ARID5B Genetic Polymorphisms Contribute to Racial Disparities in the Incidence and Treatment Outcome of Childhood Acute Lymphoblastic Leukemia

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Supplemental Text

ARID5B Genetic Polymorphisms Contribute to Racial Disparities in the Incidence and Treatment Outcome of Childhood Acute Lymphoblastic Leukemia

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Identification of correlation among *ARID5B* SNPs

Because linkage disequilibrium exists at the *ARID5B* locus, we sought to determine how many independent markers are represented by 49 *ARID5B* SNPs.

To this end, we

1) created two lists: Independent SNP list (it initially includes no SNPs) and Candidate SNP list (it initially includes all 49 SNPs)
2) calculated pair-wise r^2 between genotypes at any 2 of the 49 SNPs, and $r^2>0.1$ is considered as definition for "correlated/correlation",
3) identified the SNP with the largest number of correlations (i.e. it is correlated with the largest number of SNPs), and moved this SNP from the Candidate SNP list to the Independent SNP list as Independent SNP #1,
4) screened SNPs in the Candidate SNP list, and moved the one that was least associated with SNP #1 (smallest r^2) from the Candidate SNP list to the Independent SNP list as Independent SNP #2
5) repeated steps 3-4 until all SNPs in the Candidate SNP list were correlated with at least one of the SNPs in the Independent SNP list ($r^2>0.1$)
6) the number of SNPs in the Independent SNP list is the number used for adjusting for multiple testing (Bonferroni correction).
7) to determine membership of the 12 SNP clusters (which SNPs are clustered together), we screened each SNP in the Candidate SNP list, and assigned it to the SNP in the Independent SNP list with which it was most strongly correlated (i.e. largest r^2), until all SNPs in the Candidate SNP list were assigned.

The full script of the above analysis (in R language) is available upon request.

Supplemental Table 1S. Clinical features of patients enrolled on COG P9904/9905 protocols[1]

Clinical Features and Treatment Outcome	COG P9904		P value[2]	COG P9905		P value[2]
	Included in genetic analyses (N=717)	Not included in genetic analyses (N=111)		Included in genetic analyses (N=888)	Not included in genetic analyses (N=166)	
Race (self-reported)						
White	569 (81.2)	79 (75.2)	0.19	684 (77.1)	119 (71.7)	0.14
Other	132 (18.8)	26 (24.8)		204 (22.9)	47 (28.3)	
Gender						
Male	388 (54.1)	56 (50.5)	0.48	437 (49.2)	82 (49.4)	1
Female	329 (45.9)	55 (49.5)		451 (50.8)	84 (50.6)	
Age at diagnosis (years)						
<10	717 (100)	111 (100)	1	690 (77.7)	129 (77.7)	1
≥10	0 (0)	0 (0)		198 (22.3)	37 (22.3)	
Leukocyte count at diagnosis (/µl)						
<50,000	717 (100)	111 (100)	1	736 (82.9)	128 (77.1)	0.08
≥50,000	0 (0)	0 (0)		152 (17.1)	38 (22.9)	
5-year relapse-free survival rate	92.1%	91.4%	0.53	80.0%	74.1%	0.06

[1]Data are presented as number (%) of patients unless otherwise indicated. [2]P values were estimated by χ^2 test for race, gender, age, and leukocyte count comparison, and by Cox regression test for survival rate analyses.

Supplementary Table 2S. Associations between *ARID5B* SNPs and ALL susceptibility in whites and Hispanics

