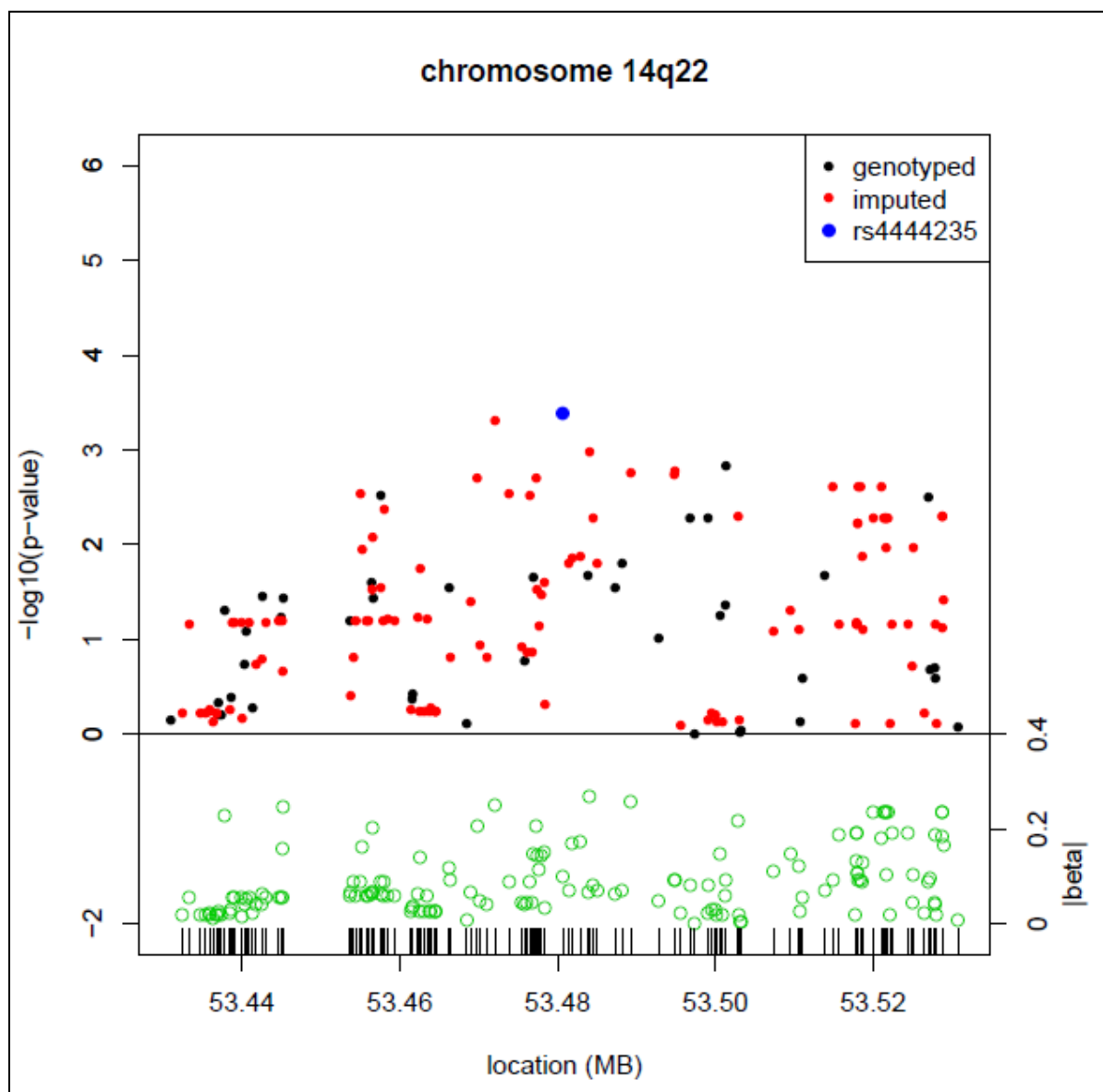


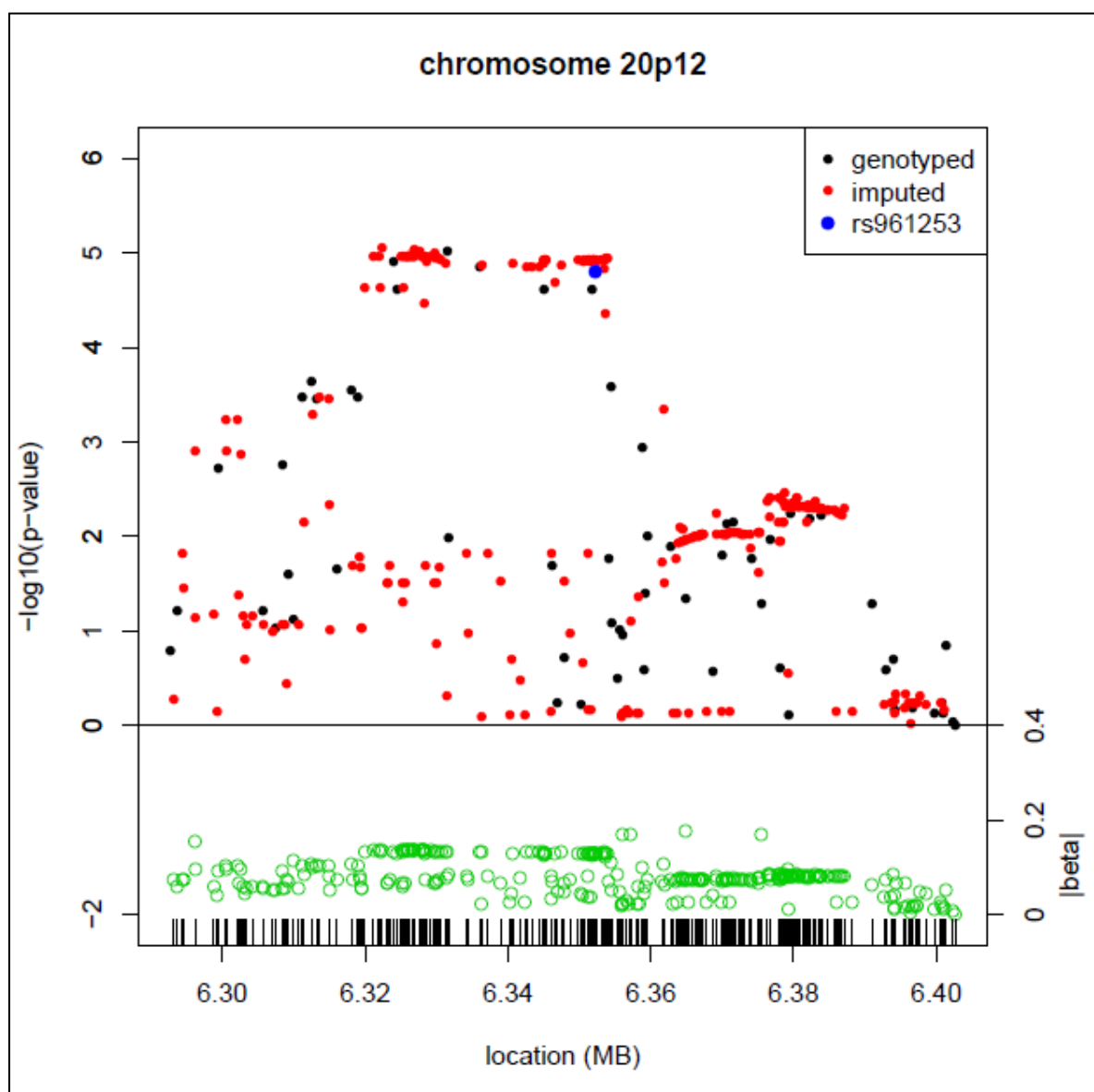
Supplemental Figure 1. Fine mapping around the known CRC risk SNPs close to (a) *BMP4* (14q22) and (b) *BMP2* (20p12).

Results for meta-analysis of UK2 and Scotland2 are shown. Both significance of association ( $-\log_{10}(P)$ ) and effect size ( $\beta$ ) are presented. The original CRC-associated tagSNPs are shown in blue. Near *BMP4*, the strongest signal is at the original tagSNP, rs4444235. rs961253, the original tagSNP near *BMP2*, lies in a region of about 40kb in which SNPs are in strong LD and thus show very similar signals of association.

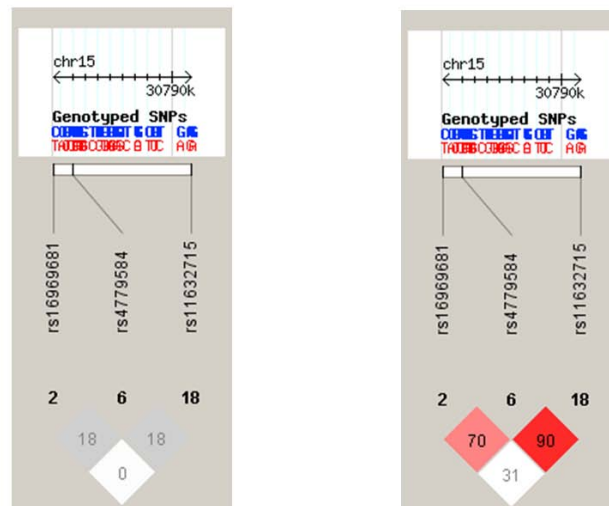
(a)



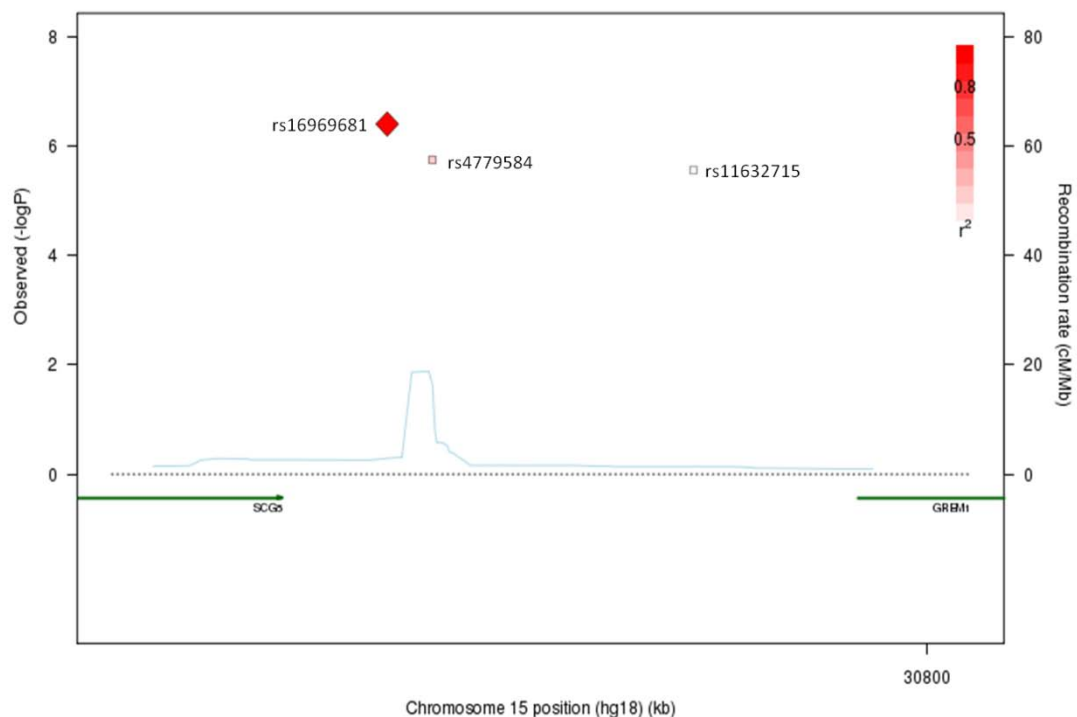
(b)



Supplemental Figure 2. Pairwise linkage disequilibrium between rs4779584, rs16969681 and rs11632715 near GREM1 (upper) and position of recombination hotspot (lower).  $r^2$  is shown left and  $D'$ , right. Data are from HapMap 2 CEU. Standard Haploview colour schemes are used (<http://www.haploview.org/>).



