A population study for 30 insertion-deletion markers in a Korean population

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Introduction

Insertion-deletion polymorphisms (Indels) have received broad attention from the field of forensic genetics, since they have advantages over both short tandem repeat (STR) and single-nucleotide polymorphism (SNP) analyses. Indels, like STRs, can be easily typed with simple procedures, without the laborious procedures most widely used in SNP typing. In addition, they can be analyzed with smaller amplicons than STRs and have benefits such as the absence of stutter peaks and the possibility of mixed stain analysis. In this study, we analyzed 30 Indels in 100 Koreans using Investigator DIPplex® kit (Qiagen, Hilden, Germany). To test forensic efficiency, we compared the data with several STR-based studies that were also performed in a Korean population , as well as with other published population studies using the DIPplex® kit.

Materials and Methods

DNA Samples

A total of 100 unrelated Koreans participated, after giving their consent using procedures approved by the Institutional Review Board of Severance Hospital, Yonsei University in Seoul, Korea. DNA was extracted from buccal swab using a QIAamp® DNA Mini Kit (Qiagen).

PCR amplification and genotyping

PCR amplification was carried out in a Veriti® 96-Well Thermal Cycler (Applied Biosystems, Foster City, CA, USA) following the manufacturer's guidelines. PCR products were analyzed using an ABI PRISM® 310 Genetic Analyzer (Applied Biosystems) and genotyped automatically with GeneMapper® ID v.3.2 software (Applied Biosystems).

Statistical Analysis

Basic statistical parameters, including the value of the allele frequencies for each Indel and observed heterozygosity (Ho), were calculated using counting methods. Forensic efficiency information was assessed by calculating expected heterozygosity (He), match probability (MP), power of discrimination (PD), polymorphic information content (PIC), and power of exclusion (PE). Deviations from Hardy-Weinberg Equilibrium (HWE) were evaluated as described by Guo and Thompson. The allele frequencies for 30 Indels using the DIPplex® kit in other populations were compared to our study using Arlequin software ver. 3.5 (http://cmpg.unibe.ch/software/arlequin35/) to compute an exact test of population differentiation at the 0.05 significant level.

Results

In the 100 Korean samples, all Indel markers were successfully amplified and genotyped with no significant deviation from Hardy-Weinberg Equilibrium (p>0.05). The forensic parameters for the 30 Indel loci are listed in Table 1. The observed heterozygosity ranged from 0.110 to 0.560, and the PD varied from 0.211 to 0.647 with the combined PD of 0.99999999995.

