

Supplementary Figures and Tables

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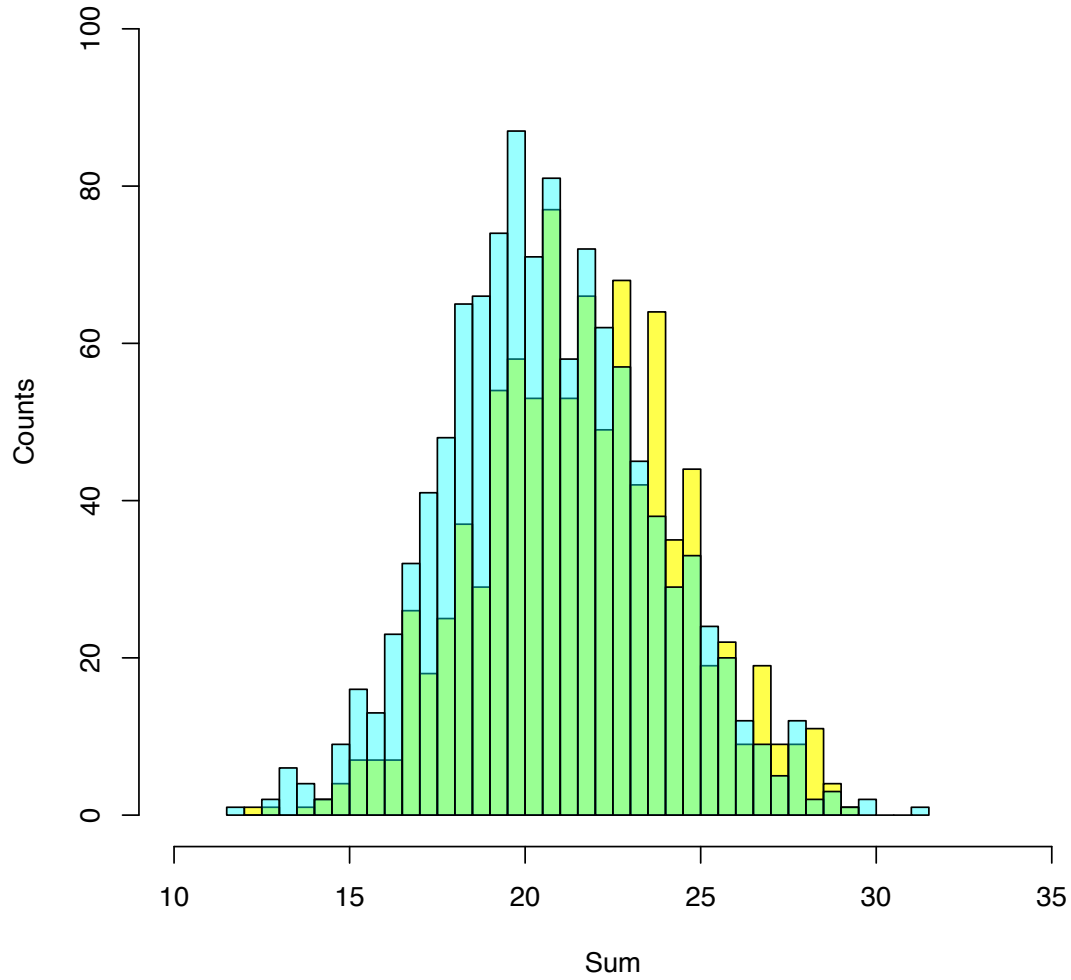
Supplementary Figure 1a and 1b: Histogram of *unweighted* sum of risk alleles for case and controls across (1a) 23 new PCa variants and (1b) 63 total PCa variants.

Supplementary Figure 2a and 2b: Histogram of *weighted* sum of risk alleles for case and controls across (1a) 23 new PCa variants and (1b) 63 total PCa variants.