The plot from SNAP shows location of recombination hotspot (peak of blue line, right-hand Y-axis) between rs16969681 and rs11632715. Left-hand Y-axis shows single-SNP association  $-\log_{10}(P)$  from logistic regression analysis based on samples genotyped for all 3 SNPs. X-axis shows physical distance.



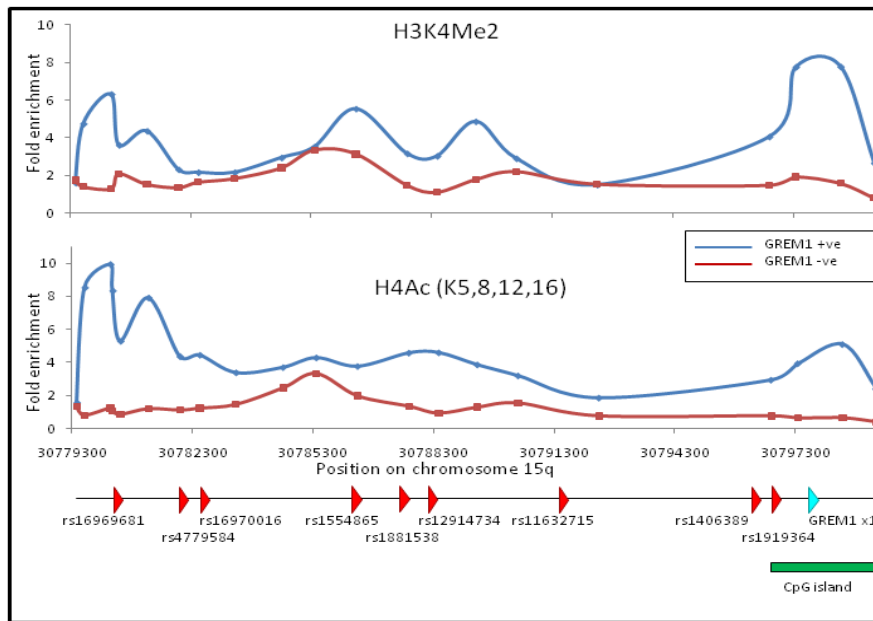
*Supplemental Figure 3. Histone methylation and acetylation marks upstream of GREM1.*

To search for possible regulatory elements tagged by SNPs in the 15q13.3 region, we carried out chromatin immunoprecipitation (ChIP) experiments to look for histone modifications between chr15:30,779,300 and the transcriptional start site of *GREM1*. Histone H4 acetylation; and histone H3 methylation at lysine 4 mark active chromatin and intergenic regions showing enrichment for such modifications may contain enhancer elements. We selected three CRC cell lines that express *GREM1* – LS180, C99 and HCC56 – and a control non-expressing cell line, SW48 and carried out ChIP on native chromatin using PCR assays spaced at ~1kb intervals.

ChIP experiments were carried out as previously described (9). Briefly,  $\sim 5 \times 10^7$  cells were collected from four colorectal cancer cell lines (LS180, C99, HCC56 and SW48) and washed in PBS. Nuclei were purified through a sucrose cushion and incubated with MNase to obtain fragments of one to five nucleosomes in length. Approximately 20  $\mu\text{g}$  of native chromatin was incubated with 5-10  $\mu\text{g}$  of antibody overnight at 4°C. The following antibodies were used: H3AcK1, 5, 9 and K14 (06-866) and H3K4me2 (07-030; Millipore). The antibody chromatin complexes were captured with Protein A magnetic beads (Invitrogen). After washing and elution DNA was extracted from the input chromatin, and bound fractions. Q-PCR analysis was carried out using Fast SYBR Green Master Mix using a 7900HT Fast Real-time PCR system (Applied Biosystems). Results were normalized to the Rhodopsin gene (a non-expressed control) and the relative enrichment of the bound fraction compared to the input was calculated using the  $\Delta\Delta\text{Ct}$  method. Primer and probe sequences are available on request.