Table 1. Forensic parameters for 30 Indels of the DIPplex® kit in Koreans

rs number	Locus	p(-)	p(+)	Ho	He	MP	PD	PIC	PE	HWE
rs1611048	D77	0.450	0.550	0.560	0.497	0.415	0.585	0.372	0.246	0.229
rs2307959	D45	0.445	0.555	0.430	0.496	0.353	0.647	0.372	0.133	0.226
rs1611001	D131	0.590	0.410	0.460	0.486	0.374	0.626	0.367	0.155	0.679
rs2307652	D70	0.365	0.635	0.470	0.466	0.398	0.602	0.356	0.163	1.000
rs1610905	D6	0.590	0.410	0.480	0.486	0.382	0.618	0.367	0.171	1.000
rs1305047	D111	0.925	0.075	0.150	0.139	0.745	0.255	0.129	0.018	1.000
rs1610937	D58	0.600	0.400	0.460	0.482	0.377	0.623	0.365	0.155	0.680
rs2308292	D56	0.470	0.530	0.540	0.501	0.399	0.601	0.374	0.225	0.546
rs16438	D118	0.065	0.935	0.110	0.122	0.787	0.213	0.114	0.010	0.338
rs17174476	D92	0.610	0.390	0.420	0.478	0.369	0.631	0.363	0.127	0.291
rs2307570	D93	0.355	0.645	0.450	0.460	0.396	0.604	0.353	0.147	0.830
rs2308163	D99	0.060	0.940	0.120	0.113	0.789	0.211	0.106	0.012	1.000
rs8190570	D88	0.400	0.600	0.520	0.482	0.406	0.594	0.365	0.206	0.534
rs2307433	D101	0.570	0.430	0.540	0.493	0.407	0.593	0.370	0.225	0.413
rs1305056	D67	0.360	0.640	0.520	0.463	0.425	0.575	0.355	0.206	0.275
rs2308072	D83	0.625	0.375	0.510	0.471	0.411	0.589	0.359	0.196	0.521
rs2307581	D114	0.695	0.305	0.490	0.426	0.446	0.554	0.334	0.179	0.161
rs28369942	D48	0.610	0.390	0.540	0.478	0.422	0.578	0.363	0.225	0.214
rs6481	D124	0.490	0.510	0.520	0.502	0.386	0.614	0.375	0.206	0.841
rs8178524	D122	0.740	0.260	0.420	0.387	0.460	0.540	0.311	0.127	0.444
rs16388	D125	0.645	0.355	0.390	0.460	0.380	0.620	0.353	0.108	0.133
rs1610935	D64	0.170	0.830	0.340	0.284	0.551	0.449	0.242	0.081	0.068
rs17879936	D81	0.085	0.915	0.150	0.156	0.728	0.272	0.143	0.018	0.524
rs16363	D136	0.390	0.610	0.520	0.478	0.410	0.590	0.363	0.206	0.408
rs2067235	D133	0.620	0.380	0.500	0.474	0.404	0.596	0.360	0.188	0.672
rs17238892	D97	0.745	0.255	0.410	0.382	0.462	0.538	0.308	0.120	0.599
rs2307956	D40	0.285	0.715	0.390	0.410	0.431	0.569	0.325	0.108	0.631
rs2307924	D128	0.675	0.325	0.450	0.441	0.415	0.585	0.342	0.147	1.000
rs17878444	D39	0.860	0.140	0.240	0.242	0.606	0.394	0.212	0.042	1.000
rs3081400	D84	0.230	0.770	0.380	0.356	0.482	0.518	0.291	0.102	0.581

Table 2. Comparison of discrimination power for the DIPplex® and other STR kits in other published Korean population studies

	Min	Max	Mean	MP	Combined PD	Type of markers
DIPplex (In this study)	0.211	0.647	0.533	4.970×10^{-11}	0.99999999995	30 Indels
COfiler	0.811	0.921	0.869	3.798×10^{-6}	0.999996	6 STRs
Profiler plus	0.876	0.996	0.934	2.307×10^{-12}	0.9999999999998	9 STRs
Identifiler	0.818	0.965	0.912	2.855×10^{-17}	0.99999999999999997	15 STRs

Table 3. Comparison of allele frequencies in other published population studies using 30 Indels in the DIPplex® kit

