Supplementary Materials

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Supplementary Methods and Results

Power Calculation:

We used Quanto (Version 1.2.4) to assess the statistical power based on the genome wide significance level ($p < 5x10^{-8}$) and the characteristic of our dataset. Assuming the population mean and SD of %ΔCr are 22.5 and 35.9, respectively as our discovery dataset, with a total sample size of 873, we will have 80% power to detect 4.4% of %ΔCr variation (R_G^2) explained by a genetic variant with MAF of 0.03 (e.g. rs13317787) or 0.09 (e.g. rs10262995). When sample size reached 1253 as our total sample size, we will have 80% power to detect the proportion of %ΔCr variation as small as 3.1% explained by a genetic variant with MAF of 0.03 or 0.09 as our top SNPs. The range of R_G^2 presented in this power calculation is similar to what we have observed in the comparison of clinical and clinical-genomic models.

BBS9 Gene - Structure and Known Functional Variation

Bardet-Biedl syndrome 9 (*BBS9*) gene is located on chromosome 7p17 (33,168,856-33,645,680). It has 16 splice variants, with the longest transcript spanning 22 coding exons. Of a total of 16 variants within the BBS9 gene predicted to have functional consequences, 10 have been directly associated with Bardet-Biedl syndrome[1, 2] . None are represented on genotyping arrays nor are part of either 1000Genomes or HapMap datasets, thus precluding assessment of LD with the *BBS9* variants identified in this study. However, rs10262995 is part of a 6 kb LD block located immediately upstream (5') to a recombination hotspot in intron 20 (Figure S2). It should be noted that other BBS9 variants were also identified using GWAS study design for cardiovascular and metabolic phenotypes in ambulatory populations (blood pressure, metabolic syndrome and cytokine responses)[3-5], which may be of potential relevance to the development of AKI in cardiac surgical patients.

Figure S1: Genome wide association results for acute kidney injury from the discovery dataset (PEGASUS) are depicted by Manhattan (1A) and quantile-quantile (QQ) plots (1B).