SNP ID	Location (Chr10)[1]	Allele (A/B)[2]	White				Hispanic			
			B Allele Frequency (control)	B Allele Frequency (case)	P value[3]	Odds Ratio[4]	B Allele Frequency (control)	B Allele Frequency (case)	P value[3]	Odds Ratio[4]
rs10821936	63723577	T/C*	0.33	0.48	**8.38×10^{-20}**	1.83(1.60-2.08)	0.47	0.62	**1×10^{-6}**	1.82(1.43-2.31)
rs7896246	63724390	G/A*	0.33	0.48	**1.03×10^{-19}**	1.83(1.60-2.08)	0.47	0.61	**5.45×10^{-6}**	1.74(1.37-2.20)
rs10821938	63724773	C/A*	0.42	0.54	**1.47×10^{-14}**	1.64(1.45-1.87)	0.54	0.68	**2.96×10^{-6}**	1.80(1.40-2.30)
rs7923074	63723440	G/T*	0.42	0.54	**1.5×10^{-13}**	1.60(1.41-1.82)	0.53	0.68	**4.69×10^{-7}**	1.88(1.47-2.41)
rs10994982	63710104	G/A*	0.50	0.58	**2.66×10^{-7}**	1.39(1.23-1.58)	0.57	0.70	**1.32×10^{-5}**	1.70(1.34-2.16)
rs7087125	63773039	G/A*	0.46	0.53	**9.22×10^{-6}**	1.32(1.17-1.50)	0.43	0.45	0.555	1.07(0.85-1.35)
rs2893881	63688672	T/C*	0.14	0.18	**0.001**	1.33(1.12-1.57)	0.30	0.34	**0.0423**	1.29(1.01-1.65)
rs9415636	63826186	A/C*	0.91	0.93	**0.0015**	1.45(1.15-1.82)	0.95	0.96	0.18	1.46(0.84-2.54)
rs7922394	63666691	C/T*	0.53	0.58	**0.0025**	1.21(1.07-1.38)	0.59	0.61	0.19	1.17(0.92-1.49)
rs6479778	63689077	C/T*	0.14	0.18	**0.0029**	1.29(1.09-1.53)	0.29	0.33	**0.0296**	1.32(1.03-1.69)
rs10994983	63712827	G/C*	0.91	0.94	**0.003**	1.44(1.13-1.84)	0.97	0.97	0.41	1.33(0.68-2.61)
rs4948488	63685154	T/C*	0.16	0.20	**0.0043**	1.26(1.08-1.48)	0.41	0.46	**0.0345**	1.28(1.02-1.61)
rs6415872	63660689	A/G*	0.50	0.54	**0.0049**	1.20(1.06-1.36)	0.55	0.57	0.149	1.19(0.94-1.51)
rs4948487	63669865	A/C*	0.51	0.55	**0.0096**	1.18(1.04-1.34)	0.56	0.59	**0.0457**	1.28(1.00-1.62)
rs6479779	63695048	G/C*	0.38	0.41	**0.013**	1.17(1.04-1.33)	0.40	0.46	**0.0364**	1.27(1.02-1.59)
rs2393782	63670859	C/G*	0.12	0.13	0.088	1.17(0.98-1.41)	0.27	0.30	**0.029**	1.32(1.03-1.70)
rs12778514	63832279	G/A	0.39	0.42	0.134	1.10(0.97-1.25)	0.31	0.30	0.323	0.88(0.69-1.14)
rs1806771	63682387	G/T	0.91	0.93	0.136	1.19(0.95-1.49)	0.87	0.85	0.169	0.79(0.56-1.11)
rs9633556	63834853	C/G	0.39	0.42	0.146	1.10(0.97-1.24)	0.31	0.30	0.34	0.88(0.69-1.14)
rs3740354	63832863	A/C	0.39	0.42	0.152	1.10(0.97-1.24)	0.31	0.30	0.32	0.88(0.69-1.12)
rs10821951	63814914	T/C	0.94	0.95	0.161	1.21(0.93-1.57)	0.69	0.70	0.61	0.93(0.72-1.20)
rs10994971	63694451	A/T	0.98	0.99	0.164	1.39(0.87-2.20)	0.89	0.92	0.156	1.33(0.90-1.99)
rs2393732	63767229	C/T*	0.03	0.03	0.205	1.28(0.88-1.86)	0.23	0.27	**0.0126**	1.40(1.08-1.83)
rs1122157	63861600	G/A	0.29	0.31	0.226	1.09(0.95-1.24)	0.14	0.13	0.238	0.80(0.56-1.16)
rs7898839	63825010	G/A	0.97	0.98	0.228	1.29(0.85-1.93)	0.97	0.95	0.271	0.72(0.41-1.28)

Supplementary Table 2S (Cont'd)

SNP ID	Location (Chr10)[1]	Allele (A/B)[2]	White				Hispanic			
			B Allele Frequency (control)	B Allele Frequency (case)	P value[3]	Odds Ratio[4]	B Allele Frequency (control)	B Allele Frequency (case)	P value[3]	Odds Ratio[4]
rs17215180	63688728	T/C*	0.53	0.55	0.251	1.08(0.95-1.22)	0.70	0.74	**0.0181**	1.37(1.05-1.77)
rs7915732	63825163	A/G	0.97	0.98	0.261	1.27(0.84-1.92)	0.98	0.95	0.059	0.52(0.26-1.03)
rs10509166	63833922	T/C	0.96	0.97	0.261	1.21(0.87-1.70)	0.74	0.74	0.24	0.85(0.65-1.11)
rs16916971	63838595	C/G	0.96	0.97	0.261	1.21(0.87-1.70)	0.64	0.65	0.39	0.90(0.70-1.15)
rs12357548	63803472	G/A	0.55	0.57	0.274	1.07(0.95-1.21)	0.36	0.39	0.853	0.98(0.77-1.23)
rs10740059	63809527	A/G	0.58	0.60	0.341	1.06(0.94-1.21)	0.64	0.64	0.849	0.98(0.77-1.23)
rs12571478	63687869	G/A	0.93	0.94	0.399	1.11(0.87-1.43)	0.87	0.85	0.182	0.79(0.57-1.11)
rs2393735	63787846	T/C	0.96	0.96	0.483	1.12(0.81-1.54)	0.73	0.73	0.218	0.85(0.65-1.10)
rs10995014	63784082	C/A	0.96	0.96	0.486	1.12(0.82-1.54)	0.73	0.73	0.144	0.82(0.63-1.08)
rs4948293	63789018	C/T	0.21	0.22	0.499	1.05(0.91-1.22)	0.17	0.15	0.458	0.89(0.65-1.22)
rs7913907	63849790	T/C	0.86	0.86	0.503	1.06(0.89-1.27)	0.51	0.52	0.102	0.82(0.65-1.04)
rs16916915	63785369	A/G	0.96	0.96	0.533	1.11(0.80-1.52)	0.72	0.73	0.228	0.85(0.65-1.11)
rs10821950	63811967	A/G	0.55	0.56	0.56	1.04(0.92-1.17)	0.36	0.39	0.505	0.93(0.72-1.18)
rs7906079	63844810	C/G	0.80	0.81	0.633	1.04(0.89-1.21)	0.83	0.84	0.946	0.99(0.73-1.33)
rs9415639	63848456	C/G	0.86	0.86	0.638	1.04(0.87-1.25)	0.52	0.53	0.139	0.83(0.65-1.06)
rs2278305	63843112	T/C	0.81	0.82	0.669	1.03(0.88-1.21)	0.83	0.84	0.812	0.96(0.71-1.32)
rs2393726	63854407	T/C	0.01	0.01	0.707	1.12(0.62-2.02)	0.34	0.35	0.121	1.21(0.95-1.55)
rs10821956	63862634	A/G	0.88	0.89	0.756	1.03(0.85-1.25)	0.95	0.93	0.955	0.99(0.61-1.59)
rs12764378	63800004	G/A	0.22	0.22	0.762	1.02(0.88-1.19)	0.17	0.14	0.501	0.90(0.66-1.23)
rs16916996	63861826	G/C	0.91	0.91	0.823	1.02(0.83-1.27)	0.84	0.85	0.856	0.97(0.70-1.33)
rs7922857	63818083	G/C	0.70	0.70	0.833	1.01(0.89-1.16)	0.69	0.71	0.973	1.00(0.78-1.28)
rs10821944	63785089	G/T	0.72	0.72	0.907	1.01(0.88-1.16)	0.52	0.55	0.631	0.94(0.75-1.19)
rs11599405	63860283	C/T	0.23	0.23	0.923	1.01(0.87-1.16)	0.15	0.13	0.211	0.81(0.58-1.12)
rs9415637	63840265	T/G	0.12	0.12	0.948	1.01(0.83-1.22)	0.06	0.08	0.223	1.32(0.84-2.08)