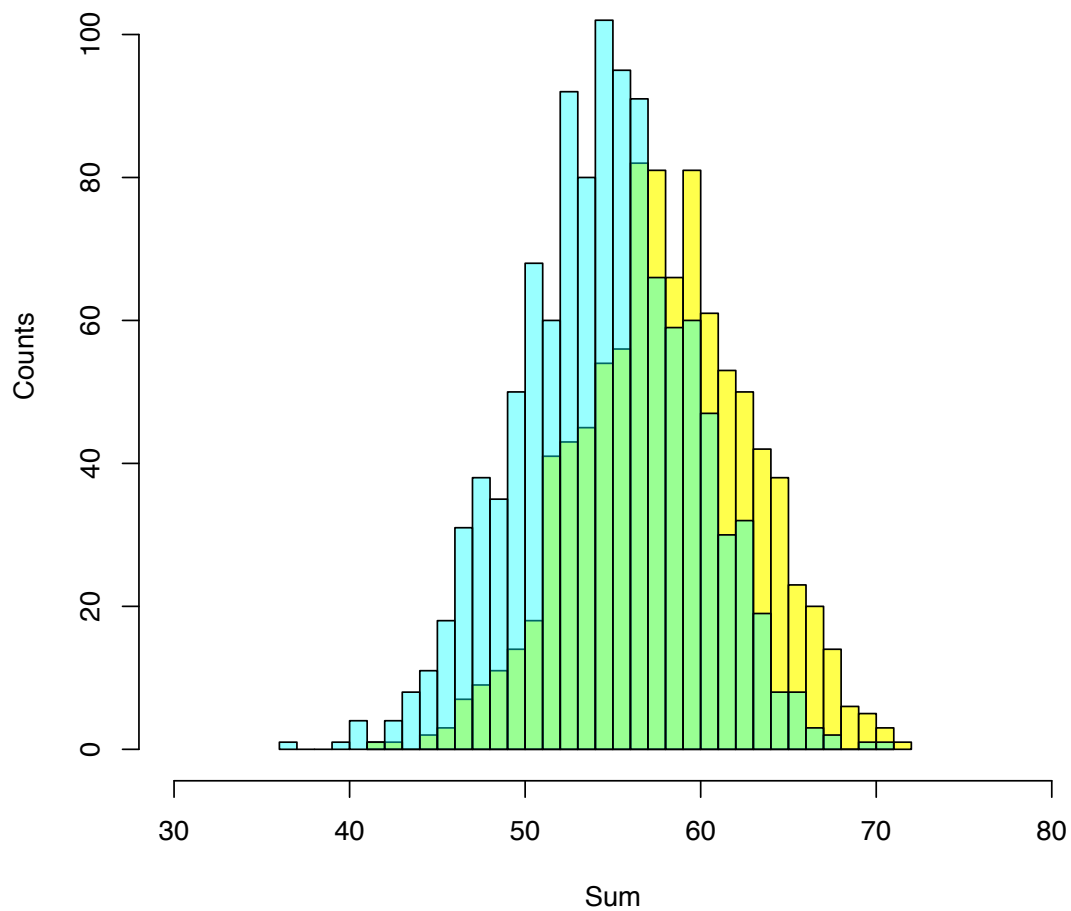
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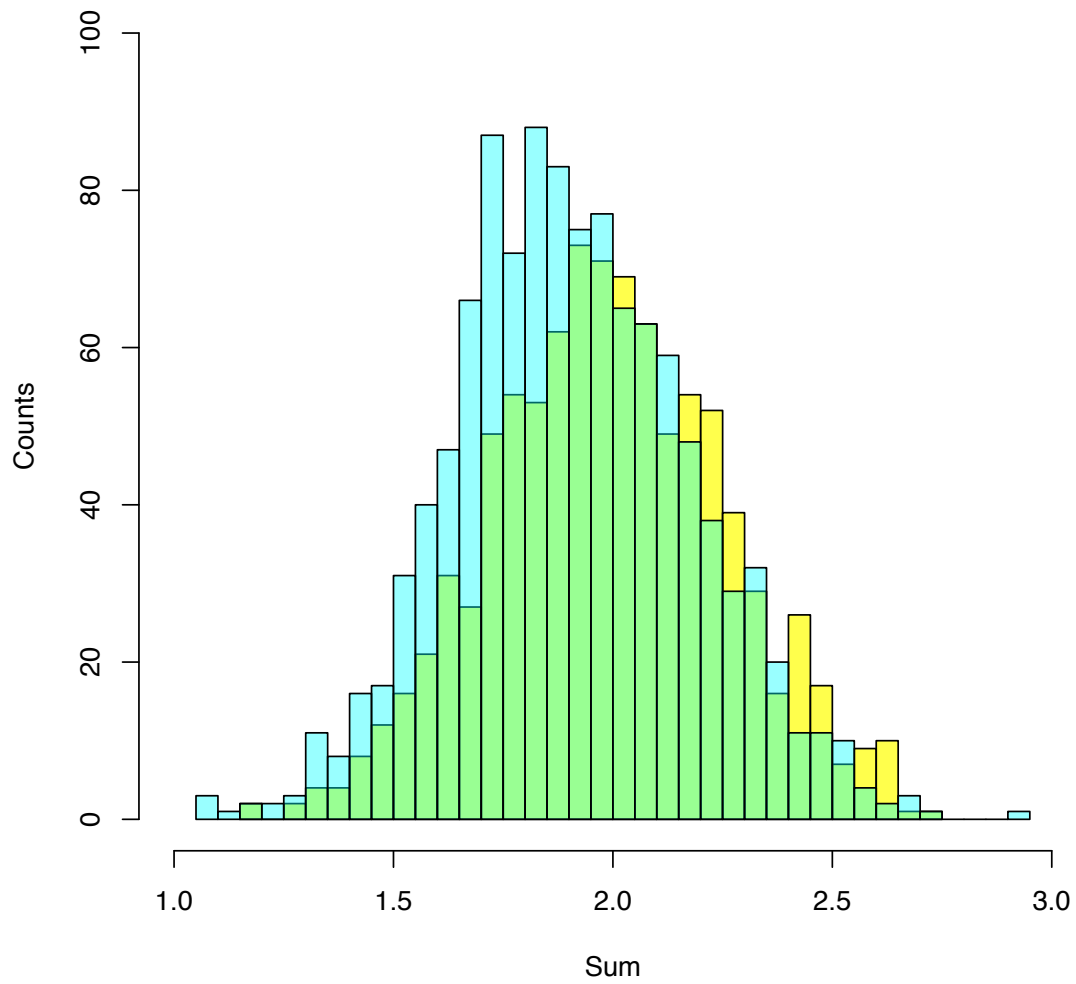
Supplementary Table 1: List of 40 established variants included in aggregate risk-allele testing.