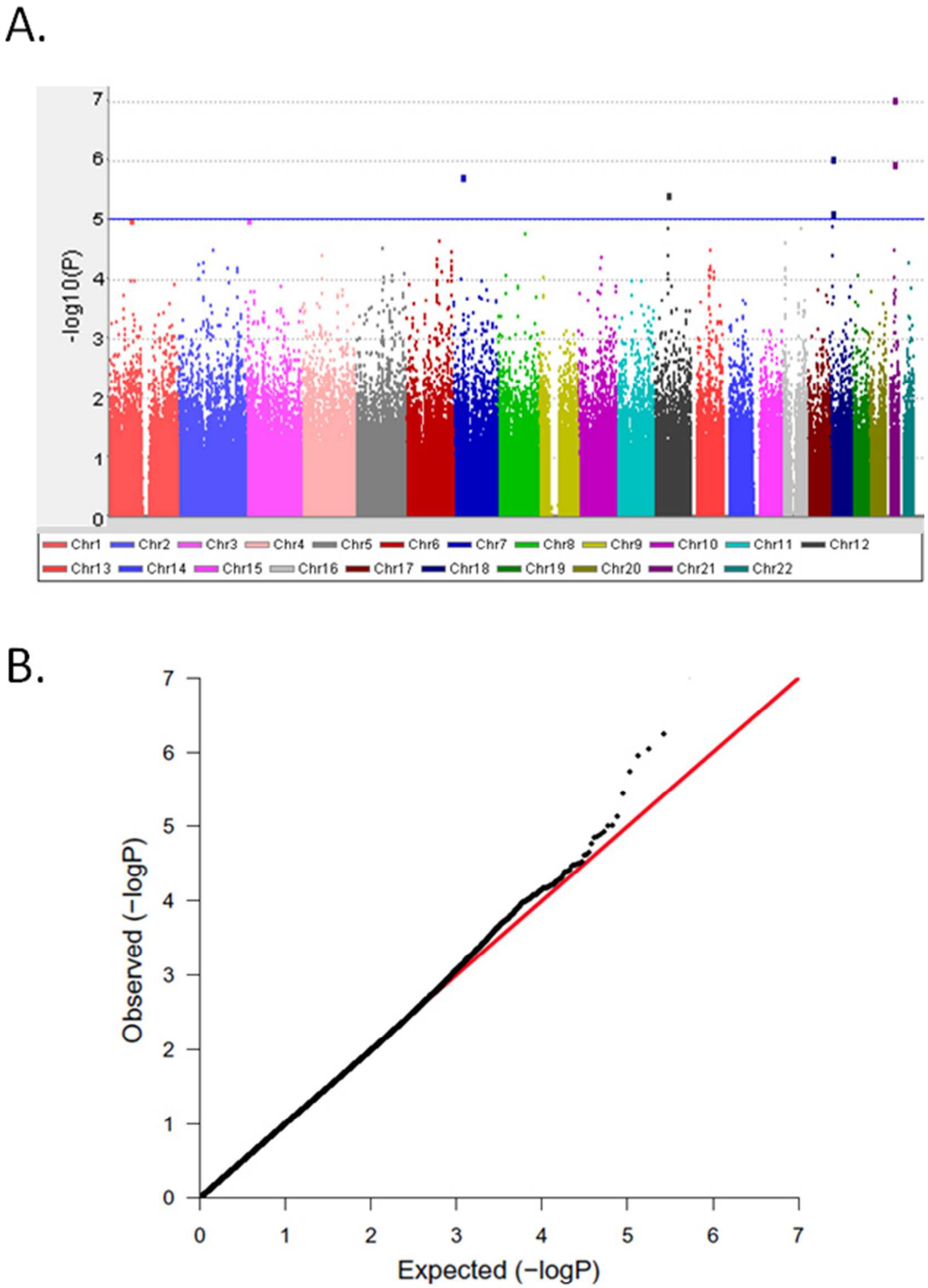


Figure S2: Haplotype block structure of the *BBS9* gene using the HapMap CEU analysis panel. Increasing correlation (r2) between SNPs is reflected in increasing darker shading within each intersecting square. Correlations and block structure were estimated using HaploView 4.2. A 6kb LD block containing rs10262995 is located immediately 5’ from a recombination hotspot.