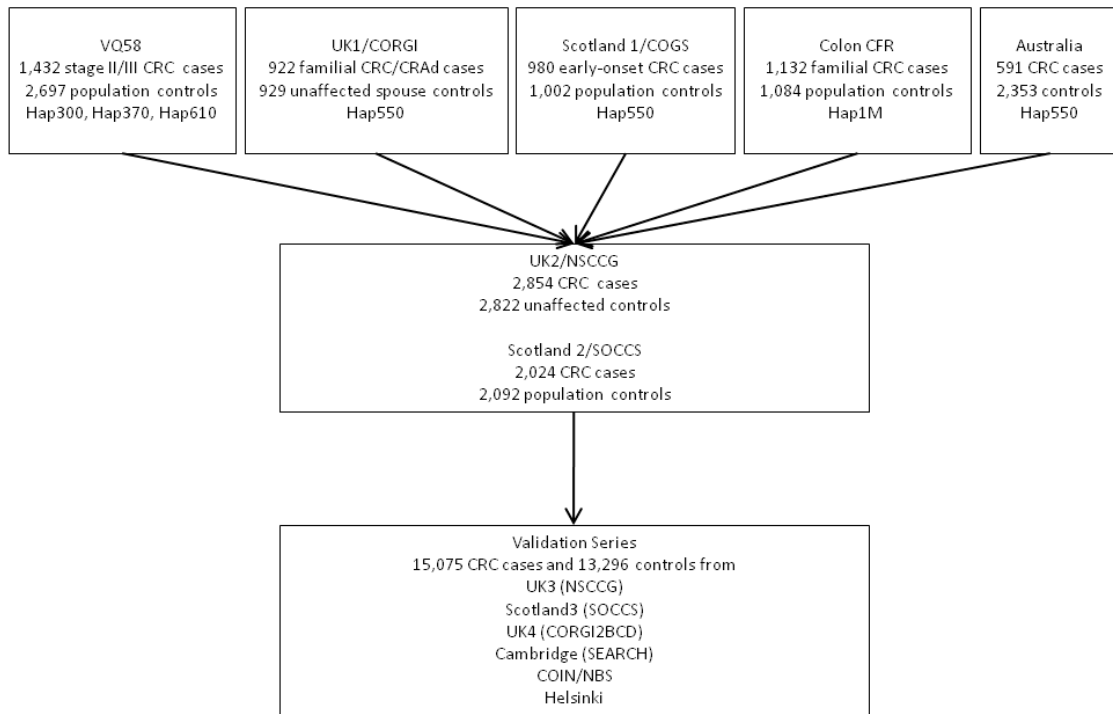
Plots show the enrichment of antibody bound chromatin relative to input chromatin plotted against the chromosome 15 co-ordinates for the average of the three *GREM1* expressing lines compared with the non-expressing line. The positions of selected SNPs are shown. Peaks were found, as expected, at the *GREM1* transcriptional start site, but there was a double peak of both acetylation and lysine 4 methylation centred on the region containing rs16969681. This peak was not seen in the control line. rs16969681 is therefore an excellent candidate functional SNP at the *GREM1* locus. The importance of the double-peak centred on rs1881538 is unclear given that it may also be present in the control. We tested rs1881538 in unconditional logistic regression analysis with rs16969681 and rs4779584 to determine whether it might be an association signal tagged by rs4779584 and independent of rs16969681. However, rs4779584 consistently captured more of the variation in disease risk than rs1881538 whether or not rs16969681 was included in the regression

model. rs11632715 was not associated with transcription control elements, whether from the ENCODE project or from our own data. It was, however, in LD with several SNPs in potential functionally important regions, including strong association with rs1919364 at the start of the *GREM1* promoter CpG island.