[1]Chromosomal locations are based on hg19. [2]Asterisk denotes that the B allele had a significantly higher frequency in children with ALL than in the non-ALL controls (P<0.05 in whites and/or Hispanics). [3]P values<0.05 are shown in bold. [4]Odds ratio for the likelihood of ALL among individuals carrying an additional copy of the B allele (versus A allele) at each SNP.

Supplementary Table 3S. SNP clusters at the *ARID5B* Locus

SNP ID	Cluster ID	SNP ID	Cluster ID
rs2393726	1	rs10821956	5
rs7913907	1	rs9415637	5
rs16916915	1	rs1806771	6
rs10509166	1	rs12571478	6
rs10821951	1	rs6415872	6
rs9415639	1	rs4948487	6
rs16916971	1	rs7922394	6
rs10995014	1	rs9633556	7
rs2393732	1	rs10821950	7
rs2393735	1	rs11599405	7
rs7087125	2	rs12778514	7
rs4948293	2	rs3740354	7
rs16916996	3	rs10740059	7
rs7922857	3	rs1122157	7
rs12764378	3	rs10821944	7
rs6479778	4	rs12357548	7
rs4948488	4	rs10994983	8
rs2893881	4	rs7906079	9
rs10994982	4	rs2278305	9
rs6479779	4	rs10994971	10
rs10821936	4	rs7915732	11
rs2393782	4	rs7898839	11
rs10821938	4	rs9415636	12
rs7896246	4		
rs17215180	4		
rs7923074	4		

Supplementary Table 4S. Correlation between *ARID5B* SNPs and ALL subtypes, age at diagnosis, and gender

SNP ID[1]	P value[5]					
	ALL Subtype[2]		Age[3]		Gender[4]	
	White	Hispanic	White	Hispanic	White	Hispanic
rs10821936	**0.00282**	**0.0131**	0.118	0.835	0.572	0.545
rs7896246	**0.00264**	**0.0388**	0.128	0.696	0.545	0.498
rs10821938	**9.09×10^{-4}**	**0.00136**	0.217	0.85	0.6108	0.8963
rs7923074	**0.00213**	**0.0063**	0.284	0.927	0.73	0.785
rs10994982	**0.0134**	**0.008**	0.075	0.694	0.694	0.818
rs7087125	0.927	0.967	0.171	0.473	0.692	0.299
rs2893881	0.18	0.0926	0.918	0.33	0.862	0.815
rs9415636	0.175	0.562	0.620	0.8	0.875	0.605
rs7922394	0.422	0.386	0.411	0.786	0.204	0.484
rs6479778	0.183	0.115	0.919	0.432	0.933	0.756
rs10994983	0.147	**0.0022**	0.562	0.303	0.811	0.891
rs4948488	0.248	**0.0311**	0.843	0.486	0.938	0.409
rs6415872	0.451	0.341	0.590	0.912	0.961	0.532
rs4948487	0.484	0.176	0.598	0.935	0.649	0.633
rs6479779	**0.0151**	0.113	0.808	0.063	0.238	0.735
rs2393782	0.197	0.327	0.835	0.979	0.811	0.34
rs12778514	0.166	**0.0299**	0.574	0.716	0.179	0.354
rs1806771	0.56	0.824	0.339	0.669	0.061	0.652
rs9633556	0.195	**0.0393**	0.575	0.696	0.178	0.345
rs3740354	0.196	**0.0299**	0.567	0.716	0.185	0.354
rs10821951	0.789	0.256	**0.0204**	0.488	0.431	0.836
rs10994971	0.674	0.334	0.415	0.769	0.808	0.537
rs2393732	0.449	0.452	0.101	0.72	0.988	0.883
rs1122157	0.672	0.48	0.201	0.583	0.256	0.404
rs7898839	0.464	0.114	0.411	0.934	0.899	0.212

Supplementary Table 4S (Cont'd)