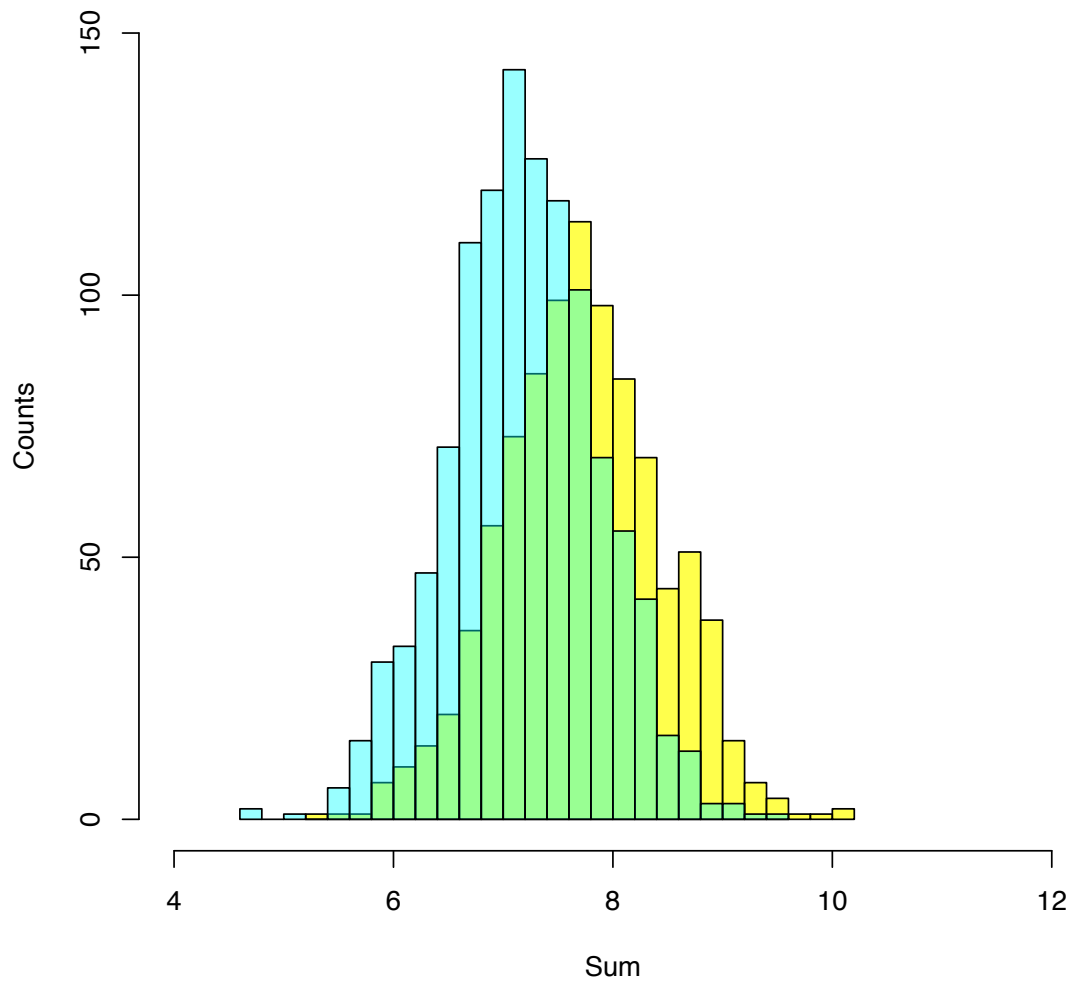
Supplementary Figure 1a. Histogram of *unweighted* total number of risk alleles for early-onset cases (n=931; yellow and green) and controls (n=1126; blue and green) for 23 new PCa variants identified in Eeles et al. (20). The green region represents the overlap of the distributions.



