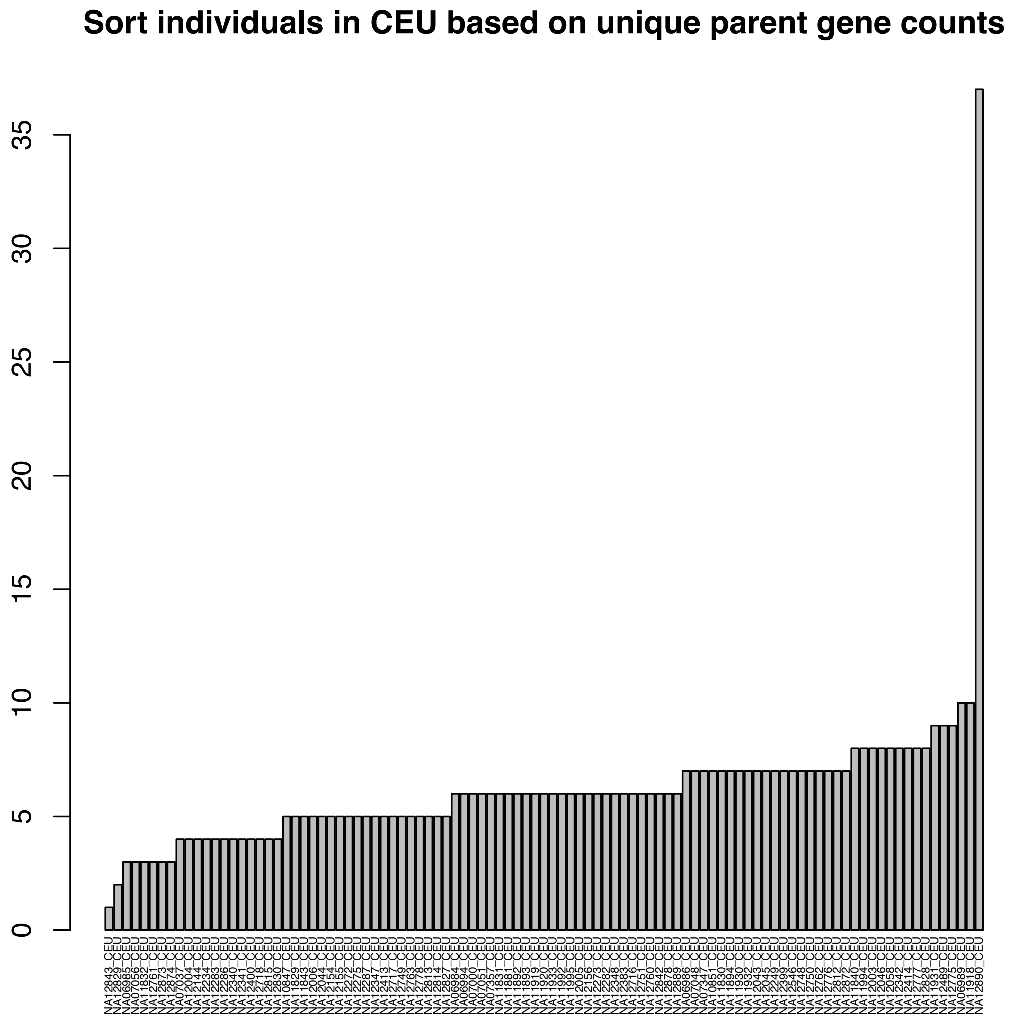
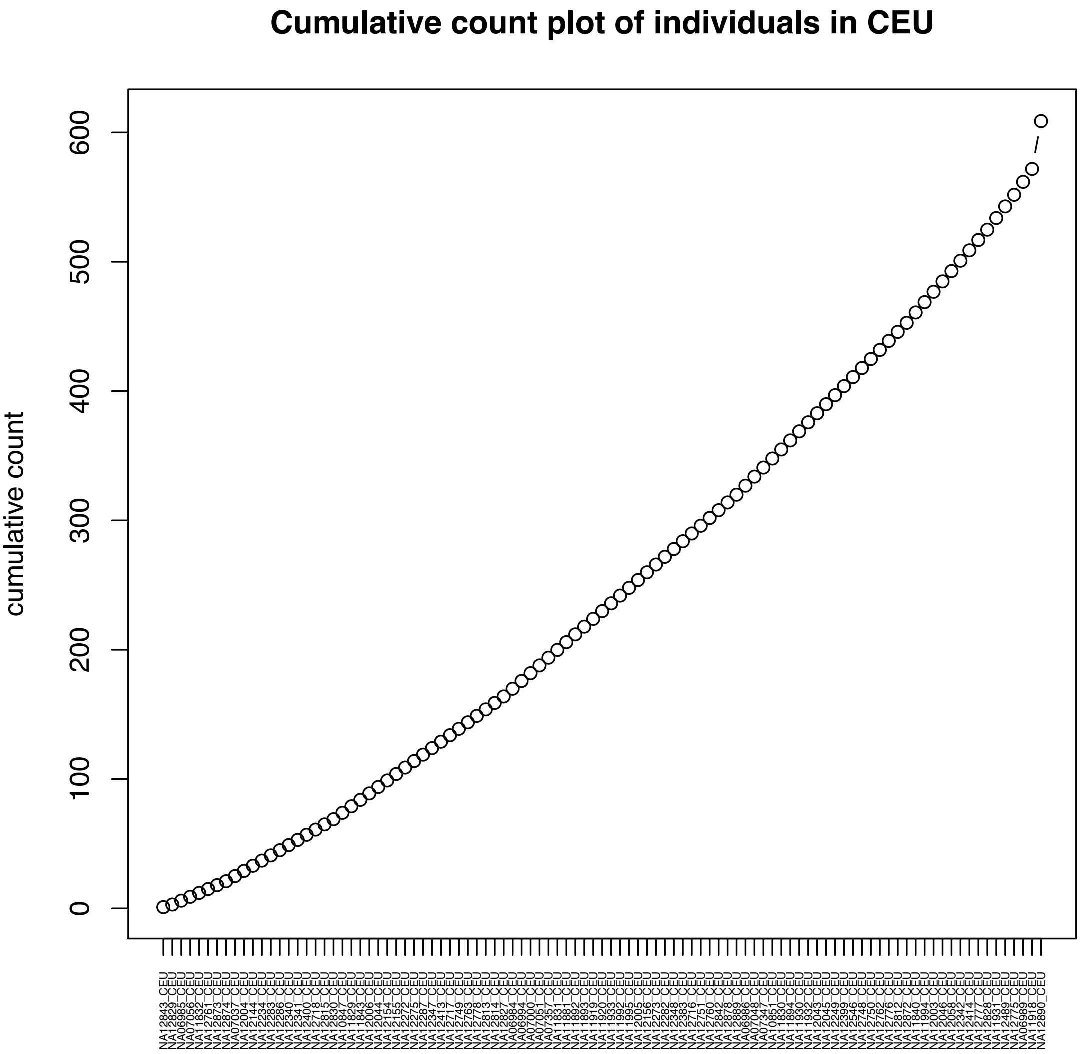
a)