SNP ID[1]	P value[5]					
	Subtype[2]		Age[3]		Gender[4]	
	White	Hispanic	White	Hispanic	White	Hispanic
rs17215180	0.0696	**0.0469**	0.939	0.082	0.088	0.735
rs7915732	0.452	0.18	0.370	0.803	0.779	0.418
rs10509166	0.83	0.705	0.428	0.543	0.759	0.568
rs16916971	0.83	0.801	0.428	0.523	0.759	0.677
rs12357548	0.198	0.0602	0.445	0.542	0.952	0.48
rs10740059	0.65	0.059	0.592	0.731	0.781	0.747
rs12571478	0.524	0.939	0.460	0.432	0.932	0.194
rs2393735	0.852	0.592	**0.0395**	0.71	0.353	0.324
rs10995014	0.558	0.705	**0.0017**	0.71	0.151	0.324
rs4948293	0.344	0.0937	0.142	0.446	0.87	0.435
rs7913907	0.1	0.477	0.843	0.664	0.399	0.774
rs16916915	0.849	0.677	**0.0408**	0.755	0.314	0.222
rs10821950	0.33	0.122	0.433	0.635	0.949	0.561
rs7906079	0.706	0.251	0.525	0.603	0.135	0.511
rs9415639	0.119	0.344	0.788	0.652	0.423	0.681
rs2278305	0.401	0.299	0.589	0.611	0.087	0.612
rs2393726	0.0892	0.848	0.400	0.996	0.839	0.66
rs10821956	0.991	0.892	0.366	0.548	0.236	0.311
rs12764378	0.532	0.132	0.197	0.499	0.963	0.251
rs16916996	0.104	0.53	0.451	0.734	0.819	0.572
rs7922857	0.313	0.0604	**0.012**	0.421	0.913	0.789
rs10821944	0.666	0.446	0.574	0.612	0.932	0.981
rs11599405	0.982	0.658	0.352	0.66	0.284	0.988
rs9415637	0.721	0.839	0.719	0.093	0.47	0.345

[1]SNPs associated with ALL susceptibility or relapse risk are highlighted in red. [2]ALL subtypes are defined as hyperdiploid, *TCF3-PBX1*,*ETV6-RUNX1* and B-other (whites: N=296, 21, 286, 375, respectively; Hispanics: N=99, 18, 78, 135, respectively). [3]Age groups are <10 and ≥10 years (whites: N=845, 133; Hispanics: N=293, 37). [4]Genders are male and female (Whites: N=510, 468; Hispanics: N=169, 161); [5]P value is estimated by χ^2 test, and P values<0.05 are shown in bold

Supplementary Table 5S. Association of *ARID5B* SNPs with the risk of ALL relapse

SNP ID[1]	Allele (A/B)[2]	ALL Relapse						Overall Survival		MRD
		Adjusting treatment arm and ancestry		Adjusting treatment arm, ancestry, and MRD		Adjusting treatment arm and ancestry in MRD-negative patients		Adjusting treatment arm and ancestry		
		P value[3]	Hazard Ratio[4]	P value	Hazard Ratio[4]	P value	Hazard Ratio[4]	P value	Hazard Ratio[4]	P value
rs6479778	C/T*	**8.1×10^{-5}**	1.48(1.22-1.80)	0.05	1.23(1.00-1.51)	0.825	1.01(0.90-1.15)	4.4×10^{-4}	1.73 (1.28-2.36)	1.3×10^{-4}
rs2893881	T/C*	**1.13×10^{-4}**	1.45(1.2-1.75)	0.036	1.23(1.01-1.52)	0.388	0.91(0.74-1.12)	3.9×10^{-4}	1.69(1.27-2.27)	2×10^{-4}
rs4948488	T/C*	**2.6×10^{-4}**	1.41(1.18-1.69)	0.021	1.25(1.03-1.51)	0.95	1.00(0.88-1.12)	0.004	1.54(1.15-2.04)	0.033
rs2393782	C/G*	**0.0087**	1.35(1.08-1.69)	0.1	1.22(0.96-1.53)	0.405	0.92(0.75-1.12)	0.023	1.50 (1.06-2.14)	0.043
rs10821938	C/A*	**0.0298**	1.2(1.02-1.45)	0.464	1.08(0.89-1.28)	0.653	0.95(0.78-1.18)	0.109	1.27(0.95-1.69)	0.055
rs7923074	G/T*	**0.0391**	1.20(1.01-1.43)	0.584	1.05(0.88-1.26)	0.202	0.83(0.63-1.1)	0.118	1.26 (0.94-1.69)	0.024
rs6479779	G/C*	**0.0419**	1.2(1.01-1.45)	0.317	1.1(0.91-1.33)	0.306	0.83(0.58-1.19)	0.005	1.49(1.12-2.00)	0.038
rs17215180	T/C*	**0.049**	1.22(1-1.49)	0.46	1.08(0.88-1.32)	0.445	1.08(0.89-1.3)	0.383	1.15(0.85-1.56)	0.308
rs10994971	A/T	0.065	1.72(0.97-3.05)	0.048	1.72(1.00-2.95)	0.119	1.15(0.96-1.38)	0.064	2.99 (0.94-9.51)	0.769
rs10994982	G/A	0.123	1.15(0.96-1.39)	0.658	1.04(0.86-1.27)	0.843	1.01(0.9-1.14)	0.075	1.32(0.97-1.79)	0.155
rs7896246	G/A	0.175	1.12(0.95-1.33)	0.997	1.00(0.84-1.19)	0.975	0.99(0.72-1.37)	0.047	1.35(1.00-1.82)	0.011
rs16916915	G/A	0.225	1.23(0.88-1.75)	0.702	1.06(0.76-1.52)	0.658	1.04(0.86-1.27)	0.263	1.32(0.81-2.17)	0.035
rs6415872	A/G	0.24	1.11(0.93-1.33)	0.314	1.10(0.91-1.34)	0.063	0.38(0.13-1.06)	0.603	0.93(0.69-1.23)	0.603
rs10994983	G/C	0.256	1.3(0.83-2.04)	0.803	1.06(0.67-1.67)	0.257	1.11(0.93-1.33)	0.589	1.22(0.60-2.44)	0.028
rs10995014	A/C	0.267	1.21(0.86-1.70)	0.778	1.05(0.74-1.48)	0.364	0.83(0.55-1.23)	0.289	1.30 (0.80-2.11)	0.038
rs16916971	C/G	0.275	1.22(0.85-1.74)	0.051	1.43(1.00-2.05)	0.731	1.03(0.89-1.18)	0.592	1.15 (0.69-1.92)	0.072
rs16916996	G/C	0.285	1.16(0.89-1.51)	0.092	1.27(0.96-1.68)	0.478	1.05(0.91-1.21)	0.992	1.00(0.63-1.59)	0.73
rs2393732	C/T	0.331	1.17(0.85-1.61)	0.729	1.06(0.75-1.52)	0.266	0.87(0.69-1.11)	0.41	0.82(0.51-1.32)	0.951
rs7915732	G/A	0.334	1.22(0.81-1.85)	0.561	1.14(0.74-1.72)	0.0131	0.73(0.57-0.93)	0.864	1.05(0.57-1.96)	0.729
rs7922394	C/T	0.344	1.09(0.91-1.31)	0.567	1.06(0.87-1.29)	0.9	1.01(0.83-1.24)	0.917	0.98(0.73-1.32)	0.552
rs10821936	T/C	0.355	1.09(0.92-1.28)	0.777	0.97(0.82-1.16)	0.44	0.93(0.75-1.14)	0.176	1.22(0.92-1.61)	0.037
rs10821944	T/G	0.358	1.1(0.9-1.33)	0.781	1.03(0.85-1.25)	0.116	1.18(0.96-1.45)	0.999	1.00 (0.74-1.35)	0.088
rs9415637	T/G	0.363	1.12(0.87-1.45)	0.45	1.11(0.85-1.45)	0.809	0.95(0.64-1.41)	0.107	1.37(0.93-2.04)	0.939
rs9415636	A/C	0.371	1.22(0.79-1.90)	0.321	1.26(0.80-2.00)	0.994	1.00(0.86-1.17)	0.187	1.72 (0.77-3.87)	0.665
rs10740059	G/A	0.385	1.08(0.91-1.27)	0.197	1.12(0.94-1.32)	0.495	0.93(0.76-1.14)	0.448	1.12(0.84-1.49)	0.355