		This study (n=100)		US Asian (n=50)		US Af-Am (n=260)		US caucasian (n=262)		US Hispanic (n=140)		Portugal (n=127)		Danes (n=80)		Czech (n=55)		German (n=80)		Central Spain (n=71)		Basque (n=60)		Global (n=171)	
rs number	Locus	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)	p(-)	P(+)	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)	p(-)	p(+)
rs1611048	D77	0.450	0.550	0.510	0.490	0.621	0.379	0.483	0.517	0.561	0.439	0.562	0.437	0.394	0.606	0.455	0.545	0.438	0.563	0.599	0.401	0.658	0.342	0.516	0.484
rs2307959	D45	0.445	0.555	0.400	0.600	0.585	0.415	0.471	0.529	0.400	0.600	0.507	0.492	0.494	0.506	0.455	0.545	0.431	0.569	0.465	0.535	0.500	0.500	0.459	0.541
rs1611001	D131	0.590	0.410	0.600	0.400	0.235	0.765	0.448	0.552	0.496	0.504	0.484	0.515	0.475	0.525	0.382	0.618	0.456	0.544	0.500	0.500	0.617	0.383	0.475	0.525
rs2307652	D70	0.365	0.635	0.300	0.700	0.129	0.871	0.496	0.504	0.354	0.646	0.464	0.535	0.500	0.500	0.545	0.455	0.481	0.519	0.387	0.613	0.350	0.650	0.401	0.599
rs1610905	D6	0.590	0.410	0.550	0.450	0.596	0.404	0.511	0.489	0.529	0.471	0.555	0.444	0.475	0.525	0.518	0.482	0.450	0.550	0.493	0.507	0.458	0.542	0.538	0.462
rs1305047	D111	0.925	0.075	0.900	0.100	0.625	0.375	0.450	0.550	0.518	0.482	0.409	0.586	0.463	0.538	0.482	0.518	0.506	0.494	0.500	0.500	0.442	0.558	0.567	0.433
rs1610937	D58	0.600	0.400	0.600	0.400	0.833	0.167	0.502	0.498	0.671	0.329	0.511	0.480	0.438	0.563	0.382	0.618	0.488	0.512	0.458	0.542	0.367	0.633	0.569	0.431
rs2308292	D56	0.470	0.530	0.530	0.470	0.460	0.540	0.340	0.660	0.329	0.671	0.303	0.696	0.350	0.650	0.327	0.673	0.344	0.656	0.247	0.754	0.383	0.617	0.365	0.635
rs16438	D118	0.065	0.935	0.080	0.920	0.706	0.294	0.565	0.435	0.618	0.382	0.551	0.440	0.544	0.456	0.473	0.527	0.562	0.438	0.585	0.416	0.575	0.425	0.574	0.426
rs17174476	D92	0.610	0.390	0.530	0.470	0.696	0.304	0.540	0.460	0.604	0.396	0.515	0.476	0.531	0.469	0.573	0.427	0.550	0.450	0.514	0.486	0.583	0.417	0.655	0.345
rs2307570	D93	0.355	0.645	0.360	0.640	0.508	0.492	0.445	0.555	0.389	0.611	0.421	0.578	0.394	0.606	0.445	0.555	0.450	0.550	0.493	0.507	0.517	0.483	0.354	0.646
rs2308163	D99	0.060	0.940	0.130	0.870	0.394	0.591	0.431	0.569	0.457	0.539	0.370	0.629	0.431	0.569	0.400	0.600	0.481	0.519	0.401	0.599	0.367	0.633	0.420	0.580
rs8190570	D88	0.400	0.600	0.540	0.460	0.325	0.675	0.460	0.540	0.414	0.586	0.488	0.511	0.531	0.469	0.573	0.427	0.556	0.444	0.578	0.423	0.600	0.400	0.451	0.549
rs2307433	D101	0.570	0.430	0.560	0.440	0.233	0.767	0.559	0.441	0.475	0.525	0.515	0.484	0.631	0.369	0.455	0.545	0.456	0.544	0.486	0.514	0.567	0.433	0.452	0.548
rs1305056	D67	0.360	0.640	0.290	0.710	0.310	0.690	0.370	0.630	0.414	0.586	0.409	0.590	0.406	0.594	0.491	0.509	0.300	0.700	0.373	0.627	0.533	0.467	0.440	0.560
rs2308072	D83	0.625	0.375	0.660	0.340	0.392	0.608	0.481	0.519	0.586	0.414	0.488	0.511	0.444	0.556	0.564	0.436	0.606	0.394	0.479	0.521	0.442	0.558	0.573	0.427
rs2307581	D114	0.695	0.305	0.770	0.230	0.225	0.775	0.557	0.443	0.525	0.475	0.543	0.456	0.631	0.369	0.664	0.336	0.631	0.369	0.514	0.486	0.675	0.325	0.510	0.490