Sort individuals in CEU based on unique parent gene counts
0
5
10
15
20
25
30
35
NA12843_CEU
NA12829_CEU
NA06985_CEU
NA07056_CEU
NA11832_CEU
NA12761_CEU
NA12873_CEU
NA12874_CEU
NA07037_CEU
NA12004_CEU
NA12144_CEU
NA12234_CEU
NA12283_CEU
NA12286_CEU
NA12340_CEU
NA12341_CEU
NA12400_CEU
NA12718_CEU
NA12815_CEU
NA12830_CEU
NA10847_CEU
NA11829_CEU
NA11843_CEU
NA12006_CEU
NA12044_CEU
NA12154_CEU
NA12155_CEU
NA12272_CEU
NA12275_CEU
NA12287_CEU
NA12347_CEU
NA12413_CEU
NA12717_CEU
NA12749_CEU
NA12763_CEU
NA12778_CEU
NA12813_CEU
NA12814_CEU
NA12827_CEU
NA06984_CEU
NA06994_CEU
NA07000_CEU
NA07051_CEU
NA07357_CEU
NA11831_CEU
NA11881_CEU
NA11892_CEU
NA11893_CEU
NA11919_CEU
NA11920_CEU
NA11933_CEU
NA11992_CEU
NA11995_CEU
NA12005_CEU
NA12156_CEU
NA12273_CEU
NA12282_CEU
NA12348_CEU
NA12383_CEU
NA12716_CEU
NA12751_CEU
NA12760_CEU
NA12842_CEU
NA12878_CEU
NA12889_CEU
NA06986_CEU
NA07048_CEU
NA07347_CEU
NA10851_CEU
NA11830_CEU
NA11894_CEU
NA11930_CEU
NA11932_CEU
NA12043_CEU
NA12045_CEU
NA12249_CEU
NA12399_CEU
NA12546_CEU
NA12748_CEU
NA12750_CEU
NA12762_CEU
NA12776_CEU
NA12812_CEU
NA12872_CEU
NA11840_CEU
NA11994_CEU
NA12003_CEU
NA12046_CEU
NA12058_CEU
NA12342_CEU
NA12414_CEU
NA12777_CEU
NA12828_CEU
NA11931_CEU
NA12489_CEU
NA12775_CEU
NA06989_CEU
NA11918_CEU
NA12890_CEU

b)


Cumulative count plot of individuals in CEU
cumulative count
0
100
200
300
400
500
600
NA12843_CEU
NA12829_CEU
NA06985_CEU
NA07056_CEU
NA11832_CEU
NA12761_CEU
NA12873_CEU
NA12874_CEU
NA07037_CEU
NA12004_CEU
NA12144_CEU
NA12234_CEU
NA12283_CEU
NA12286_CEU
NA12340_CEU
NA12341_CEU
NA12400_CEU
NA12718_CEU
NA12815_CEU
NA12830_CEU
NA10847_CEU
NA11829_CEU
NA11843_CEU
NA12006_CEU
NA12044_CEU
NA12154_CEU
NA12155_CEU
NA12272_CEU
NA12275_CEU
NA12287_CEU
NA12347_CEU
NA12413_CEU
NA12717_CEU
NA12749_CEU
NA12763_CEU
NA12778_CEU
NA12813_CEU
NA12814_CEU
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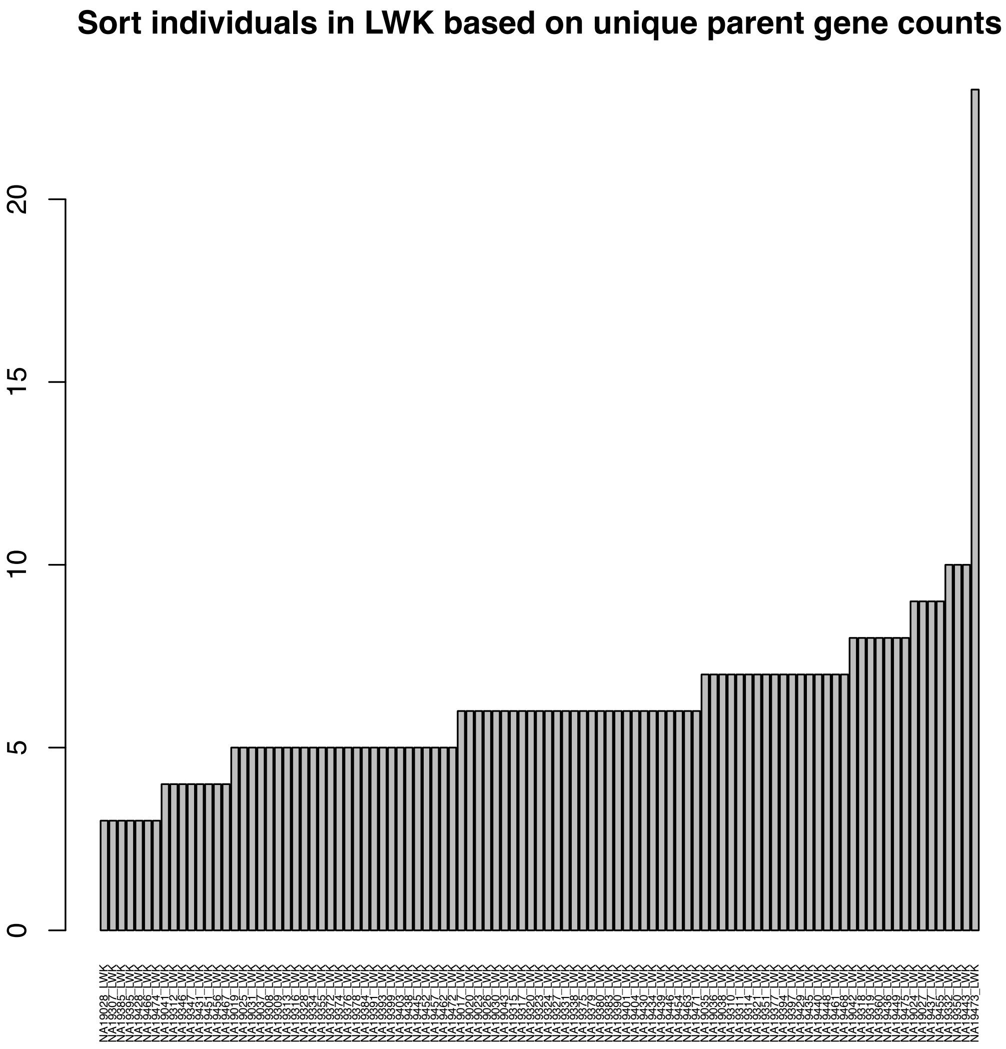
NA11893_CEU
NA11919_CEU
NA11920_CEU
NA11933_CEU
NA11992_CEU
NA11995_CEU
NA12005_CEU
NA12156_CEU
NA12273_CEU
NA12282_CEU
NA12348_CEU
NA12383_CEU
NA12716_CEU
NA12751_CEU
NA12760_CEU
NA12842_CEU
NA12878_CEU
NA12889_CEU
NA06986_CEU
NA07048_CEU
NA07347_CEU
NA10851_CEU
NA11830_CEU
NA11894_CEU
NA11930_CEU
NA11932_CEU
NA12043_CEU
NA12045_CEU
NA12249_CEU
NA12399_CEU
NA12546_CEU
NA12748_CEU
NA12750_CEU
NA12762_CEU
NA12776_CEU
NA12812_CEU
NA12872_CEU
NA11840_CEU
NA11994_CEU
NA12003_CEU
NA12046_CEU
NA12058_CEU
NA12342_CEU
NA12414_CEU
NA12777_CEU
NA12828_CEU
NA11931_CEU
NA12489_CEU
NA12775_CEU
NA06989_CEU
NA11918_CEU
NA12890_CEU

c)