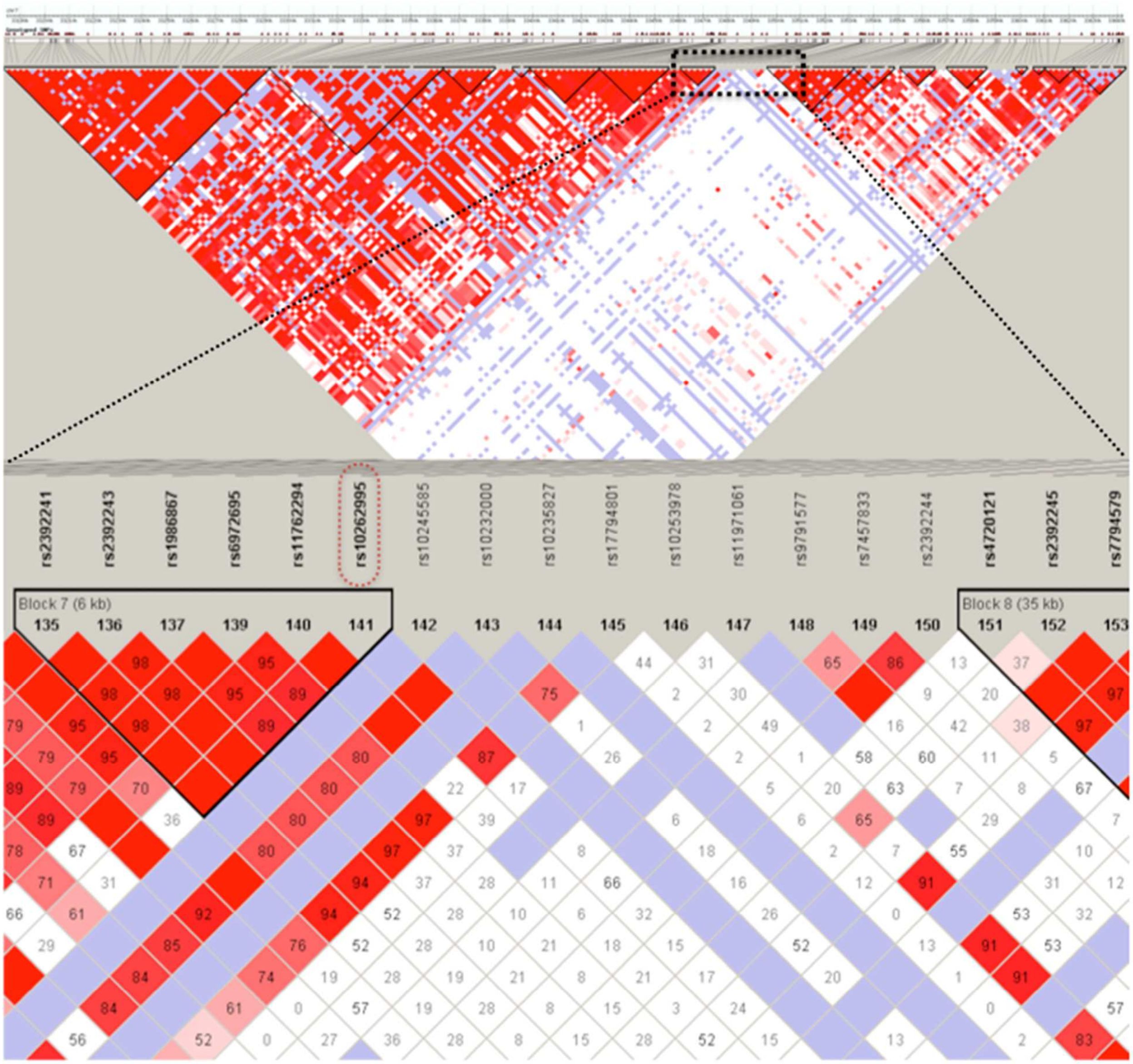


Figure S3: Genotype clusters obtained from Illumina GenomeStudio for rs13317787 in GRM7-LMCD1-AS1 intergenic region from two batches of genotype data (787 and 159 samples) for PEGASUS.

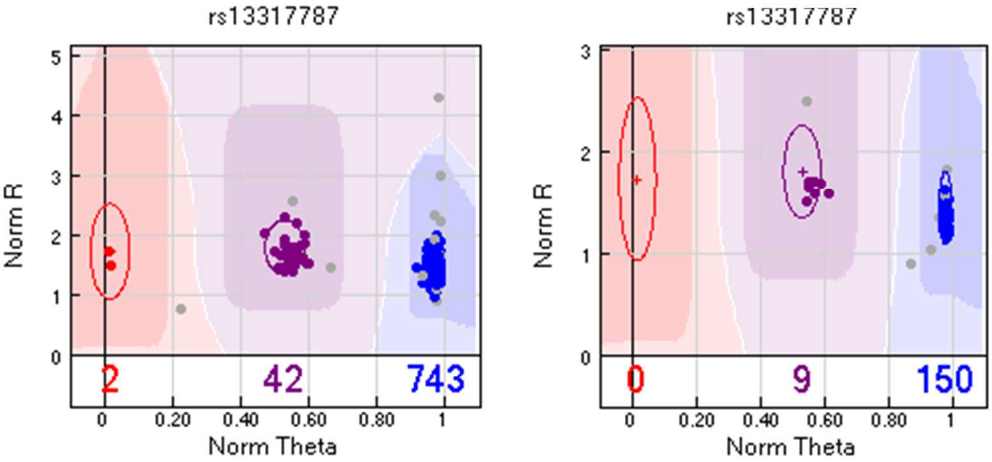


Table S1: Top-scoring directly genotyped and imputed SNPs in the *GRM7|LMCD1-AS1* Intergenic Region and in *BBS9*.