Supplementary Table 5S (Cont'd)

SNP ID[1]	Allele (A/B)[2]	ALL Relapse						Overall Survival		MRD
		Adjusting treatment arm and ancestry		Adjusting treatment arm, ancestry, and MRD		Adjusting treatment arm and ancestry in MRD-negative Patients		Adjusting treatment arm and ancestry		
		P value[3]	Hazard Ratio[4]	P value	Hazard Ratio[4]	P value	Hazard Ratio[4]	P value	Hazard Ratio[4]	P value
rs1806771	G/T	0.386	1.16(0.83-1.61)	0.406	1.16(0.82-1.64)	0.305	1.14(0.89-1.46)	0.212	1.45 (0.81-2.58)	0.709
rs2393726	C/T	0.387	1.19(0.81-1.75)	0.1	1.39(0.94-2.07)	0.889	1.02(0.78-1.33)	0.549	1.18 (0.68-2.06)	0.156
rs2393735	C/T	0.39	1.16(0.83-1.63)	0.924	1.02(0.72-1.43)	0.68	0.96(0.78-1.18)	0.38	1.24 (0.77-2.00)	0.031
rs12571478	G/A	0.396	1.16(0.82-1.64)	0.739	1.06(0.74-1.52)	0.014	1.23(1.04-1.47)	0.119	1.72(0.87-3.33)	0.068
rs10821951	C/T	0.406	1.14(0.85-1.49)	0.951	1.01(0.75-1.35)	0.0147	0.84(0.73-0.97)	0.743	1.08(0.71-1.61)	0.29
rs12357548	A/G	0.471	1.07(0.89-1.28)	0.576	1.05(0.88-1.27)	0.0267	2.16(1.09-4.27)	0.802	1.04 (0.78-1.38)	0.601
rs10821950	G/A	0.519	1.06(0.88-1.27)	0.671	1.04(0.87-1.25)	0.057	1.22(0.99-1.52)	0.717	1.05(0.79-1.41)	0.411
rs7913907	T/C	0.541	1.08(0.85-1.37)	0.589	1.08(0.83-1.39)	0.228	0.90(0.76-1.06)	0.106	1.37(0.93-2.00)	0.282
rs9633556	G/C	0.541	1.05(0.88-1.25)	0.548	1.05(0.88-1.27)	0.987	1.00(0.88-1.12)	0.576	1.09(0.81-1.45)	0.811
rs12778514	A/G	0.6	1.05(0.88-1.25)	0.666	1.04(0.87-1.24)	0.984	1.00(0.79-1.26)	0.608	1.08 (0.81-1.45)	0.948
rs3740354	C/A	0.628	1.04(0.88-1.25)	0.688	1.04(0.87-1.23)	0.114	0.85(0.68-1.04)	0.648	1.08(0.80-1.43)	0.929
rs4948293	C/T	0.64	1.05(0.85-1.31)	0.742	1.04(0.83-1.30)	0.386	0.85(0.59-1.22)	0.858	1.03 (0.72-1.48)	0.495
rs4948487	A/C	0.654	1.04(0.87-1.26)	0.722	1.04(0.85-1.26)	0.315	0.90(0.73-1.11)	0.462	0.90(0.67-1.20)	0.637