Sort individuals in LWK based on unique parent gene counts
0
5
10
15
20
NA19028_LWK
NA19307_LWK
NA19385_LWK
NA19395_LWK
NA19428_LWK
NA19466_LWK
NA19474_LWK
NA19041_LWK
NA19312_LWK
NA19346_LWK
NA19347_LWK
NA19431_LWK
NA19451_LWK
NA19456_LWK
NA19467_LWK
NA19019_LWK
NA19025_LWK
NA19031_LWK
NA19037_LWK
NA19308_LWK
NA19309_LWK
NA19313_LWK
NA19316_LWK
NA19328_LWK
NA19334_LWK
NA19355_LWK
NA19372_LWK
NA19374_LWK
NA19376_LWK
NA19378_LWK
NA19384_LWK
NA19391_LWK
NA19393_LWK
NA19399_LWK
NA19403_LWK
NA19438_LWK
NA19445_LWK
NA19452_LWK
NA19457_LWK
NA19462_LWK
NA19472_LWK
NA19017_LWK
NA19020_LWK
NA19023_LWK
NA19026_LWK
NA19030_LWK
NA19043_LWK
NA19315_LWK
NA19317_LWK
NA19320_LWK
NA19323_LWK
NA19324_LWK
NA19327_LWK
NA19331_LWK
NA19338_LWK
NA19375_LWK
NA19379_LWK
NA19380_LWK
NA19383_LWK
NA19390_LWK
NA19401_LWK
NA19404_LWK
NA19430_LWK
NA19434_LWK
NA19439_LWK
NA19446_LWK
NA19454_LWK
NA19463_LWK
NA19471_LWK
NA19035_LWK
NA19036_LWK
NA19038_LWK
NA19310_LWK
NA19311_LWK
NA19314_LWK
NA19321_LWK
NA19351_LWK
NA19377_LWK
NA19394_LWK
NA19397_LWK
NA19429_LWK
NA19435_LWK
NA19440_LWK
NA19448_LWK
NA19461_LWK
NA19468_LWK
NA19042_LWK
NA19318_LWK
NA19319_LWK
NA19360_LWK
NA19436_LWK
NA19449_LWK
NA19475_LWK
NA19024_LWK
NA19027_LWK
NA19437_LWK
NA19455_LWK
NA19332_LWK
NA19350_LWK
NA19443_LWK
NA19473_LWK

d)

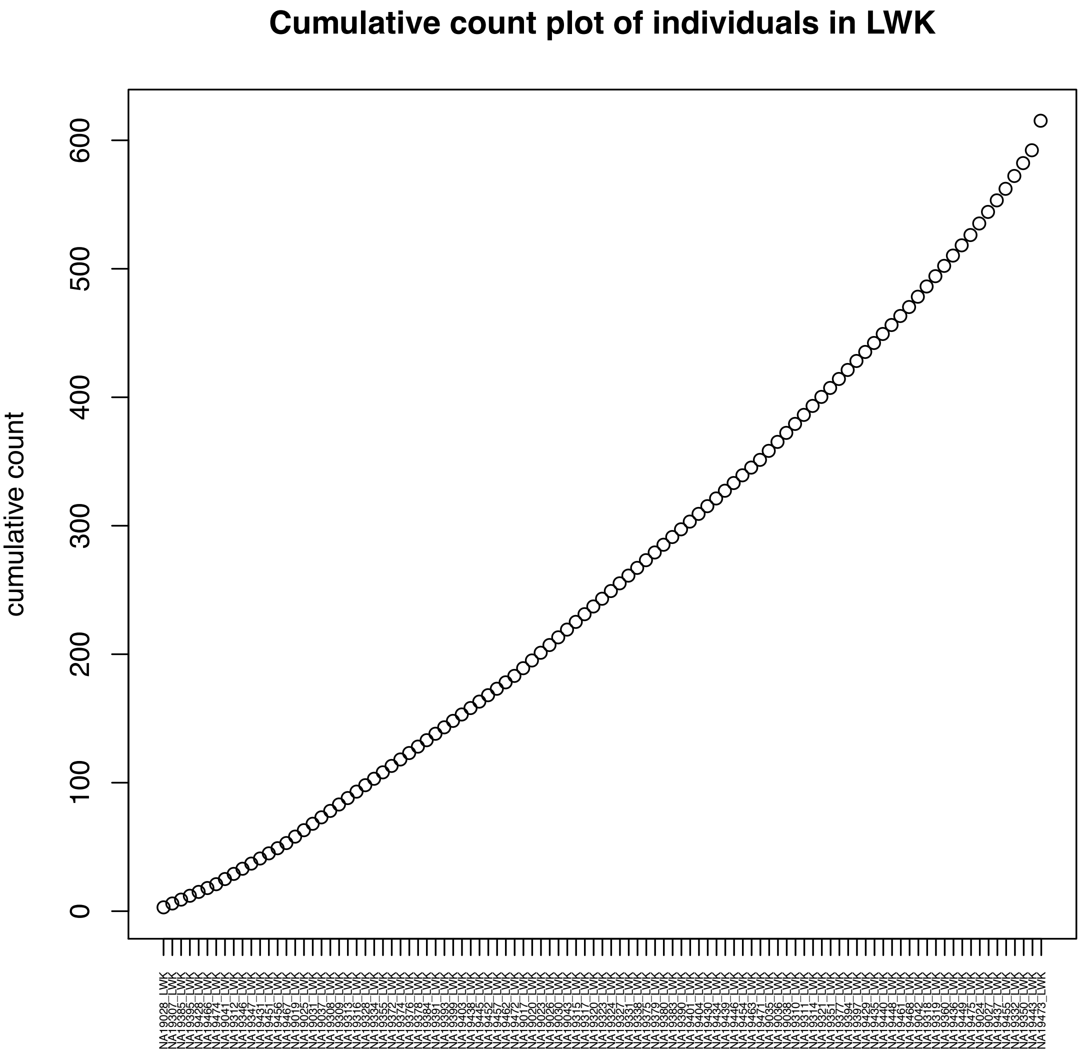
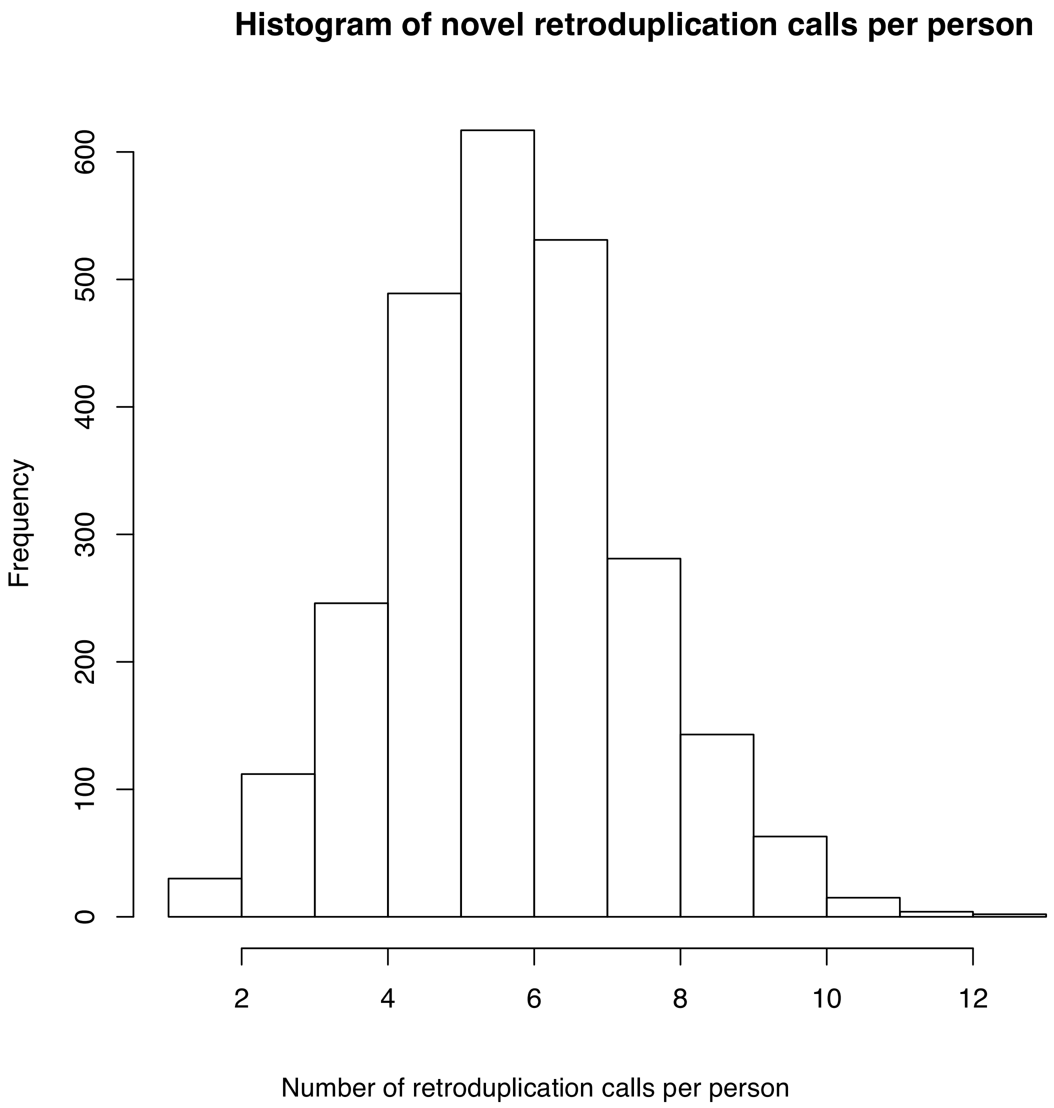