				Discovery Cohort: PEGASUS				Replication Cohort: CATHGEN				Combined	
Chr	SNP	Base Pair	Minor Allele	MAF	Beta	SE	p value	MAF	Beta	SE	p value	Meta-p	r^{2a}
GRM7|LMCD1-AS1intergenic region													
3	rs511731	8099146	A	0.02	26.84	5.10	1.81×10^{-7}	0.03	14.87	7.34	0.043	4.28×10^{-8}	0.74
3	rs11131106	8099368	C	0.02	26.84	5.10	1.81×10^{-7}	0.03	14.87	7.34	0.043	4.28×10^{-8}	0.74
3	rs4566523	8099591	A	0.02	26.84	5.10	1.81×10^{-7}	0.03	14.87	7.34	0.043	4.28×10^{-8}	0.74
3	rs76087876	8100556	A	0.02	26.84	5.10	1.81×10^{-7}	0.03	14.87	7.34	0.043	4.28×10^{-8}	0.74
3	rs78993528	8100558	G	0.02	26.84	5.10	1.81×10^{-7}	0.03	14.87	7.34	0.043	4.28×10^{-8}	0.74
3	rs522639	8108291	G	0.02	26.72	5.16	2.85×10^{-7}	0.03	15.41	7.28	0.035	5.06×10^{-8}	0.74
3	rs484787	8109679	A	0.02	26.88	5.10	1.73×10^{-7}	0.03	14.87	7.34	0.043	4.13×10^{-8}	0.74
3	rs4277672	8113945	C	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	3-8115655	8115655	C	0.03	21.70	4.57	2.4×10^{-6}	0.04	10.50	6.89	0.128	1.58×10^{-6}	0.62
3	3-8115878	8115878	T	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	3-8116001	8116001	A	0.03	22.17	4.63	1.94×10^{-6}	0.04	10.64	6.83	0.120	1.28×10^{-6}	0.61
3	rs115325749	8117103	G	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	rs116377711	8118197	T	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	3-8118455	8118455	T	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	3-8119772	8119772	G	0.01	33.70	6.18	6.41×10^{-8} $(4.07\times10^{-5})^{b}$	0.01	45.34	11.49	9.55×10^{-5} $(1.7\times10^{-3})^{b}$	2.49×10^{-11}	Ref
3	rs80134927	8120165	A	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	rs115902483	8120607	A	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	rs78603199	8120821	A	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	rs4387953	8120958	C	0.03	21.72	4.57	2.32×10^{-6}	0.04	10.50	6.89	0.128	1.54×10^{-6}	0.62
3	rs9820883	8122644	G	0.03	21.70	4.57	2.45×10^{-6}	0.04	10.50	6.89	0.128	1.61×10^{-6}	0.62
3	rs6797446	8125433	A	0.03	21.70	4.57	2.45×10^{-6}	0.04	10.50	6.89	0.128	1.61×10^{-6}	0.62
3	rs1607021	8129194	G	0.03	20.79	4.54	5.31×10^{-6}	0.04	10.48	6.88	0.128	3.08×10^{-6}	0.60
3	rs77820906	8130190	T	0.03	22.18	4.51	1.02×10^{-6}	0.04	9.06	7.02	0.197	1.3×10^{-6}	0.57
3	rs536793	8132902	G	0.02	24.55	5.14	2.06×10^{-6}	0.01	37.05	11.02	8.6×10^{-4}	8.74×10^{-9}	0.77
3	rs493271	8134937	A	0.02	24.57	5.13	2.0×10^{-6}	0.02	31.94	10.59	0.003	1.88×10^{-8}	0.77
3	rs9848276	8135200	T	0.02	23.43	5.09	4.74×10^{-6}	0.02	31.90	10.62	0.003	5.04×10^{-8}	0.77
3	rs576239	8135597	A	0.02	24.41	5.08	1.81×10^{-6}	0.02	31.94	10.59	0.003	1.71×10^{-8}	0.77
3	rs574408	8135797	T	0.02	24.38	5.08	1.82×10^{-6}	0.02	31.94	10.59	0.003	1.75×10^{-8}	0.77
3	rs548604	8136314	A	0.03	24.38	5.08	1.82×10^{-6}	0.02	31.94	10.59	0.003	1.75×10^{-8}	0.77
3	rs541878	8136712	T	0.03	24.38	5.08	1.82×10^{-6}	0.02	31.94	10.59	0.003	1.75×10^{-8}	0.77
3	rs79084800	8137685	A	0.03	24.38	5.08	1.82×10^{-6}	0.02	26.47	10.23	0.010	4.94×10^{-8}	0.77