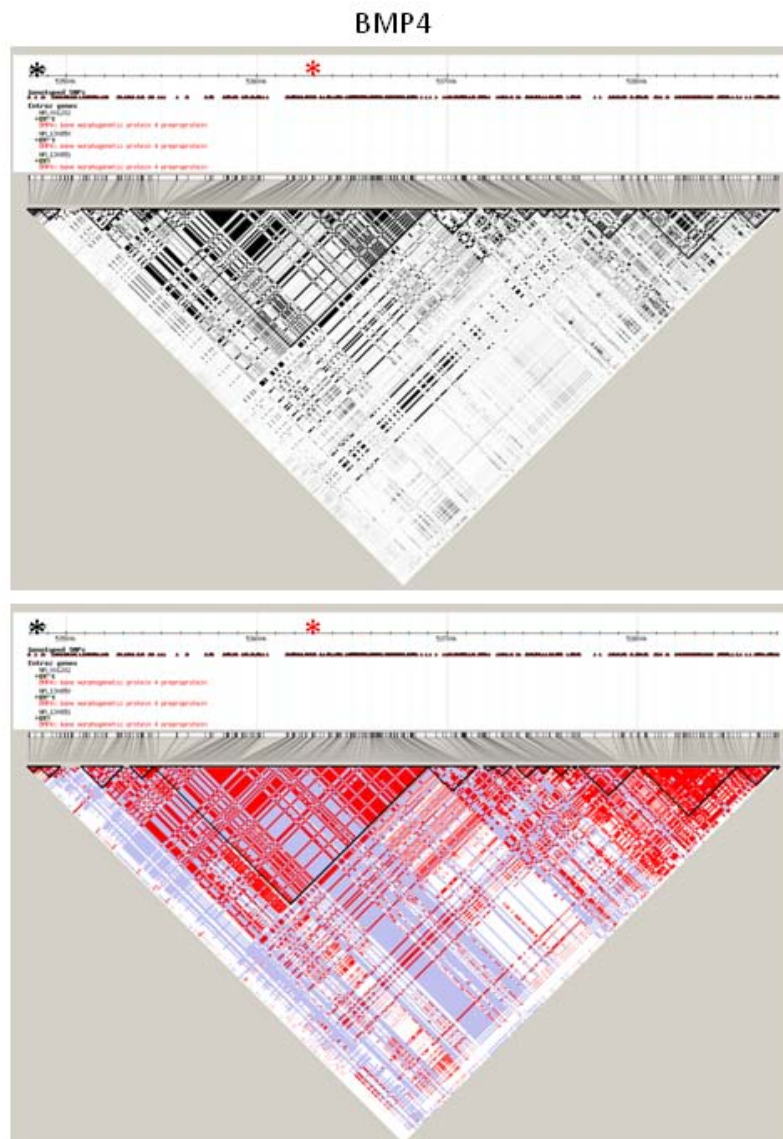


*Supplemental Figure 4. Study design for discovery and validation phases.*

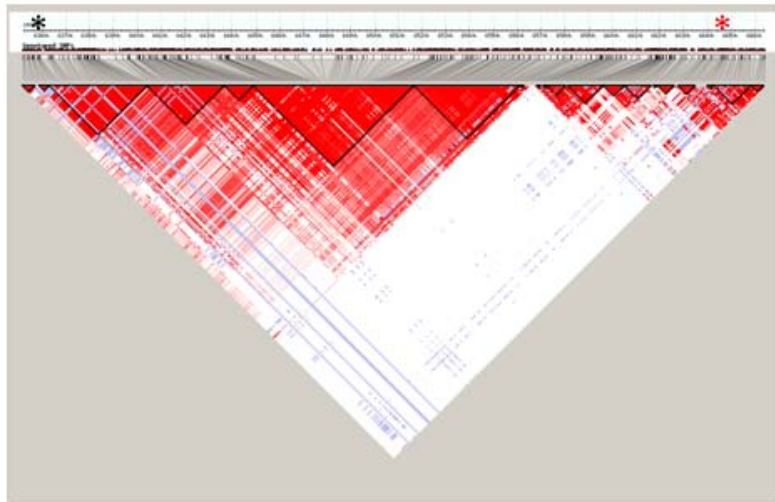
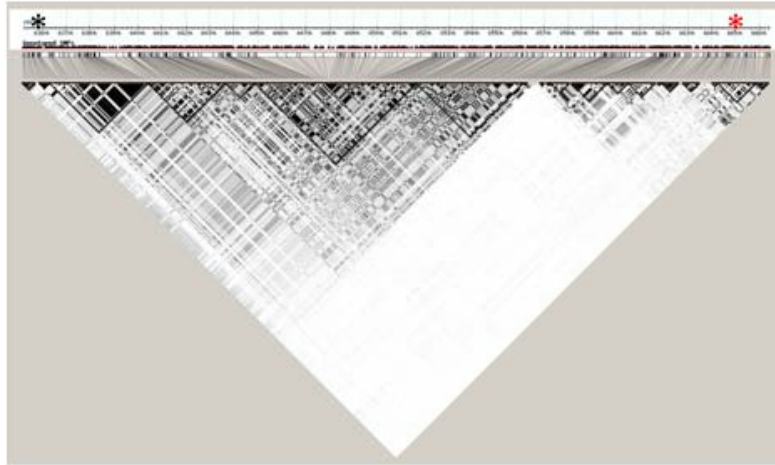
The proprietary Illumina arrays used for the 5 GWA studies are shown.



Supplemental Figure 5. Large-scale LD structure in regions around BMP4 and BMP2. For each of BMP2 and BMP4, the upper panel shows  $r^2$  and the middle panel,  $D'$  (from SNAPData are from HapMap2 CEU samples in Haploview). In all cases, X-axes show physical distance. The original tagSNP is shown by a black star and the new signal by a red star.



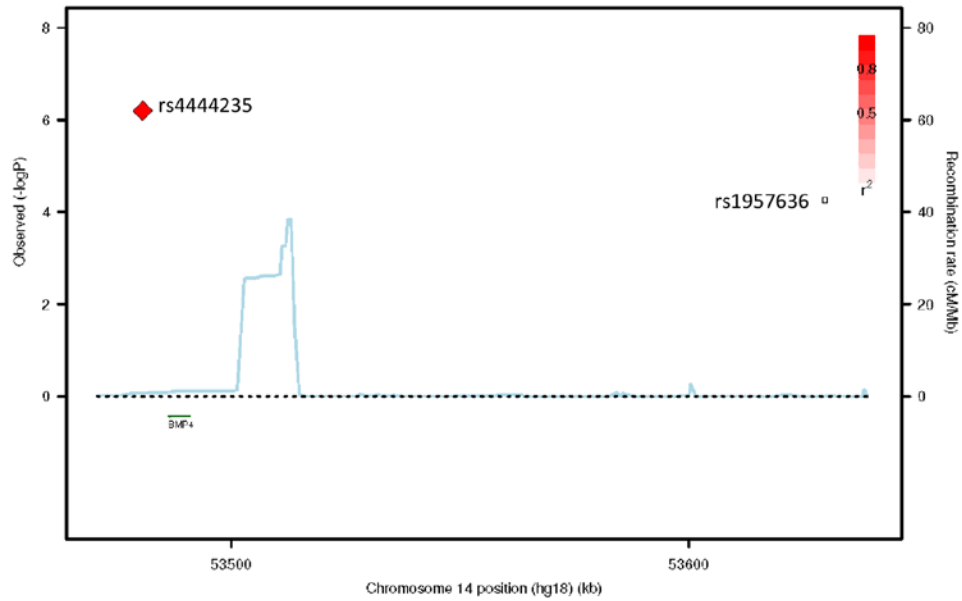
## BMP2



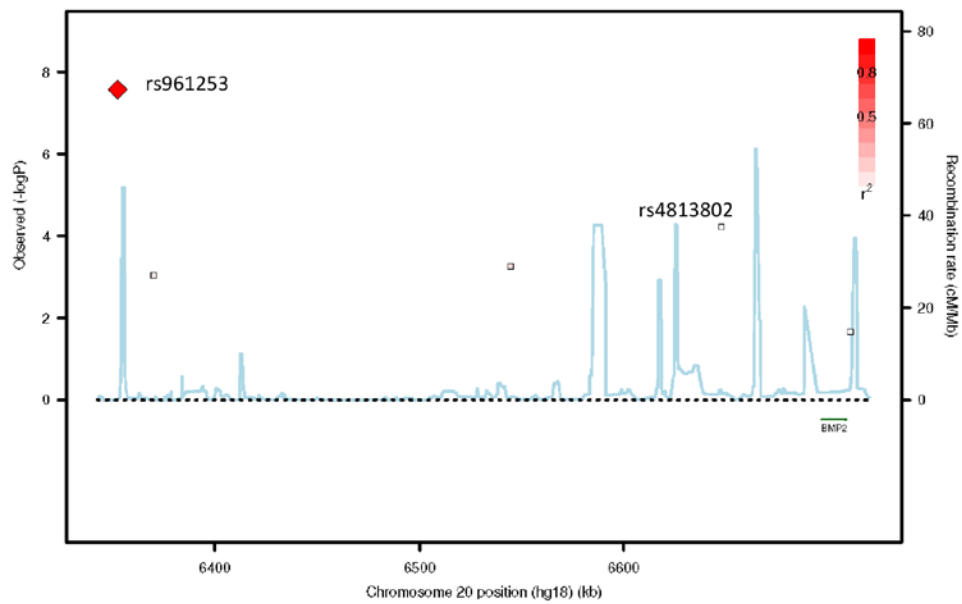


Supplemental Figure 6. Locations of recombination hotspots in regions around *BMP4* and *BMP2*. The plots, from SNAP, show location of recombination hotspots (peaks of blue line, right-hand Y-axis) for the regions between the original tag SNPs near *BMP4* (rs4444235) and *BMP2* (rs961253) and the new signals (rs1957636 and rs4813802 respectively). X-axes show physical distance. Note the presence of hotspots between the locations of the pairs of SNPs.