Fig A. Diagnosis plots for detection of outlier individuals that have exceptionally high number of retroduplication calls. In each population, we sort the indivuals based on the number of unique parent genes having novel retroduplications. We have detected two individuals with exceptionally high number of retroduplication calls: NA12890 in CEU, and NA19473 in LWK. Diagnosis plots of CEU (panel a, b) and LWK (panel c, d) are shown here. Individuals in each population are sorted by increasing number of retroduplication calls.

a)


Histogram of novel retroduplication calls per person
Frequency
0
100
200
300
400
500
600
2
4
6
8
10
12
Number of retroduplication calls per person

b)

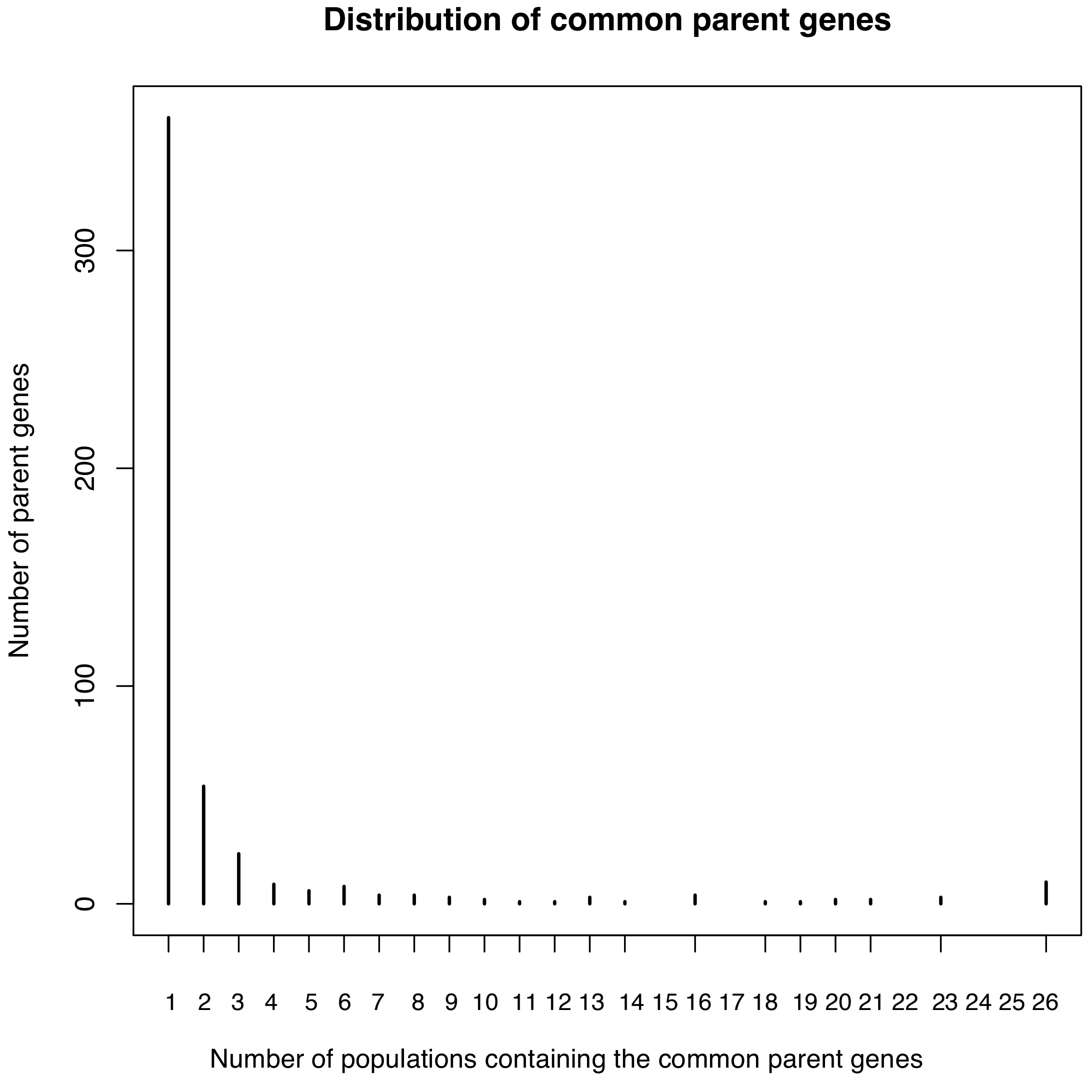
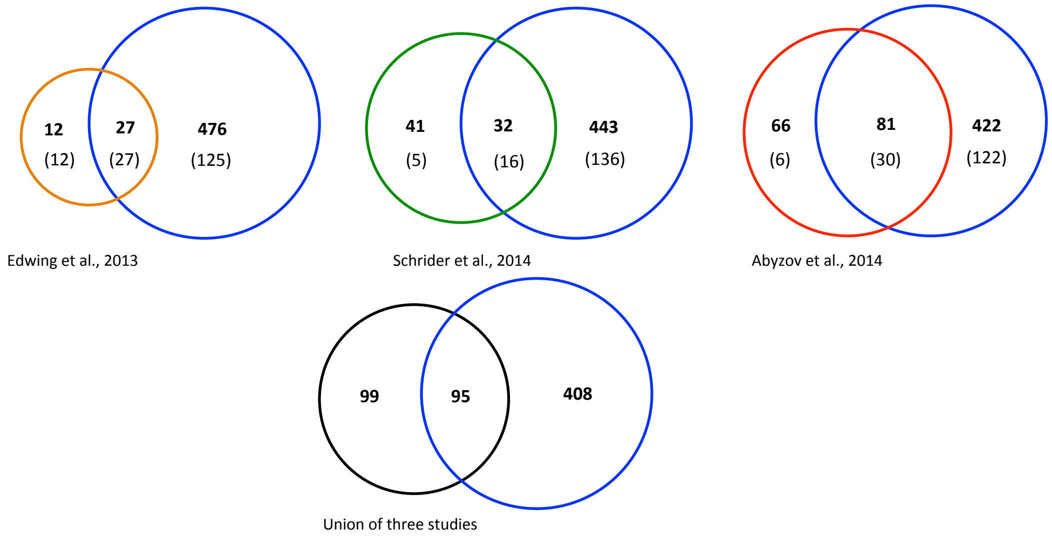


Fig B. Summary statistics of the retroduplication call set generated based exon junction libraries. a) – Histogram of novel retroduplication calls per person. b) – Distribution of common parent genes among populations. Two outlier individuals, NA12890 in CEU and NA19473 in LWK, have been excluded while generating the plots.