Supplementary Figure 1b. Histogram of *unweighted* total number of risk alleles for early-onset cases (n=931; yellow and green) and controls (n=1126; blue and green) for 63 combined new and established PCa variants in Eeles et al. (20). and Guo et al. (29). The green region represents the overlap of the distributions.



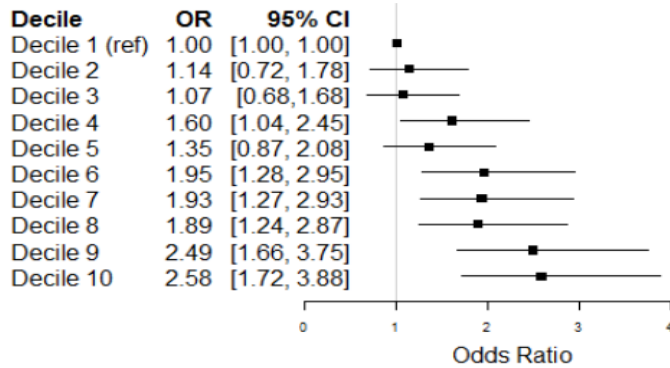
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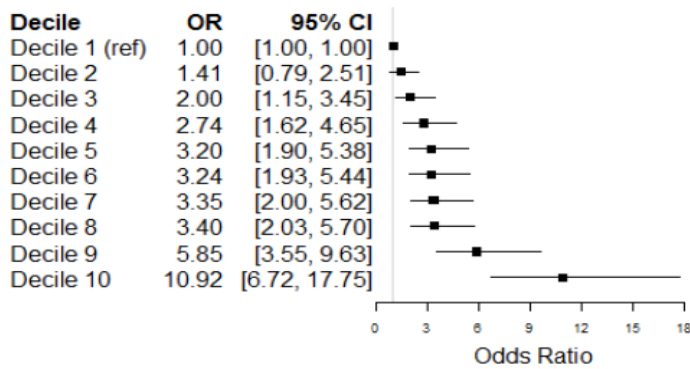
Supplementary Table 2b. Histogram of *weighted* (ln[OR], OR from Eeles et al. (20) and Guo et al. (29)) total number of risk alleles for early-onset cases (n=931; yellow and green) and controls (n=1126; blue and green) for 63 combined new and established PCa variants in Eeles et al. (20) and Guo et al. (29). The green region represents the overlap of the distributions.

