DXS8051	108–130	12	0.79	0.84	0.88	0.8105	
	DXS987	203–229	13	0.71	0.80	0.83	0.6984	
	DXS1226	275–307	15	0.84	0.84	0.84	0.8295	
	DXS1214	284–300	9	0.75	0.75	0.79	0.7208	
	DXS1068	247–263	9	0.69	0.65	0.79	0.6221	
	DXS993	269–291	8	0.67	0.68	0.79	0.5903	
	DXS991	316–348	12	0.70	0.78	0.80	0.6863	
	DXS986	159–201	16	0.82	0.89	0.77	0.8815	
	DXS990	120–134	8	0.78	0.65	0.74	0.7267	
	DXS1106	124–136	7	0.21	0.27	0.67	0.2212	
	DXS8055	310–320	6	0.26	0.21	0.65	0.2411	
	DXS1001	191–215	12	0.81	0.81	0.82	0.7927	
	DXS1047	149–173	12	0.78	0.82	0.81	0.8252	
	DXS1227	77–97	10	0.62	0.54	0.73	0.5448	
	DXS8043	147–171	12	0.78	0.76	0.80	0.7155	
	DXS8091	81–93	7	0.51	0.55	0.78	0.5106	
	DXS1073	303–335	11	0.59	0.64	0.80	0.5569	

population. Heterozygosity in the Caucasians ranged from 0.58 (D22S539) to 0.91 (D14S68), with an average of 0.79 (SD $\pm$ 0.06). Most markers (99.5%) had a heterozygosity of $\geq$0.6 in the Caucasian population. Overall, heterozygosity in the Korean population shared greater similarity with the Taiwanese population than with the Caucasian population.

A detailed comparison of heterozygosity in the four populations is shown in Fig. 1. Four hundred ABI MD-10 markers were analyzed for Koreans (this study), Japanese (Ikari et al. 2001) and Caucasians (Ikari et al. 2001; http://www.cephb.fr); 399 ABI MD-10 markers (all except D3S1311) were analyzed for Taiwanese (Lu et al. 2004). At a level of heterozygosity ranging from 0.7 to 0.8, frequencies of the markers in the four populations were similar. At other levels of heterozygosity, however, frequencies varied among the different populations. Heterozygosities of markers from Korean, Taiwanese and Japanese populations differed considerably from Caucasians. The Asian populations had similar frequencies at heterozygosity levels of $<$0.5, 0.5–0.6 and 0.7–0.8, but Koreans differed slightly from Taiwanese and Japanese at heterozygosity levels between 0.6 and 0.7 and $\geq$0.8.

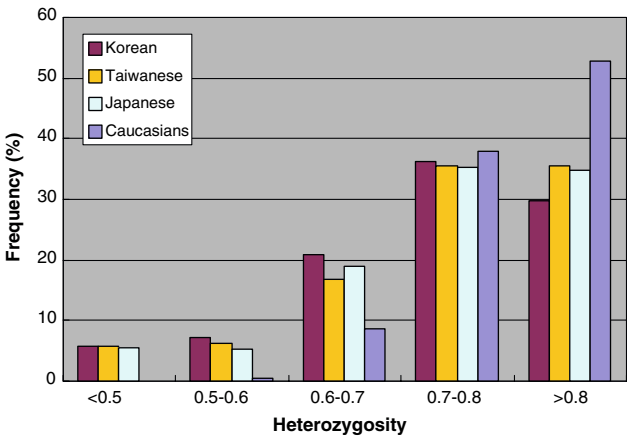

Fig. 1 Distribution of heterozygosities for 400 microsatellite markers in Korean, Taiwanese (Lu et al. 2004, 399 markers), Japanese (Ikari et al. 2001) and Caucasian (Ikari et al. 2001; http://www.cephb.fr) populations

Distribution of heterozygosities relative to mean IBD values

To confirm the frequency of each level of heterozygosity with a maximum number of individuals, we analyzed the distribution of heterozygosity with 578 sib individuals from 249 families. For autosomal markers, 578 individuals were used, and for X chromosome markers, 326 females were used. The heterozygosity distribution of 249 unrelated individuals and 578 sib individuals is shown in Fig. 2. There were no differences at any level of heterozygosity ($P = 0.93$).