rs11599405	T/C	0.735	1.04(0.83-1.3)	0.741	1.04(0.83-1.32)	0.175	0.90(0.78-1.04)	0.247	1.26(0.85-1.82)	0.434
rs9415639	C/G	0.771	1.04(0.81-1.32)	0.812	1.03(0.79-1.34)	0.927	0.99(0.89-1.11)	0.142	1.34 (0.91-1.97)	0.206
rs7898839	A/G	0.784	1.06(0.70-1.61)	0.802	1.06(0.69-1.61)	0.246	0.86(0.66-1.11)	0.917	1.03(0.57-1.89)	0.726
rs10509166	T/C	0.784	1.05(0.73-1.52)	0.259	1.25(0.85-1.85)	0.114	1.12(0.97-1.32)	0.824	0.94(0.55-1.61)	0.017
rs7906079	G/C	0.896	1.01(0.81-1.27)	0.421	1.1(0.87-1.39)	0.973	1.00(0.76-1.33)	0.376	0.83(0.56-1.25)	0.111
rs12764378	G/A	0.927	1.01(0.81-1.27)	0.848	1.02(0.81-1.28)	0.28	0.89(0.74-1.1)	0.979	1.00 (0.69-1.43)	0.741
rs7922857	G/C	0.951	1.01(0.83-1.22)	0.727	0.97(0.81-1.16)	0.0145	1.35(1.06-1.72)	0.56	1.10(0.80-1.49)	0.323
rs1122157	A/G	0.981	1.00(0.81-1.24)	0.802	1.03(0.83-1.28)	0.241	0.89(0.73-1.08)	0.314	0.84(0.61-1.18)	0.164
rs7087125	A/G	0.989	1.00(0.84-1.19)	0.572	1.05(0.88-1.26)	0.591	1.04(0.91-1.18)	0.444	0.89(0.67-1.20)	0.604
rs10821956	A/G	0.995	1.00(0.74-1.35)	0.784	0.96(0.71-1.3)	0.0196	1.17(1.02-1.33)	0.632	0.89(0.55-1.45)	0.582
rs2278305	T/C	0.997	1.00(0.8-1.25)	0.494	0.92(0.72-1.16)	0.0301	1.25(1.02-1.52)	0.366	1.20(0.81-1.82)	0.244

[1]SNPs associated with ALL susceptibility are highlighted in red. [2]Asterisk denotes that the B allele was associated with higher risk of relapse, lower survival rate, or higher rate of MRD positivity. [3]P values <0.05 are shown in bold. [4]Hazard ratio for the likelihood of ALL relapse (for relapse analyses) or death (for survival analyses) among individuals carrying an additional copy of the B allele at each SNP.

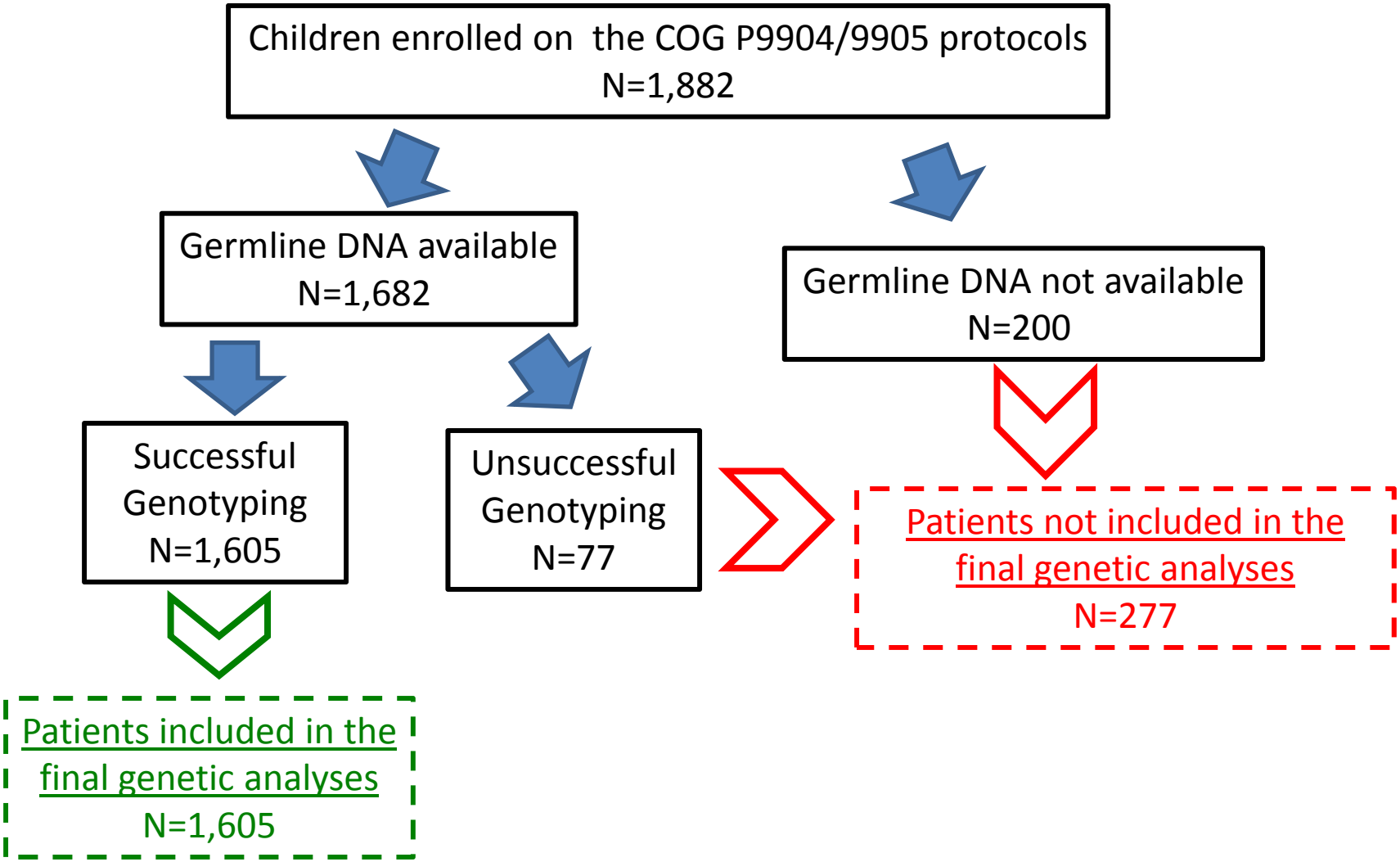
Supplementary Table 6S. Correlation between 49 *ARID5B* SNPs and *IKZF1* SNP rs11978267.