Edwing et al., 2013

Schrider et al., 2014

Abyzov et al., 2014

Union of three studies

Fig C. Venn digram of callset comparison between this study and three previous studies. Concordances are called based on insertion sites if they are available in both datasets. When insertion sites are unknown, we use gene names. Numbers in parentheses are the number of insertion points in agreement. Thses circles are not drawn proportional to actual data size.

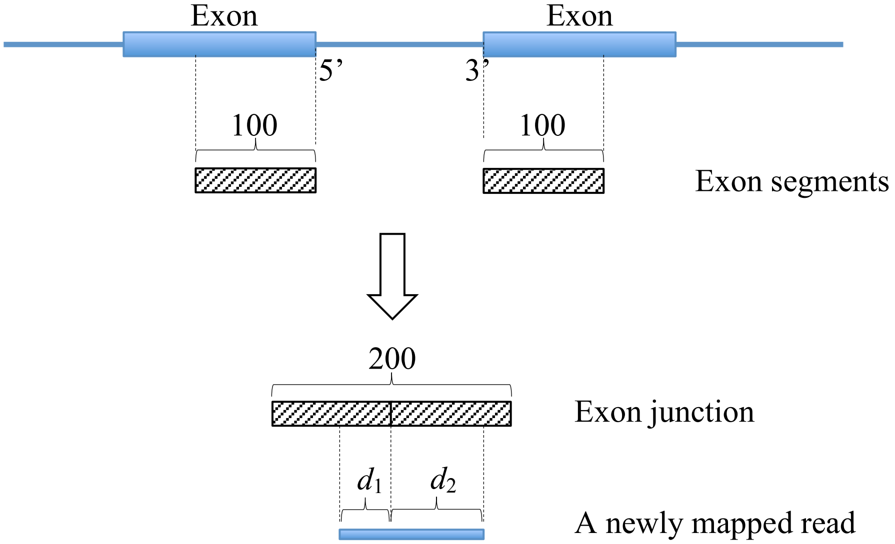


Fig D. Generating exon junctions, and mapping reads to an exon junction. Minimum distance allowed between two exons being joined is 70 bases. Two exon segments adjacent to the joining splice site are extrated, and combined to form an exon junction of length 200 bases. Unmapped reads are mapped against exon junctions. d_1 and d_2 are the number of bases that the read maps to either exon segment. $\min(d_1, d_2) \geq d$ is required for a newly mapped read to be reported from our pipeline. We also calculate the mismatch rate r for each mapped read. d and r are parameters automatically tuned in the range [1, 15] and [0.00, 0.05], respectively, ensuring the most number of calls from the true exon junction library while satisfying no false call from any decoy library.

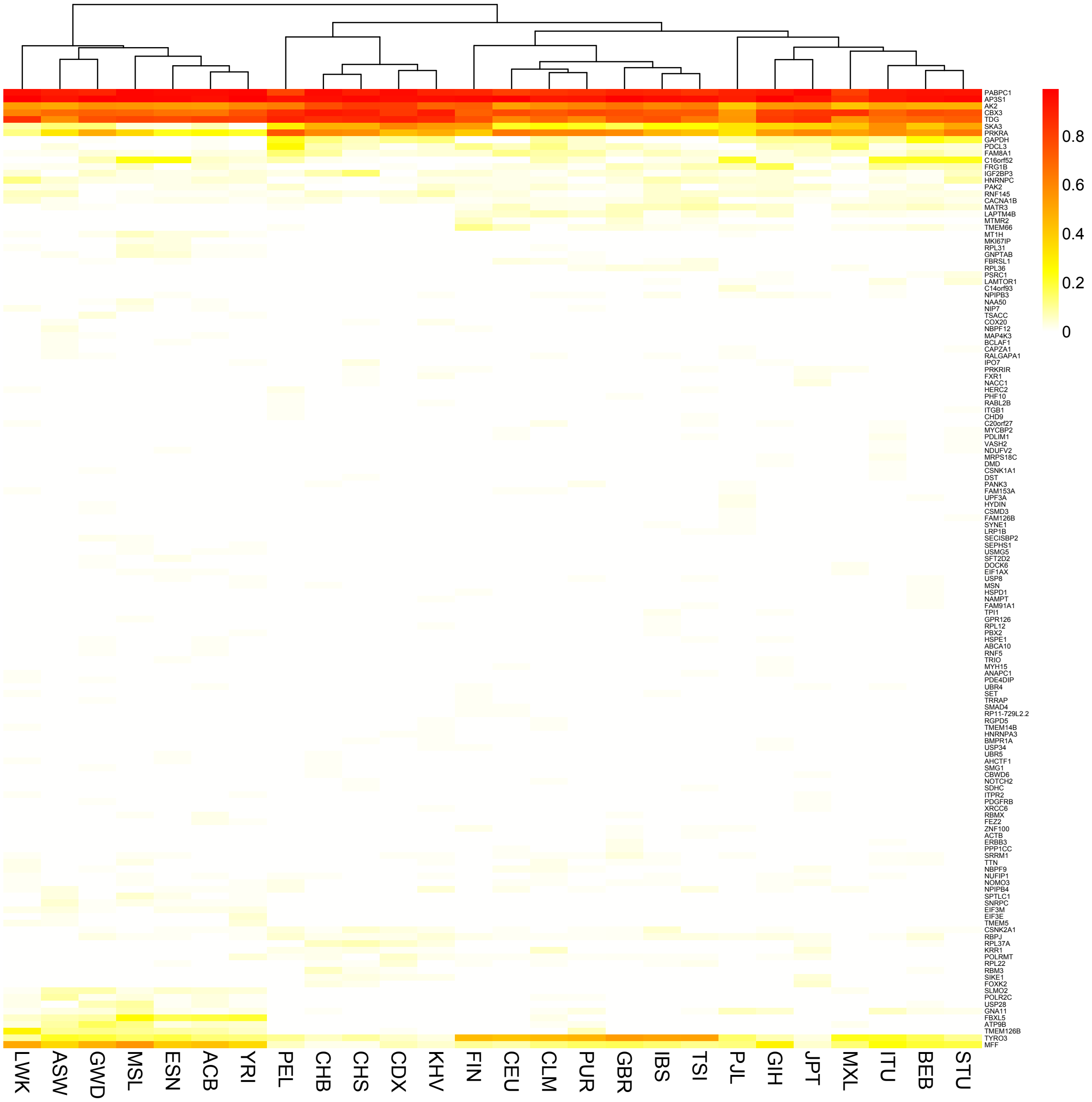
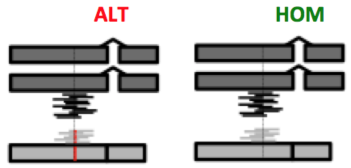


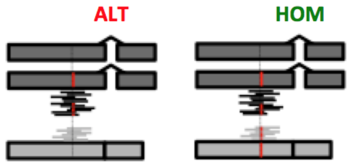
Fig E. Exploration of 142 retroduplication events based on frequency spectrum. Frequency spectrum of 142 retroduplication events that are detected in at least two populations. Hierarchical clustering was used.