rs28369942	D48	0.610	0.390	0.730	0.270	0.278	0.722	0.483	0.517	0.282	0.718	0.440	0.559	0.319	0.681	0.473	0.527	0.450	0.550	0.444	0.556	0.467	0.533	0.460	0.540
rs6481	D124	0.490	0.510	0.410	0.590	0.779	0.221	0.365	0.635	0.443	0.557	0.370	0.629	0.444	0.556	0.300	0.700	0.375	0.625	0.352	0.648	0.317	0.683	0.464	0.536
rs8178524	D122	0.740	0.260	0.790	0.210	0.637	0.363	0.561	0.439	0.736	0.264	0.503	0.496	0.619	0.381	0.491	0.509	0.606	0.394	0.599	0.401	0.667	0.333	0.565	0.435
rs16388	D125	0.645	0.355	0.650	0.350	0.722	0.278	0.439	0.561	0.625	0.375	0.440	0.559	0.456	0.544	0.445	0.555	0.444	0.556	0.535	0.465	0.525	0.475	0.575	0.425
rs1610935	D64	0.170	0.830	0.140	0.860	0.223	0.777	0.458	0.542	0.289	0.711	0.429	0.570	0.419	0.581	0.527	0.473	0.463	0.537	0.401	0.599	0.483	0.517	0.318	0.682
rs17879936	D81	0.085	0.915	0.110	0.890	0.481	0.519	0.578	0.422	0.421	0.579	0.547	0.444	0.531	0.469	0.545	0.455	0.506	0.494	0.578	0.423	0.483	0.517	0.533	0.467
rs16363	D136	0.390	0.610	0.390	0.610	0.221	0.779	0.504	0.496	0.414	0.586	0.279	0.720	0.506	0.494	0.545	0.455	0.506	0.494	0.444	0.556	0.300	0.700	0.422	0.578
rs2067235	D133	0.620	0.380	0.550	0.450	0.675	0.325	0.462	0.538	0.529	0.471	0.476	0.523	0.394	0.606	0.436	0.564	0.456	0.544	0.373	0.627	0.383	0.617	0.526	0.474
rs17238892	D97	0.745	0.255	0.760	0.240	0.590	0.410	0.464	0.536	0.550	0.450	0.523	0.476	0.469	0.531	0.482	0.518	0.488	0.512	0.479	0.521	0.392	0.608	0.521	0.479
rs2307956	D40	0.285	0.715	0.340	0.660	0.700	0.300	0.582	0.418	0.554	0.446	0.460	0.535	0.581	0.419	0.591	0.409	0.581	0.419	0.592	0.409	0.567	0.433	0.489	0.511
rs2307924	D128	0.675	0.325	0.720	0.280	0.342	0.658	0.519	0.481	0.514	0.486	0.594	0.405	0.569	0.431	0.555	0.445	0.506	0.494	0.549	0.451	0.492	0.508	0.574	0.426
rs17878444	D39	0.860	0.140	0.820	0.180	0.440	0.560	0.668	0.332	0.593	0.407	0.673	0.326	0.700	0.300	0.682	0.318	0.612	0.388	0.599	0.401	0.725	0.275	0.511	0.489
rs3081400	D84	0.230	0.770	0.310	0.690	0.389	0.602	0.452	0.548	0.436	0.564	0.433	0.566	0.481	0.519	0.491	0.509	0.406	0.594	0.394	0.606	0.417	0.583	0.402	0.598

Conclusion

- **By comparing the PD of 30 Indels with that of other STR kits in a Korean population, the 30 Indels of the DIPplex® kit proved to be more discriminative than the six STRs from the COfiler® (Applied Biosystems), but less discriminative than the nine STRs in the Profiler Plus® (Applied Biosystems) in other published Korean population studies.**
- **In the exact test of population differentiation, we detected statistically significant differences in allele frequency distribution at the D111, D118, D99, D81, D97, D40, D39, and D84 loci between the Korean population and other population groups (p<0.05) except for US Asians.**
- **A deletion at D111 and insertions at D118, D81, and D99 were observed frequently (allele frequency of>0.900) in Koreans as well as in US Asians (allele frequency of>0.870). Therefore, these Indels in the DIPplex® kit could serve as ancestry informative markers for Asian populations.**

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For more information, please refer to the paper Int J Legal Med 2013; In press. (http://forensic.yonsei.ac.kr/)