SNP ID[1]	P value[2]			
	White (control) N=1,046	White (case) N=978	Hispanic (control) N=541	Hispanic (case) N=330
rs10821936	0.566	0.339	0.868	0.523
rs7896246	0.564	0.264	0.982	0.782
rs10821938	0.983	0.17	0.547	0.919
rs7923074	0.997	0.204	0.36	0.97
rs10994982	0.123	0.222	0.908	0.707
rs7087125	0.398	0.156	0.112	0.914
rs2893881	0.234	0.436	0.63	0.165
rs9415636	0.671	0.432	0.773	0.389
rs7922394	**0.0051**	0.73	0.138	0.822
rs6479778	0.32	0.631	0.412	0.26
rs10994983	0.059	0.462	0.331	0.719
rs4948488	0.573	0.852	0.234	0.406
rs6415872	**0.0044**	0.723	**0.039**	0.99
rs4948487	**0.0121**	0.63	**0.0373**	0.822
rs6479779	**0.0167**	0.753	0.316	0.125
rs2393782	0.344	0.379	0.636	0.217
rs12778514	0.635	0.106	0.545	0.744
rs1806771	0.769	0.148	0.085	0.798
rs9633556	0.611	0.104	0.545	0.797
rs3740354	0.611	0.102	0.585	0.744
rs10821951	0.555	0.771	0.77	0.751
rs10994971	0.379	0.622	0.258	**0.0063**
rs2393732	0.747	0.359	0.951	0.73
rs1122157	0.511	0.122	0.68	0.252
rs7898839	0.982	0.499	0.534	0.839

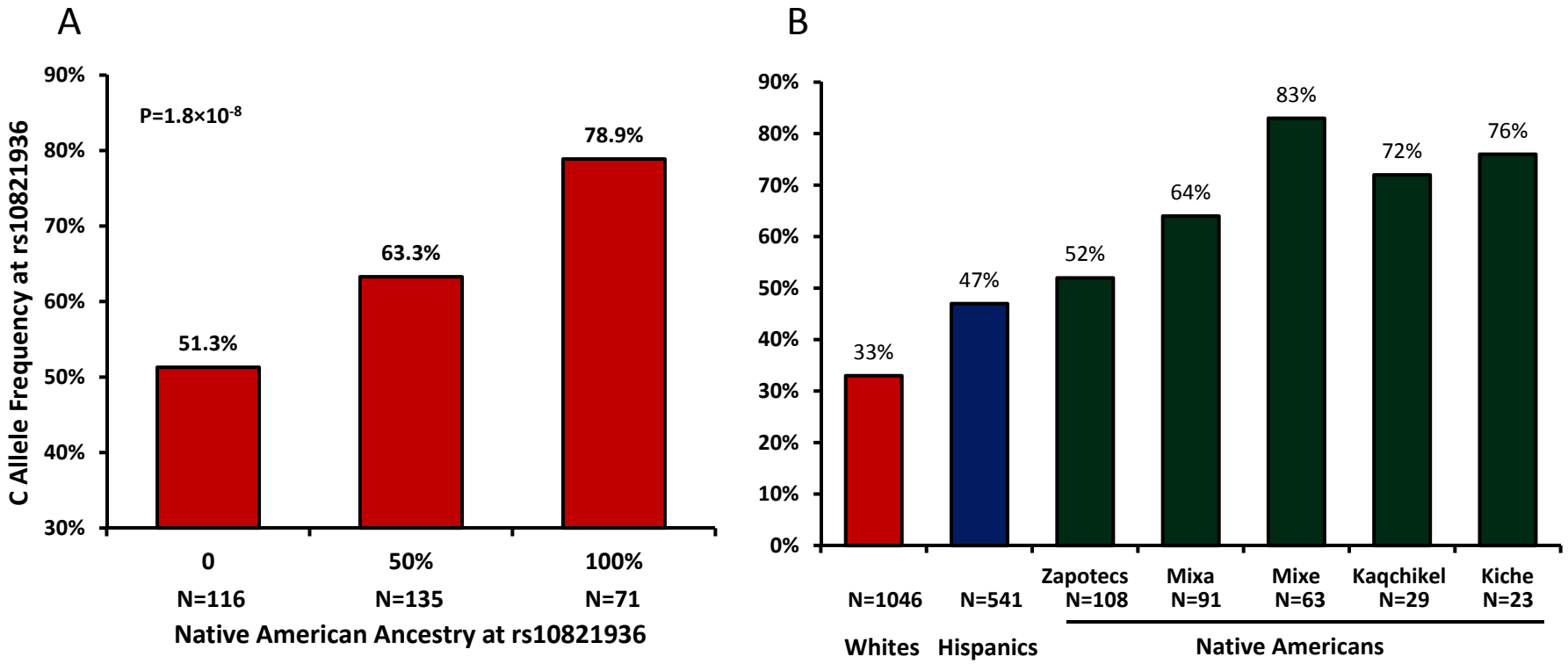
Supplementary Table 6S (Cont'd)