Parent gene is hom, the retrodup is…



If the depth is …	10X	50X	100X
No retrodup	99.1%	>99.9%	>99.9%
Alt. retrodup	6.76%	0.03%	<0.01%
Ref. retrodup	99.7%	>99.9%	>99.9%

Parent gene is alt, the retrodup is…



If the depth is …	10X	50X	100X
No retrodup	89.1%	99.3%	>99.9%
Alt. retrodup	59.7%	57.5%	55.4%
Ref. retrodup	92.9%	>99.9%	>99.9%

Fig F. A simplified model of retroduplications affecting SNP calling. We first define the likelihood functions for three genotypes: Pois(n, depth*(1-e)) (AA), Binom(n, depth, 0.5) (AB) and Pois(n, depth*e) (BB). The error rate e = 0.01. We generate all reads from a Poisson distribution with an error rate of 0.01. For genotyping, we picked the one with the highest likelihood and compare it with the ground truth to derive the accuracy as shown in the table. HOM/hom: homozygous/reference allele; ALT/alt: alternative allele.

Table A. Update of Phase 3 retroduplication identifications from Phase 1. In our previous study (Abyzov et al., 2013), we identified retroduplications from the 1000 Genomes Project Phase 1 low-coverage whole-genome sequencing data. In the new study, we identified retroduplications from Phase 3 high-coverage sequencing data. Update of this study is summarized in the table.

	Previous study (Abyzov et al., 2013)	New study update
Detection of novel retroduplications using exon junction libraries		
Data	Low-coverage whole-genome sequencing (WGS)	ILLUMINA high-coverage whole-exome sequencing (WES)
Populations	986 WGS of 14 populations + 2 WGS trios (YRI trio, CEU trio)	2,535 WES of 26 populations
Number of retroduplication calls per person	On average 6-10	Median: 6, IQR: 2
Number of unique genes with novel exon junctions	147	503
Outlier individuals	6 JPT individuals	1 CEU individual and 1 LWK individual
Insertion site detection using mapping of paired end reads		
Data	968 WGS	2,535 WGS
Number of insertion sites detected	36 unique genes	152 unique genes

Table B. Population differentiation measure of each retroduplication parent gene. Observed F_{ST} is the observed test statistic from the true populations set. The empirical p-value is calculated from permutations tests, comparing observed F_{ST} with the null distribution of F_{ST} derived from 1000 fake population sets. The parent genes are assorted with ascending BH (Benjamini-Hochberg procedure) adjusted p-value. The top 43 parent genes have BH adjusted p-value < 0.001, and they are significant retroduplication parent genes that can differentiate superpopulations.

	Parent Gene Ensembl ID	Observed F_{ST}	p-value	Adjusted p-value (BH)
1	ENSG00000092445	0.138278681	0	0
2	ENSG00000168958	0.137309409	0	0
3	ENSG00000165480	0.120808178	0	0
4	ENSG00000118564	0.109889405	0	0
5	ENSG00000171204	0.07846155	0	0
6	ENSG00000111640	0.060451025	0	0
7	ENSG00000185716	0.058092375	0	0
8	ENSG00000180228	0.056955187	0	0
9	ENSG00000166377	0.04989263	0	0
10	ENSG00000115539	0.038428269	0	0
11	ENSG00000197756	0.035297492	0	0
12	ENSG00000149531	0.032854703	0	0
13	ENSG00000101166	0.031702645	0	0
14	ENSG00000004455	0.02975187	0	0
15	ENSG00000122565	0.029516431	0	0
16	ENSG00000139372	0.026314177	0	0
17	ENSG00000015479	0.024405028	0	0
18	ENSG00000048028	0.023831726	0	0
19	ENSG00000070756	0.022783149	0	0
20	ENSG00000087053	0.020313783	0	0
21	ENSG00000052723	0.020214209	0	0
22	ENSG00000133872	0.02011706	0	0
23	ENSG00000104341	0.017653856	0	0
24	ENSG00000102978	0.017058594	0	0
25	ENSG00000141568	0.015530902	0	0
26	ENSG00000205358	0.014956016	0	0
27	ENSG00000088256	0.014498964	0	0
28	ENSG00000111615	0.013778157	0	0
29	ENSG00000149100	0.013289565	0	0
30	ENSG00000149357	0.012697414	0	0
31	ENSG00000102317	0.01203019	0	0
32	ENSG00000130255	0.010837415	0	0
33	ENSG00000111670	0.010644515	0	0

34	ENSG00000137414	0.010048388	0	0
35	ENSG00000092199	0.009994358	0	0
36	ENSG00000090054	0.009955327	0	0
37	ENSG00000124562	0.009955327	0	0
38	ENSG00000177879	0.008665282	0	0
39	ENSG00000100802	0.008163628	0	0
40	ENSG00000101444	0.008163628	0	0
41	ENSG00000134222	0.008163628	0	0
42	ENSG00000104408	0.006629006	0	0
43	ENSG00000112787	0.006022602	0	0
44	ENSG00000071082	0.009566276	0.001	0.010934783
45	ENSG00000118600	0.007736901	0.001	0.010934783
46	ENSG00000120438	0.006629006	0.001	0.010934783
47	ENSG00000114416	0.007750092	0.002	0.021404255
48	ENSG00000121579	0.005521986	0.004	0.041061224
49	ENSG00000155438	0.005521986	0.004	0.041061224
50	ENSG00000160877	0.006197622	0.005	0.0503
51	ENSG00000163467	0.005521986	0.006	0.059176471
52	ENSG00000136231	0.0052821	0.008	0.075924528
53	ENSG00000163319	0.004894305	0.008	0.075924528
54	ENSG00000169062	0.004894305	0.009	0.083833333
55	ENSG00000197020	0.004789575	0.011	0.098803571
56	ENSG00000145860	0.004779859	0.011	0.098803571
57	ENSG00000176915	0.004894305	0.013	0.114719298
58	ENSG00000186298	0.004773668	0.016	0.138758621
59	ENSG00000156467	0.004896106	0.017	0.144932203
60	ENSG00000099821	0.004572527	0.018	0.14842623
61	ENSG00000116251	0.004114264	0.018	0.14842623
62	ENSG00000132603	0.004352587	0.022	0.178483871
63	ENSG00000171055	0.003310573	0.029	0.231539683
64	ENSG00000213064	0.003310573	0.037	0.290796875
65	ENSG00000187742	0.003310573	0.04	0.309538462
66	ENSG00000077809	0.003261581	0.042	0.320090909
67	ENSG00000136144	0.003310573	0.043	0.322820896
68	ENSG00000011566	0.003310573	0.044	0.325470588
69	ENSG00000166454	0.003310573	0.047	0.342623188
70	ENSG00000173915	0.003310573	0.05	0.359285714
71	ENSG00000107438	0.003263524	0.055	0.389647887
72	ENSG00000155744	0.003261581	0.056	0.391222222
73	ENSG00000182899	0.003261581	0.063	0.43409589
74	ENSG00000198947	0.003261581	0.064	0.435027027