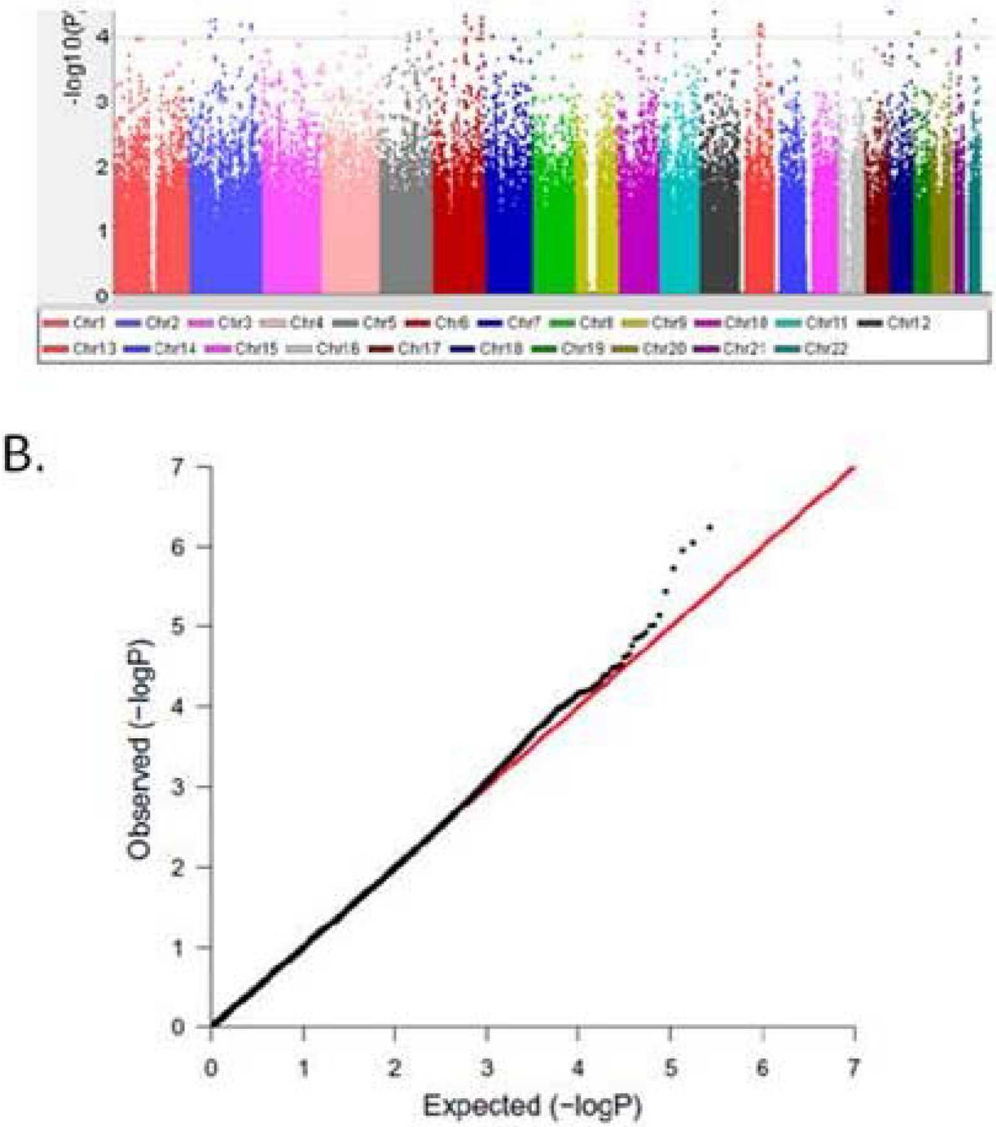
3	rs1516371	8140289	C	0.03	23.24	5.03	4.47×10^{-6}	0.02	26.45	10.24	0.010	1.26×10^{-7}	0.77
3	rs75266354	8141109	C	0.03	24.36	5.07	1.85×10^{-6}	0.02	26.48	10.21	0.010	4.92×10^{-8}	0.77
3	rs10470631	8141586	A	0.03	23.24	5.03	4.47×10^{-6}	0.02	26.45	10.24	0.010	1.26×10^{-7}	0.77
3	rs13317787[c]	8141952	A	0.03	21.56	4.84	9.67×10^{-6}	0.02	22.04	9.56	0.022	5.35×10^{-7}	0.72
3	3-8143673	8143673	T	0.03	23.67	5.03	2.92×10^{-6}	0.02	26.48	10.21	0.010	7.88×10^{-8}	0.75
3	rs73135229	8143742	G	0.03	23.56	5.04	3.45×10^{-6}	0.02	26.66	10.22	0.009	9.06×10^{-8}	0.75
3	rs9880757	8144012	A	0.03	22.00	4.90	7.94×10^{-6}	0.02	26.45	10.24	0.010	2.37×10^{-7}	0.74
3	rs9844587	8144234	A	0.03	21.73	4.85	8.45×10^{-6}	0.02	26.45	10.24	0.010	2.55×10^{-7}	0.72