Supplementary Figure 3. Association between decile categories (lowest decile group is reference category) for *unweighted* number of risk alleles carried and PCa. Decile-specific odds ratios were estimated based on the imputed dataset (931 cases and 1,126 controls) for (a) 23 newly reported PCa variants (b) 40 established PCa variants (c) 63 combined PCa variants.

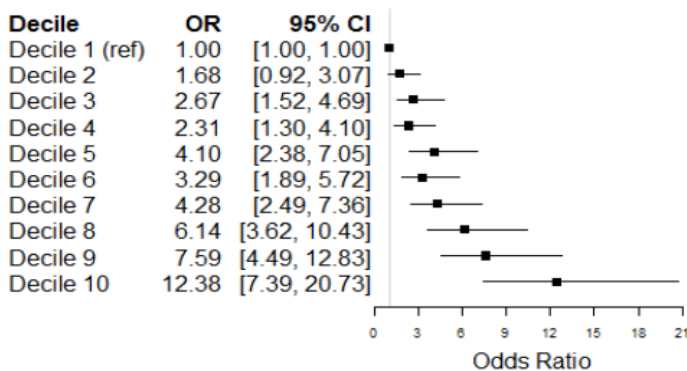
(a)



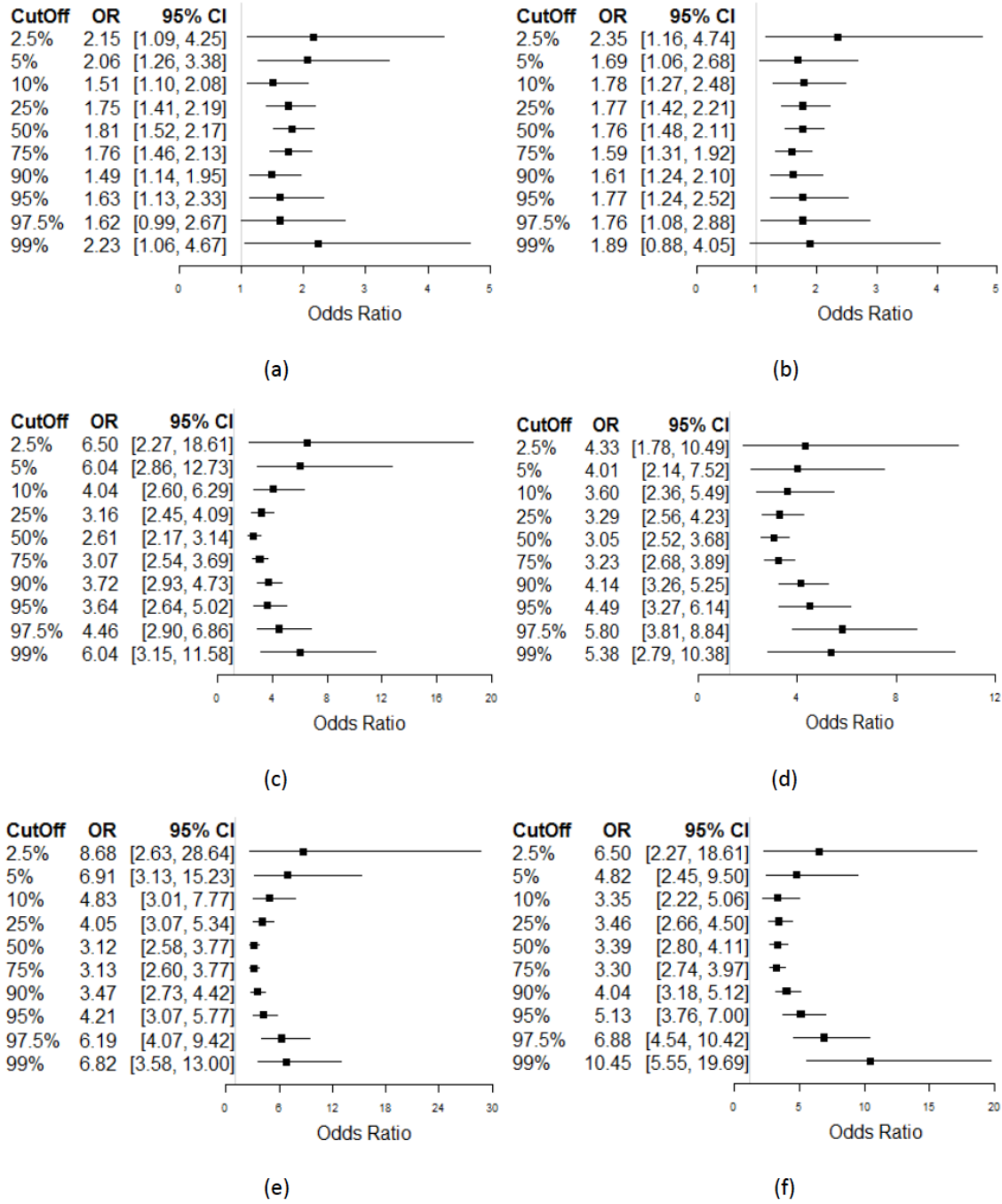
(b)