75	ENSG00000204628	0.003261581	0.065	0.435933333
76	ENSG00000143494	0.003261581	0.067	0.443434211
77	ENSG00000137492	0.003223297	0.072	0.470337662
78	ENSG00000156795	0.003181188	0.084	0.541692308
79	ENSG00000101266	0.003062007	0.098	0.611082645
80	ENSG00000141646	0.003181188	0.106	0.611082645
81	ENSG00000267699	0.003181188	0.106	0.611082645
82	ENSG00000075624	0.003181188	0.108	0.611082645
83	ENSG00000203667	0.003169033	0.11	0.611082645
84	ENSG00000203943	0.002447086	0.116	0.611082645
85	ENSG00000204790	0.003096362	0.12	0.611082645
86	ENSG00000167004	0.003096362	0.124	0.611082645
87	ENSG00000131732	0.002447086	0.124	0.611082645
88	ENSG00000066027	0.002447086	0.126	0.611082645
89	ENSG00000185842	0.002447086	0.126	0.611082645
90	ENSG00000123545	0.002447086	0.13	0.611082645
91	ENSG00000197930	0.002447086	0.13	0.611082645
92	ENSG00000169139	0.002447086	0.131	0.611082645
93	ENSG00000089157	0.002447086	0.132	0.611082645
94	ENSG00000185305	0.002447086	0.132	0.611082645
95	ENSG00000196419	0.003096362	0.133	0.611082645
96	ENSG00000132692	0.002447086	0.133	0.611082645
97	ENSG00000137601	0.002447086	0.133	0.611082645
98	ENSG00000143341	0.002447086	0.133	0.611082645
99	ENSG00000163492	0.002447086	0.133	0.611082645
100	ENSG00000135457	0.002447086	0.134	0.611082645
101	ENSG00000198554	0.002447086	0.134	0.611082645
102	ENSG00000204262	0.002447086	0.134	0.611082645
103	ENSG00000106636	0.002447086	0.135	0.611082645
104	ENSG00000116001	0.002447086	0.135	0.611082645
105	ENSG00000155313	0.002447086	0.135	0.611082645
106	ENSG00000173674	0.002503289	0.137	0.611082645
107	ENSG00000100030	0.002447086	0.137	0.611082645
108	ENSG00000113013	0.002447086	0.137	0.611082645
109	ENSG00000188647	0.002447086	0.137	0.611082645
110	ENSG00000165898	0.002447086	0.138	0.611082645
111	ENSG00000118113	0.002447086	0.139	0.611082645
112	ENSG00000164253	0.002447086	0.139	0.611082645
113	ENSG00000078304	0.002447086	0.14	0.611082645
114	ENSG00000004866	0.002447086	0.142	0.611082645
115	ENSG00000125144	0.002447086	0.142	0.611082645

116	ENSG00000153956	0.002447086	0.142	0.611082645
117	ENSG00000145730	0.002447086	0.143	0.611082645
118	ENSG00000130159	0.002447086	0.144	0.611082645
119	ENSG00000163877	0.002447086	0.146	0.611082645
120	ENSG00000164032	0.002447086	0.146	0.611082645
121	ENSG00000185261	0.002447086	0.147	0.611082645
122	ENSG00000149273	0.003096362	0.149	0.613414634
123	ENSG00000146776	0.002447086	0.15	0.613414634
124	ENSG00000170144	0.003096362	0.152	0.616580645
125	ENSG00000153391	0.003096362	0.155	0.618769841
126	ENSG00000025156	0.002447086	0.155	0.618769841
127	ENSG00000005810	0.002178645	0.157	0.621818898
128	ENSG00000170906	0.002447086	0.16	0.62875
129	ENSG00000133818	0.002447086	0.167	0.651170543
130	ENSG00000178104	0.002206176	0.197	0.760259542
131	ENSG00000086475	0.002206176	0.198	0.760259542
132	ENSG00000147274	0.002288754	0.2	0.762007463
133	ENSG00000029363	0.002206176	0.202	0.762007463
134	ENSG00000204308	0.002206176	0.203	0.762007463
135	ENSG00000065361	0.002138433	0.206	0.767540741
136	ENSG00000120137	0.002256828	0.209	0.772992647
137	ENSG00000111669	0.002138433	0.216	0.786073593
138	ENSG00000154263	0.002206176	0.218	0.786073593
139	ENSG00000128731	0.002135409	0.243	0.786073593
140	ENSG00000205339	0.002229863	0.246	0.786073593
141	ENSG00000107779	0.00208186	0.248	0.786073593
142	ENSG00000150093	0.001644321	0.264	0.786073593
143	ENSG00000150760	0.001630146	0.293	0.786073593
144	ENSG00000166743	0.001630146	0.293	0.786073593
145	ENSG00000143436	0.001630146	0.298	0.786073593
146	ENSG00000110700	0.001630146	0.301	0.786073593
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148	ENSG00000077380	0.001630146	0.309	0.786073593
149	ENSG00000133112	0.001630146	0.309	0.786073593
150	ENSG00000181163	0.001630146	0.309	0.786073593
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155	ENSG00000118307	0.001630146	0.315	0.786073593
156	ENSG00000130024	0.001624223	0.315	0.786073593

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158	ENSG00000213741	0.001630146	0.316	0.786073593
159	ENSG00000064666	0.001630146	0.317	0.786073593
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162	ENSG00000177200	0.001624223	0.317	0.786073593
163	ENSG00000089472	0.001630146	0.32	0.786073593
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165	ENSG00000048544	0.001630146	0.321	0.786073593
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167	ENSG00000100083	0.001630146	0.322	0.786073593
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169	ENSG00000116489	0.002016079	0.323	0.786073593
170	ENSG00000115760	0.001630146	0.324	0.786073593
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172	ENSG00000213585	0.001630146	0.326	0.786073593
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178	ENSG00000152208	0.001630146	0.327	0.786073593
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231	ENSG00000134250	0.001603016	0.361	0.786073593
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233	ENSG00000079974	0.001603016	0.373	0.80523176
234	ENSG00000015568	0.001603016	0.387	0.831884615
235	ENSG00000168214	0.001613257	0.408	0.873293617
236	ENSG00000180370	0.001505758	0.416	0.886644068
237	ENSG00000130158	0.00138047	0.444	0.917725166
238	ENSG00000168614	0.001532636	0.45	0.917725166

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243	ENSG00000144381	0.001215591	0.506	0.917725166
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310	ENSG00000151914	0.001194385	0.605	0.98166129
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326	ENSG00000121741	0.00154757	0.723	0.999534704
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361	ENSG00000127184	0.00154757	0.746	0.999534704

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384	ENSG00000038382	0.000971839	0.764	0.999534704
385	ENSG00000136068	0.00154757	0.768	0.999534704
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388	ENSG00000163510	0.00154757	0.772	0.999534704
389	ENSG00000133226	0.000777806	0.773	0.999534704
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443	ENSG00000132522	0.001102653	1	1

444	ENSG00000132676	0.001102653	1	1
445	ENSG00000132819	0.001102653	1	1
446	ENSG00000134109	0.001102653	1	1
447	ENSG00000134627	0.001102653	1	1
448	ENSG00000135596	0.001102653	1	1
449	ENSG00000136011	0.001102653	1	1
450	ENSG00000136104	0.001102653	1	1
451	ENSG00000137700	0.001102653	1	1
452	ENSG00000138448	0.001102653	1	1
453	ENSG00000138778	0.001102653	1	1
454	ENSG00000140853	0.001102653	1	1
455	ENSG00000140905	0.001102653	1	1
456	ENSG00000143452	0.001102653	1	1
457	ENSG00000145741	0.001102653	1	1
458	ENSG00000148356	0.001102653	1	1
459	ENSG00000149547	0.001102653	1	1
460	ENSG00000150527	0.001102653	1	1
461	ENSG00000150787	0.001102653	1	1
462	ENSG00000151422	0.001102653	1	1
463	ENSG00000151779	0.001102653	1	1
464	ENSG00000152601	0.001102653	1	1
465	ENSG00000154265	0.001102653	1	1
466	ENSG00000160188	0.001102653	1	1
467	ENSG00000160211	0.001102653	1	1
468	ENSG00000162869	0.001102653	1	1
469	ENSG00000164190	0.001102653	1	1
470	ENSG00000165390	0.001102653	1	1
471	ENSG00000165912	0.001102653	1	1
472	ENSG00000167548	0.001102653	1	1
473	ENSG00000168778	0.001102653	1	1
474	ENSG00000171132	0.001102653	1	1
475	ENSG00000172115	0.001102653	1	1
476	ENSG00000175582	0.001102653	1	1
477	ENSG00000176783	0.001102653	1	1
478	ENSG00000177156	0.001102653	1	1
479	ENSG00000182095	0.001102653	1	1
480	ENSG00000182621	0.001102653	1	1
481	ENSG00000183765	0.001102653	1	1
482	ENSG00000186439	0.001102653	1	1
483	ENSG00000187240	0.001102653	1	1
484	ENSG00000187522	0.001102653	1	1