### BMP4 region



### BMP2 region



*Supplemental Table 1. SNPs genotyped directly or predicted by imputation in the fine mapping of the regions around rs4779584, rs4444235 and rs961253 in UK2 and Scotland2.*

We undertook fine mapping of the genomic regions containing CRC-associated tag SNPs close to *GREM1* (15q13.3), *BMP4* (14q22.2) and *BMP2* (20p12.3). We identified all SNPs in the haplotype blocks and immediately flanking regions for rs4779584, rs4444235 and rs961253 from dbSNP (see Methods) and selected those with minor allele frequency >5%. After excluding SNPs that failed genotyping assay design or that fell below standard quality control (QC) thresholds, a total of 74, 113 and 255 SNPs in each region were successfully genotyped in the CRC cases and controls from the UK2 and Scotland2 sample sets. We then used 1000 Genomes and HapMap 3 reference genotypes to impute untyped SNPs mapping to these regions (1).

<b>Region</b>	<b>Location</b>	<b>SNP ID</b>	<b>Imputed or Genotyped</b>
15q13.3	30,733,560	rs12903437	Genotyped
15q13.3	30,734,914	rs11638385	Genotyped
15q13.3	30,734,931	rs11638089	Genotyped
15q13.3	30,735,171	rs7171657	Genotyped
15q13.3	30,735,386	rs12593101	Genotyped
15q13.3	30,737,358	rs55683307	Imputed
15q13.3	30,739,485	rs8023613	Genotyped
15q13.3	30,740,356	rs4238560	Genotyped
15q13.3	30,742,387	rs11071887	Genotyped
15q13.3	30,746,003	rs1406387	Genotyped
15q13.3	30,747,917	rs10083612	Genotyped
15q13.3	30,749,197	rs17228564	Genotyped
15q13.3	30,749,532	rs17228571	Imputed
15q13.3	30,749,742	rs11855680	Imputed
15q13.3	30,749,934	rs8041254	Genotyped
15q13.3	30,750,051	rs8037112	Imputed
15q13.3	30,750,497	rs16963973	Genotyped
15q13.3	30,751,048	rs16964074	Genotyped
15q13.3	30,752,649	rs12909871	Genotyped
15q13.3	30,752,922	rs11634086	Genotyped
15q13.3	30,753,521	rs11635362	Genotyped
15q13.3	30,755,075	rs62001857	Imputed
15q13.3	30,755,131	rs7161975	Genotyped
15q13.3	30,755,270	rs10775188	Genotyped
15q13.3	30,756,123	rs12148394	Genotyped
15q13.3	30,756,146	15-30756146	Imputed
15q13.3	30,756,215	rs7170561	Genotyped
15q13.3	30,756,749	rs10519737	Imputed
15q13.3	30,757,201	rs28688414	Imputed
15q13.3	30,757,349	rs7177176	Genotyped
15q13.3	30,757,435	rs6494576	Imputed
15q13.3	30,757,448	rs11633548	Genotyped
15q13.3	30,757,493	rs16965041	Imputed
15q13.3	30,757,554	rs6494577	Imputed
15q13.3	30,757,842	rs1881536	Genotyped
15q13.3	30,758,358	rs71462819	Imputed
15q13.3	30,758,440	rs11071897	Genotyped
15q13.3	30,758,464	rs34278216	Imputed
15q13.3	30,758,577	rs16965254	Imputed
15q13.3	30,758,627	rs35415313	Imputed
15q13.3	30,758,727	rs12102176	Imputed
15q13.3	30,759,050	rs3817592	Genotyped
15q13.3	30,759,226	rs7177843	Genotyped
15q13.3	30,759,546	15-30759546	Imputed