(c)



Supplementary Figure 4. Association results between percentile-cutpoint-defined dichotomous categories (lowest category group is reference category) for sum of risk alleles carried and PCa. Cutpoint-specific odds ratios were estimated based on the imputed dataset (931 cases and 1,126 controls) for (a) *unweighted* 23 newly reported PCa variants, (b) *weighted* 23 newly reported PCa variants, (c) *unweighted* 40 established PCa variants, (d) *weighted* 40 established PCa variants (e) *unweighted* 63 combined PCa variants, (f) *weighted* 63 combined PCa variants.



Supplementary Table 1. List of 40 established variants included in aggregate risk-allele testing. Individual association results for these variants with early-onset PCa can be found in Lange et al. (21)

Locus	Variant (Rare/Common [#])	Imputation Quality (R ²)
2p11	rs10187424 (G/A)	1.00
2p15	rs721048 (A/G)	1.00
2p21	rs1465618 (A/G)	0.94
2q31	rs12621278 (G/A)	1.00
2q37	rs2292884 (G/A)	1.00
3p12	rs2660753 (T/C)	0.99
3q21	rs10934853 (A/C)	1.00
3q23	rs6763931 (T/C)	1.00
3q26	rs10936632 (C/A)	0.75
4q22	rs17021918 (T/C)	0.99
4q22	rs12500426 (A/C)	0.99
4q24	rs7679673 (A/C)	0.98
5p12	rs2121875 (G/T)	1.00
5p15	rs2242652 (A/G)	0.49
6p21	rs130067 (G/T)	1.00
6q25	rs9364554 (T/C)	1.00
7p15	rs10486567 (A/G)	1.00
7q21	rs6465657 (C/T)	1.00
8p21	rs2928679 (T/C)	1.00
8p21	rs1512268 (A/G)	1.00
8q24	rs1447295 (A/C)	1.00
8q24	rs6983267 (G/T)	1.00
8q24	rs16901979 (A/C)	1.00
8q24	rs10086908 (T/C)	1.00
8q24	rs12543663 (C/A)	1.00
8q24	rs620861 (A/G)	0.97
9q33	rs1571801 (T/G)	0.99
10q11	rs10993994 (T/C)	0.99
10q26	rs4962416 (C/T)	1.00
11p15	rs7127900 (A/G)	1.00
11q13	rs7931342 (T/G)	1.00
12q13	rs10875943 (C/T)	1.00
12q13	rs902774 (A/G)	1.00
17q12	rs4430796 (A/G)	0.75
17q12	rs11649743 (A/G)	1.00
17q24	rs1859962 (G/T)	1.00
19q13	rs2735839 (A/G)	1.00
22q13	rs5759167 (T/G)	1.00
Xp11	rs5945619 (G/A)	0.72
Xq12	rs5919432 (G/A)	1.00