485	ENSG00000197121	0.001102653	1	1
486	ENSG00000197386	0.001102653	1	1
487	ENSG00000197893	0.001102653	1	1
488	ENSG00000197969	0.001102653	1	1
489	ENSG00000198355	0.001102653	1	1
490	ENSG00000198382	0.001102653	1	1
491	ENSG00000205038	0.001102653	1	1
492	ENSG00000211460	0.001102653	1	1
493	ENSG00000227345	0.001102653	1	1
494	ENSG00000241186	0.001102653	1	1
495	ENSG00000253729	0.001102653	1	1
496	ENSG00000254999	0.001102653	1	1
497	ENSG00000258941	0.001102653	1	1
498	ENSG00000261915	0.001102653	1	1
499	ENSG00000264424	0.001102653	1	1
500	ENSG00000104517	0.000930534	1	1
501	ENSG00000113721	0.000930534	1	1
502	ENSG00000157106	0.000930534	1	1
503	ENSG00000127481	0.000283085	1	1

Table C. Percentage of total variants (retroduplications, or SNPs) private to each superpopulation. The novel retroduplication set can be found in S2 File. The SNPs were extracted from the 1000 Genomes Project Phase 3 dataset (Auton et al., 2015), available at ftp://ftp.1000genomes.ebi.ac.uk/vol1/ftp/release/20130502/ALL.wgs.phase3_shapeit2_mvncall_integrated_v5b.20130502.sites.vcf.gz.

	Total variant sites detected in all genomes	**Total variant sites private to a superpopulation**	**AFR**	**AMR**	**EAS**	**EUR**	**SAS**
Retroduplications	503	397 (78.9%)	119 (23.7%)	39 (7.8%)	80 (15.9%)	65 (12.9%)	94 (18.7%)
SNPs	81,443,073	55,983,609 (68.7%)	20,120,050 (24.7%)	5,577,247 (6.8%)	11,742,915 (14.4%)	7,189,248 (8.8%)	11,354,149 (13.9%)

Table D. Disease-associated retroduplication insertions. These insertion target (inserted) genes associated with diseases are supported by literature, mined from the DISEASES database.

Insertion site chr.	Insertion site start	Insertion site end	Parent gene name	Parent gene Ensembl ID	Parent gene chr.	Parent gene start	Parent gene end	Affected population (by insertion points)	Inserted gene name	Ref	Disease, evidence
chr19	13331914	13332160	ANK1	ENSG00000029534	chr8	41510738	41754280	LWK	CACNA1A	DOID:0060178	Familial,hemiplegic,migraine,GHR,CURATED
									CACNA1A	DOID:1289	Neurodegenerative,disease,UniProtKB-KW,CURATED
									CACNA1A	DOID:1441	Spinocerebellar,ataxia,UniProtKB-KW,CURATED
									CACNA1A	DOID:963	Episodic,ataxia,GHR,CURATED
chr3	8868980	8869077	SLMO2	ENSG00000101166	chr20	57608199	57617964	ACB,ESN,GWD,YRI	CAV3	DOID:0050700	Cardiomyopathy,UniProtKB-KW,CURATED,
									CAV3	DOID:11724	limb-girdle,muscular,dystrophy,GHR,CURATED
									CAV3	DOID:11724	limb-girdle,muscular,dystrophy,UniProtKB-KW,CURATED
									CAV3	DOID:2843	Long,QT,syndrome,UniProtKB-KW,CURATED
chr8	68377448	68377749	TPI1	ENSG00000111669	chr12	6976282	6980112	GIH	CPA6	DOID:1826	Epilepsy,syndrome,UniProtKB-KW,CURATED
chr2	116376651	116376659	SET	ENSG00000119335	chr9	131445702	131458679	CEU,FIN,IBS,LWK	DPP10	DOID:2841	Asthma,UniProtKB-KW,CURATED,
chr15	67871200	67871563	COX7C	ENSG00000127184	chr5	85913720	85916779	CHS	MAP2K5	DOID:0050425	Restless,legs,syndrome,GHR,CURATED
chr10	30651932	30652023	ITSN2	ENSG00000198399	chr2	24425732	24583583	CEU	MTPAP	DOID:1289	Neurodegenerative,disease,UniProtKB-KW,CURATED
chr5	149311980	149312306	MFF	ENSG00000168958	chr2	228189866	228222550	YRI	PDE6A	DOID:10584	Retinitis,pigmentosa,GHR,CURATED
									PDE6A	DOID:10584	Retinitis,pigmentosa,UniProtKB-KW,CURATED
chr6	167114767	167114812	IGF2BP3	ENSG00000136231	chr7	23349827	23510086	BEB,CLM,GWD,JPT,YRI	RPS6KA2	DOID:162	Cancer,UniProtKB-KW,CURATED,
chr6	167114167	167114249	IGF2BP3	ENSG00000136231	chr7	23349827	23510086	CHB,ESN,IBS,LWK,MSL,PUR,YRI			,,,,
chr6	167113886	167113963	IGF2BP3	ENSG00000136231	chr7	23349827	23510086	PJL			,,,,
chr13	36934280	36934427	RALGAPA1	ENSG00000174373	chr14	36007557	36278510	ASW,IBS	SPG20	DOID:1289	Neurodegenerative,disease,UniProtKB-KW,CURATED
									SPG20	DOID:2476	Hereditary,spastic,paraplegia,UniProtKB-KW,CURATED
chrX	41032571	41032679	PFN1	ENSG00000108518	chr17	4848946	4852356	GWD	USP9X	DOID:1059	Intellectual,disability,UniProtKB-KW,CURATED

Table E. Exon-exon junction calls from two trios. Comparison of the number of calls from different platforms.

	CEU trio	YRI trio
High-coverage WGS	13	11
High-coverage WES	11	7
Shallow WGS	6 (NA12878 only, parents' data not available)	5

Estimation of FDR in real data:

Our method could take advantage of the high-coverage WES. In the previous study (Abyzov et al. 2013), retroduplications were discovered per population (i.e. all the individuals in the same population were pooled), since the coverage of Phase 1 WGS data was shallow. By analyzing the pooled shallow WGS data, there was less than 1 novel retroduplication discovered per individual. In comparison, here in this study, we identified novel retroduplications individually using high-coverage WES data, and the number of detected novel retroduplications per individual (median: 6) is significantly more than in the previous study.

Besides, Abyzov et al. also called retroduplications in two deep sequenced trios. These retroduplications have been verified both computationally and experimentally in Abyzov et al. In the CEU and YRI trios, they identified 13 and 11 novel retroduplications, respectively. The numbers are comparable to what we found in our study (median: 6 per individual). We would expect the sensitivity of our WES-based method lie between low-coverage and high-coverage WGS-based method. Indeed, we identified 11 and 7 unique retroduplications in CEU and YRI trios, which are slightly less than 13 and 11.

Furthermore, among the 6 retroduplications that we identified by exon-exon junction strategy on high-coverage WES in the CEU child (NA12878), 4 of them (SKA3, TDG, CBX3 and AP3S1) were also identified by Abyzov et al. using high-coverage WGS data but not AK2 and HNRNPC. In the YRI trio, 5/7 overlapped with the set reported by Abyzov et al. (overlapped: TMEM5, CBX3, ATP9B, MFF and AP3S1, not overlapped: PABPC1 and AK2)." But AK2 and PABPC1 are in the common retroduplication set that Abyzov et al. reported. Taken all together, our estimation of FDR using a validated, independent set is 7.7% (1/13). Noticeably, this is likely an underestimated as some of our unique retroduplications might be missed in Abyzov et al.