The estimated mean IBD was calculated for each of the 382 autosomal markers using 429 sib pairs from 249 families. The test statistic had a standard normal distribution under the null hypothesis. Thus, an alternative linkage

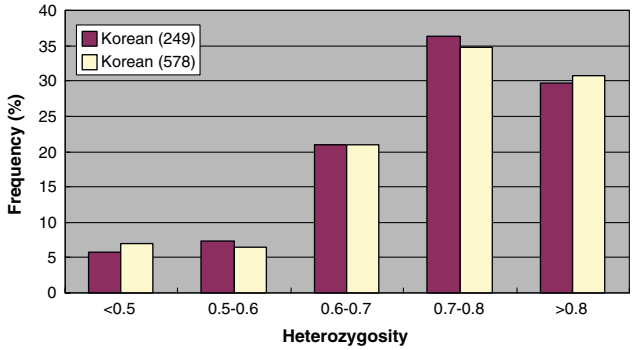

Fig. 2 Distribution of heterozygosities for 400 microsatellite markers in 249 unrelated individuals and 578 sib individuals from 249 Korean families

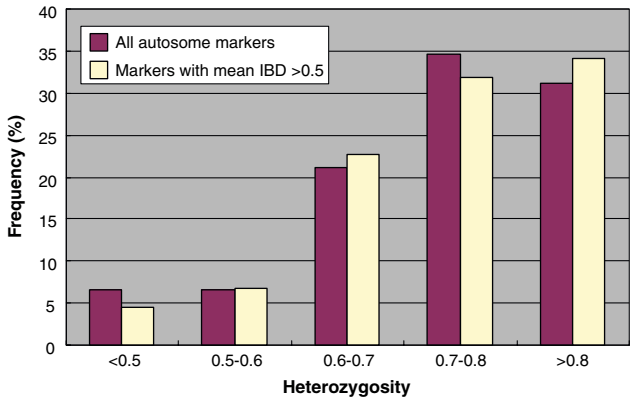

Fig. 3 Distribution of heterozygosities for all autosomal markers and 44 markers with a mean IBD > 0.5

hypothesis is given when the mean IBD value is >0.5. Of the 382 markers, 44 showed positive linkages with a mean IBD >0.5 (Table 1). A comparison of heterozygosity distributions for all markers and the 44 markers with a mean IBD >0.5 is shown in Fig. 3. The distribution for markers with a mean IBD >0.5 was similar to the distribution for all 382 autosomal markers ($P = 0.97$).

Discussion

We constructed a comprehensive dataset of allelic frequencies and heterozygosities of 400 microsatellite markers in the Korean population, information that will be useful for mapping disease-associated genes in Koreans. Overall, the levels of heterozygosity were similar between the Korean, Taiwanese and Japanese populations. However, there were slight differences in several levels of heterozygosity between these three datasets, suggesting that the Korean dataset will be a powerful resource for genetic studies in Koreans. Heterozygosity for most markers in the Asian populations was lower than that in the Caucasian population. Ten to 13% of the markers examined showed heterozygosities lower than 0.6 in the Asian populations. This level of heterozygosity was almost never observed in the Caucasian population. Thus, the Caucasian database may not be suitable for other ethnic groups. Due to significant differences in heterozygosities and allelic frequencies between populations, markers should be optimally selected for each study population in order to maximize information content and power (Ikari et al. 2001; Tan et al. 2002).

We used 249 unrelated individuals to evaluate the level of heterozygosity for each marker. We also used 578 sib individuals from 249 families to confirm the frequency of each level of heterozygosity using the maximum possible number of individuals. Computer simulation studies using sample sizes of 10–200 individuals and allele numbers ranging from 2 to 27 revealed that the number of individuals genotyped has a minimal influence on heterozygosity (Tan et al. 2002). In our study, we found no differences in the heterozygosity distributions, and thus 249 subjects were sufficient to evaluate the levels of heterozygosity.

A large number of markers (23 of 400 loci) did not meet the Hardy–Weinberg equilibrium in our study. This may reflect sampling errors, population substructure, original genetic variations of the subjects, or the presence of low-frequency alleles (Mizutani et al. 2001; Lu et al. 2004). We used 249 unrelated Korean samples to analyze population stratification with the STRUCTURE program. Fst values in $K = 2$ were 0.003 and 0.0015, and in $K = 3$ were 0.0028, 0.0036 and 0.0040 (data not shown), suggesting that the markers we used were not sufficient to detect sub-structures in the Korean population or that the 249 subjects we used were from one local region.

Heterozygosity and PIC are commonly used to indicate how informative a marker is. Highly polymorphic markers with heterozygosities ranging from 80 to 90% have been developed for linkage analysis (Ott and Rabinowitz 1997). In this study, the percentage of the markers with 80–90% heterozygosities for Korean population was 29%, while the same value for Caucasian was 52%. In addition, the percentage of PIC values with 0.7 or higher was only 60% (Table 1). Although some markers displayed low heterozygosities and PIC values, we found that the estimated IBDs from less informative autosomal markers could be also used for positive disease linkages. The distribution of heterozygosities for the 44 markers with a mean IBD >0.5 was similar to that for all 382 autosomal markers (Fig. 3). We found that it was unnecessary to exclude markers with low heterozygosities, at least when using the IBD sharing method of model-free linkage analysis.

In conclusion, heterozygosity information gleaned from this study will be a useful reference for genome-wide screens of Koreans and comparative studies of microsatellite

markers among different ethnic populations. Furthermore, the present study may contribute to linkage studies involving the IBD sharing method of model-free analysis.

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