3	rs11925840	8144902	T	0.03	21.62	4.85	9.51×10^{-6}	0.02	26.45	10.24	0.010	2.87×10^{-7}	0.70
3	rs2171523	8148053	A	0.03	21.15	4.73	8.71×10^{-6}	0.02	24.81	9.85	0.012	3.01×10^{-7}	0.65
3	rs577364	8149000	A	0.03	20.93	4.69	9.3×10^{-6}	0.02	22.38	9.55	0.020	4.77×10^{-7}	0.64
3	rs1488349	8153260	T	0.02	29.71	6.17	1.76×10^{-6} (1.1×10^{-4})[b]	0.01	50.66	12.02	3.14×10^{-5} (8.1×10^{-4})[b]	5.41×10^{-10}	0.97
3	rs1825891	8161987	T	0.02	27.96	5.70	1.12×10^{-6}	0.02	26.58	9.96	0.008	2.38×10^{-8}	0.72
3	rs320069	8199895	G	0.03	20.82	4.57	5.99×10^{-6}	0.03	11.63	8.37	0.166	3.09×10^{-6}	0.41
BBS9 gene													
7	rs28619003	33548225	T	0.08	15.58	3.05	3.92×10^{-7}	0.10	9.42	4.53	0.038	6.51×10^{-8}	Ref
7	rs10262995[c]	33550041	A	0.09	14.33	2.98	1.83×10^{-6}	0.10	9.51	4.47	0.034	2.24×10^{-7}	1.00