15q13.3 30,760,107	15-30760107	Imputed
15q13.3 30,760,231	rs12442397	Genotyped
15q13.3 30,760,289	rs12438604	Genotyped
15q13.3 30,760,617	15-30760617	Imputed
15q13.3 30,762,805	rs35703183	Imputed
15q13.3 30,762,980	rs12441136	Genotyped
15q13.3 30,763,009	rs12441140	Genotyped
15q13.3 30,763,347	rs17816224	Imputed
15q13.3 30,763,475	15-30763475	Imputed
15q13.3 30,764,393	rs7165737	Genotyped
15q13.3 30,764,688	15-30764688	Imputed
15q13.3 30,764,833	rs11634570	Imputed
15q13.3 30,765,042	rs56338436	Imputed
15q13.3 30,766,061	rs7403093	Imputed
15q13.3 30,766,905	rs16966853	Genotyped
15q13.3 30,767,015	rs11638903	Genotyped
15q13.3 30,767,310	rs8043234	Genotyped
15q13.3 30,768,135	rs28417809	Imputed
15q13.3 30,768,217	rs4780033	Imputed
15q13.3 30,768,377	rs8039575	Imputed
15q13.3 30,768,468	15-30768468	Imputed
15q13.3 30,768,526	15-30768526	Imputed
15q13.3 30,768,620	rs7178316	Genotyped
15q13.3 30,768,935	rs6494587	Genotyped
15q13.3 30,769,270	rs8024160	Imputed
15q13.3 30,771,488	rs6494593	Imputed
15q13.3 30,772,597	rs17228585	Genotyped
15q13.3 30,772,770	rs12592208	Genotyped
15q13.3 30,773,082	rs28494912	Imputed
15q13.3 30,773,246	rs1997317	Genotyped
15q13.3 30,773,279	rs1997316	Genotyped
15q13.3 30,773,663	rs17228592	Genotyped
15q13.3 30,773,727	rs68050511	Imputed
15q13.3 30,774,389	rs16968154	Imputed
15q13.3 30,774,508	15-30774508	Imputed
15q13.3 30,774,799	15-30774799	Imputed
15q13.3 30,775,388	rs1406388	Genotyped
15q13.3 30,775,430	rs7494781	Genotyped
15q13.3 30,779,005	rs16969344	Genotyped
15q13.3 30,779,950	rs28399071	Imputed
15q13.3 30,780,036	rs8035130	Genotyped
15q13.3 30,780,128	rs12708491	Imputed
15q13.3 30,780,403	rs16969681	Genotyped
15q13.3 30,780,585	rs28436737	Imputed
15q13.3 30,780,817	rs62002603	Imputed
15q13.3 30,780,864	rs28590240	Imputed
15q13.3 30,780,937	rs16969816	Genotyped
15q13.3 30,781,152	rs28630996	Imputed
15q13.3 30,781,293	rs16969862	Genotyped
15q13.3 30,781,348	rs12591992	Genotyped
15q13.3 30,781,704	rs12592056	Genotyped
15q13.3 30,781,917	rs12594722	Genotyped
15q13.3 30,782,069	rs4779585	Genotyped
15q13.3 30,782,135	rs9888701	Genotyped
15q13.3 30,782,465	rs11071915	Imputed
15q13.3 30,782,590	rs16970016	Genotyped
15q13.3 30,782,646	rs9888705	Imputed
15q13.3 30,782,760	rs6494598	Genotyped
15q13.3 30,782,792	rs6494599	Imputed
15q13.3 30,783,056	rs1124774	Imputed
15q13.3 30,783,368	rs28663519	Imputed
15q13.3 30,783,431	rs17816236	Genotyped
15q13.3 30,783,506	rs55659128	Imputed
15q13.3 30,783,535	rs28650777	Imputed
15q13.3 30,784,008	rs12901827	Genotyped
15q13.3 30,784,223	rs12906413	Imputed
15q13.3 30,784,442	rs3861195	Genotyped

15q13.3	30,784,467	rs12902616	Genotyped
15q13.3	30,784,874	rs11853552	Genotyped
15q13.3	30,784,959	rs11857190	Imputed
15q13.3	30,785,128	rs11857997	Genotyped
15q13.3	30,786,603	rs8031842	Imputed
15q13.3	30,786,715	rs6494601	Imputed
15q13.3	30,786,888	15-30786888	Imputed
15q13.3	30,787,098	rs1554865	Genotyped
15q13.3	30,788,001	rs1881538	Genotyped
15q13.3	30,788,556	rs12914734	Genotyped
15q13.3	30,788,858	rs7182252	Genotyped
15q13.3	30,789,026	rs58658771	Imputed
15q13.3	30,789,764	rs11071922	Imputed
15q13.3	30,789,986	rs34054489	Imputed
15q13.3	30,790,000	15-30790000	Imputed
15q13.3	30,790,002	15-30790002	Imputed
15q13.3	30,790,143	15-30790143	Imputed
15q13.3	30,790,156	15-30790156	Imputed
15q13.3	30,790,171	15-30790171	Imputed
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15q13.3	30,791,354	rs11638007	Genotyped
15q13.3	30,791,539	rs11632715	Genotyped
15q13.3	30,793,167	rs1534594	Genotyped
15q13.3	30,793,696	rs12591802	Genotyped
15q13.3	30,793,707	rs12594148	Imputed
15q13.3	30,793,800	rs12592288	Genotyped
15q13.3	30,793,902	rs12592312	Imputed
15q13.3	30,794,643	rs28473724	Imputed
15q13.3	30,795,651	rs11633862	Genotyped
15q13.3	30,796,770	rs1406389	Genotyped
15q13.3	30,796,866	rs1919364	Imputed
15q13.3	30,797,704	rs2293582	Imputed
15q13.3	30,798,028	rs2293581	Genotyped
15q13.3	30,798,419	rs7168877	Imputed
15q13.3	30,798,933	rs9806137	Genotyped
15q13.3	30,798,989	15-30798989	Imputed
15q13.3	30,799,143	rs8034965	Genotyped
15q13.3	30,799,524	rs11635984	Genotyped
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15q13.3	30,801,062	rs4779586	Imputed
15q13.3	30,801,587	rs7167214	Genotyped
15q13.3	30,802,498	rs1528734	Genotyped
15q13.3	30,802,694	rs7497354	Genotyped
15q13.3	30,802,752	rs9920024	Genotyped

Region	Location	SNP ID	Imputed or Genotyped
14q22.2	53,430,973	rs4898815	Genotyped
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14q22.2	53,434,718	rs56132091	Imputed
14q22.2	53,435,381	rs4901464	Imputed
14q22.2	53,435,871	rs7140284	Imputed
14q22.2	53,435,915	rs7140441	Imputed
14q22.2	53,436,318	rs4901465	Imputed
14q22.2	53,436,788	rs10144601	Imputed
14q22.2	53,436,952	rs4898817	Genotyped
14q22.2	53,437,038	rs1957847	Genotyped
14q22.2	53,437,350	rs12435627	Genotyped
14q22.2	53,437,781	rs2358427	Genotyped
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14q22.2	53,438,796	rs2147102	Imputed
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14q22.2	53,439,923	rs2181734	Imputed
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14q22.2 53,457,623	rs4243595	Imputed
14q22.2 53,457,891	rs17832101	Imputed
14q22.2 53,458,043	rs12895146	Imputed
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14q22.2 53,459,337	rs12323369	Imputed
14q22.2 53,461,392	rs1957856	Imputed
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14q22.2 53,463,489	rs2147104	Imputed
14q22.2 53,463,762	rs2358429	Imputed
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14q22.2 53,464,479	rs4901468	Imputed
14q22.2 53,464,481	rs4901469	Imputed
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14q22.2 53,469,007	rs12587398	Imputed
14q22.2 53,469,825	rs942315	Imputed
14q22.2 53,470,173	rs12432196	Imputed
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14q22.2 53,476,491	rs34763890	Imputed
14q22.2 53,476,772	rs2224835	Imputed
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14q22.2 53,477,396	rs12435446	Imputed
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14q22.2 53,497,352	rs12434228	Genotyped
14q22.2 53,499,042	rs72680539	Imputed
14q22.2 53,499,105	rs1957860	Genotyped
14q22.2 53,499,535	rs17127103	Imputed
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14q22.2 53,503,140	rs6572927	Genotyped
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14q22.2 53,530,761 rs17127134 Genotyped