SNP ID[1]	P value[2]			
	White (control) N=1,046	White (case) N=978	Hispanic (control) N=541	Hispanic (case) N=330
rs17215180	0.137	0.462	0.535	0.902
rs7915732	0.516	0.623	0.524	0.738
rs10509166	0.966	0.172	0.954	0.514
rs16916971	0.966	0.172	0.784	0.782
rs12357548	0.939	0.724	0.396	0.884
rs10740059	0.716	0.991	0.808	0.571
rs12571478	0.131	0.189	0.054	0.732
rs2393735	0.493	0.25	0.739	0.631
rs10995014	0.322	0.133	0.782	0.439
rs4948293	0.968	0.228	0.533	0.833
rs7913907	0.327	0.265	0.569	0.951
rs16916915	0.488	0.235	0.634	0.508
rs10821950	0.948	0.703	0.438	0.859
rs7906079	0.101	0.64	0.208	0.626
rs9415639	0.314	0.385	0.633	0.923
rs2278305	0.14	0.837	0.558	0.609
rs2393726	0.43	**0.029**	0.906	0.999
rs10821956	0.53	0.116	0.898	0.683
rs12764378	0.867	0.211	0.65	0.753
rs16916996	0.89	0.467	0.622	0.94
rs7922857	0.677	0.677	0.895	0.608
rs10821944	0.734	0.096	0.679	0.785
rs11599405	0.594	0.346	0.923	0.828
rs9415637	**0.0386**	0.194	0.577	0.996

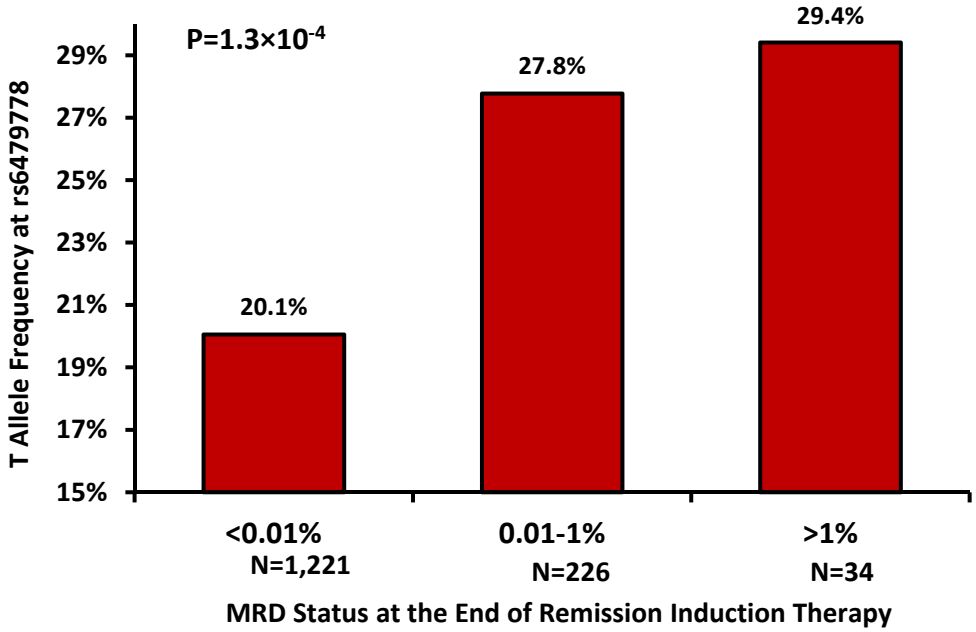
[1]SNPs associated with ALL susceptibility or relapse risk are highlighted in red. [2]P values were estimated by Spearman Rank test and P<0.05 are shown in bold.



Supplementary Figure 1S. Flow chart of COG P9904/9905 patients included/excluded for the genetic analyses.



Supplementary Figure 2S. Relationship between genotype and NA ancestry at rs10821936. (A) C allele frequency is positively correlated with local NA ancestry (as inferred by LAMP). P value was estimated by Spearman rank correlation. (B) C allele at rs10821936 is more common in indigenous Native American populations than whites and Hispanics.



Supplementary Figure 3S. Genotype at rs6479778 is associated with minimal residual disease (MRD) status at the end of remission induction therapy. Children carrying the T allele were more likely to have positive MRD status in the COGP9904/9905 studies. P value was determined by Spearman rank correlation.