Abbreviations: SNP - single nucleotide polymorphism; Chr – chromosome; MAF – minor allele frequency; Beta – regression coefficient SE – standard error; PEGASUS, CATHGEN – see text.

[a] r^2 was compared for each SNP relative to the "Ref" (best performing) SNP.

[b] p-values in parenthesis are from permutation with 10^6 repeats.

[c] Genotyped SNPs initially identified in GWAS and replication dataset are in red font.



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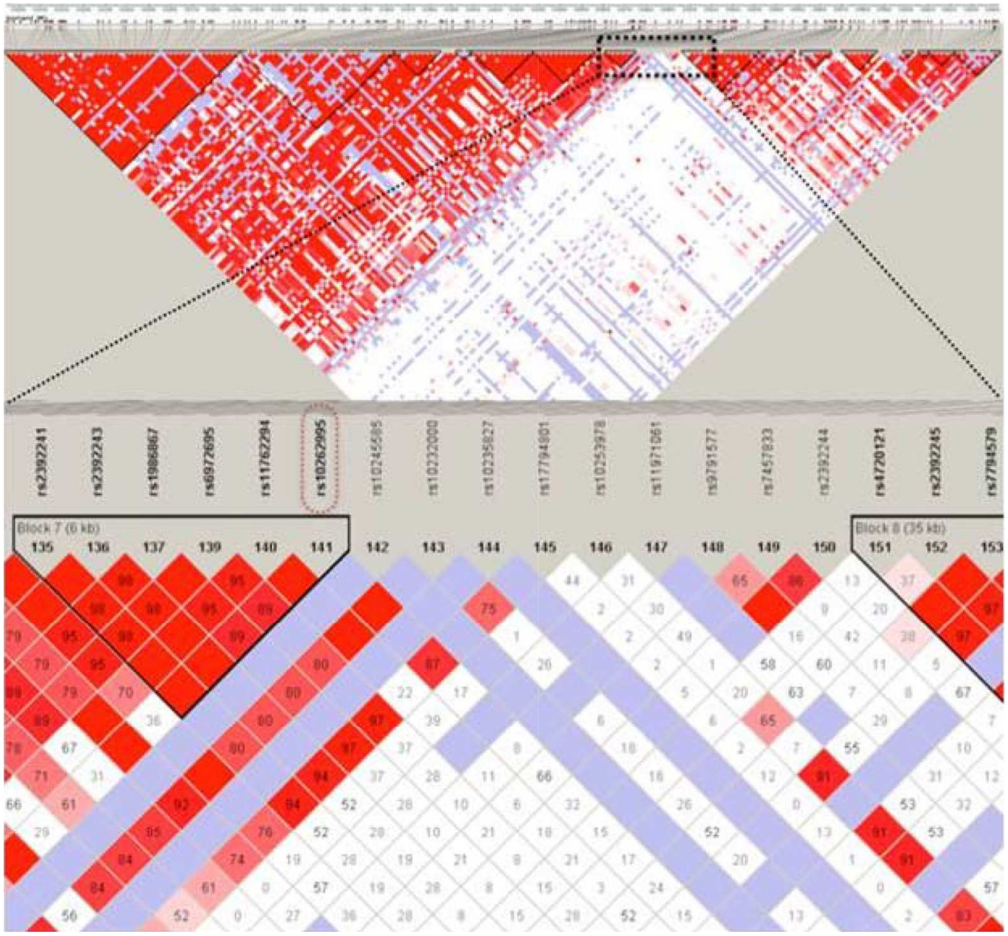

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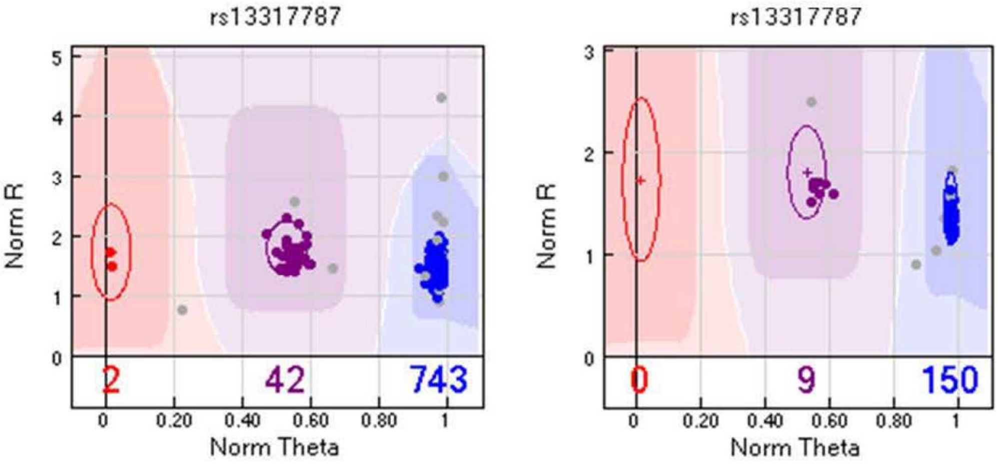

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