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20p12.3 6,363,824	rs6054232	Imputed
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20p12.3 6,372,857	rs6054248	Imputed
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20p12.3 6,373,899	rs6085559	Imputed
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20p12.3 6,375,518	rs6054255	Genotyped
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20p12.3 6,376,622	rs1156511	Imputed
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20p12.3 6,378,101	rs11087731	Genotyped
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20p12.3 6,378,556	rs13038613	Imputed
20p12.3 6,378,639	rs6139998	Imputed
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20p12.3 6,379,457	rs6054266	Imputed
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20p12.3 6,379,914	rs6054268	Imputed
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20p12.3 6,380,618	rs6054272	Imputed
20p12.3 6,380,735	rs2876033	Imputed
20p12.3 6,380,797	rs2326785	Imputed
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20p12.3 6,382,117	rs6054275	Imputed
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20p12.3 6,388,258	rs7509140	Imputed
20p12.3 6,390,961	rs6077004	Genotyped
20p12.3 6,392,659	rs13036856	Imputed
20p12.3 6,392,931	rs7269050	Genotyped
20p12.3 6,393,632	rs62199997	Imputed
20p12.3 6,393,985	rs6054289	Genotyped
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20p12.3 6,394,162	rs6117272	Genotyped
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20p12.3 6,395,663	rs12626134	Imputed
20p12.3 6,396,094	rs7262110	Imputed
20p12.3 6,396,432	rs6117275	Imputed
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20p12.3 6,397,281	rs6085566	Imputed
20p12.3 6,397,722	rs62199999	Imputed
20p12.3 6,398,549	rs990123	Imputed
20p12.3 6,399,752	rs2326787	Genotyped
20p12.3 6,400,601	rs6054290	Imputed
20p12.3 6,400,773	rs6054291	Genotyped
20p12.3 6,400,982	rs6085568	Genotyped
20p12.3 6,401,105	rs6085569	Imputed
20p12.3 6,401,324	rs4815903	Genotyped
20p12.3 6,402,309	rs6077007	Genotyped
20p12.3 6,402,661	rs6054292	Genotyped

*Supplemental Table 2. Haplotype risk analysis at rs16969681 and rs4779584.*

Haploview (<http://www.haploview.org/>) was used to estimate haplotype frequencies in our data at SNPs close to rs16969681 and rs4779584. We then used PLINK to perform haplotype association analysis at rs16969681 and rs4779584.

LOCUS	HAPLOTYPE	F A	F U	CHISQ	DF	P	SNPs
WIN1	OMNIBUS	NA	NA	24.91	3	$1.609 \times 10^{-5}$	rs16969681 rs4779584
WIN1	TT	0.0632	0.0525	16.01	1	$6.29 \times 10^{-5}$	rs16969681 rs4779584
WIN1	CT	0.1470	0.1380	4.938	1	0.02628	rs16969681 rs4779584
WIN1	TC	0.0326	0.0306	1.008	1	0.3154	rs16969681 rs4779584
WIN1	CC	0.7571	0.7789	19.94	1	$7.974 \times 10^{-6}$	rs16969681 rs4779584

*Supplemental Table 3. Logistic regression model analysis of CRC risk and genotypes at rs4779584, rs16969681 and rs11632715.*

Samples typed for all 3 SNPs are included. The best fitting model (minimum Akaike Information Criterion) included rs16969681 and rs11632715. Inclusion of rs4779584 did not improve the fit of the model. When all 3 SNPs were included in the logistic regression model: for rs11632715,  $P=1.36 \times 10^{-5}$ ; for rs16969681,  $P=3.96 \times 10^{-5}$ ; and for rs4779584,  $P=0.14$ .

<u>SNPs included in model</u>	<u>AIC</u>
rs4779584+rs16969681+rs11632715	25541
rs4779584+rs16969681	25558
rs4779584+rs11632715	25556
rs16969681+rs11632715	25541
rs4779584	25570
rs16969681	25565
rs11632715	25564

Although the data for the SNPs near *GREM1* are by far most compatible with 2 independent CRC variants at or tagged by rs16969681 and rs11632715, we cannot entirely exclude the remote possibility of the signals at rs16969681 and rs11632715 capturing a single very rare disease variant on a haplotype which we estimate to have a frequency of ~1%. However, no such variant was evident on imputation using 1000 genomes project data as a reference (see above). Moreover, such a variant might have a sufficiently large effect size that it would be detectable by linkage screens, and no evidence of a such a linkage signal at *GREM1* has emerged from linkage studies of CRC in white northern European populations (2-7). It is also highly implausible that these SNPs are reporting the effects of the high-penetrance *HMPS/CRAC1* gene found in Ashkenazim (8), since HMPS families are generally large, have distinct phenotypes and tumour histology. Moreover, the *HMPS/CRAC1* ancestral mutation resides on a haplotype that does not include the risk allele at rs16969681 or rs11632715.

*Supplemental Table 4. TagSNPs around GREM1, BMP4 and BMP2 analysed for new associations.*

<b>CHR</b>	<b>BP</b>	<b>SNP</b>
15q13.3	30,775,388	rs1406388
15q13.3	30,775,430	rs7494781
15q13.3	30,779,005	rs16969344
15q13.3	30,779,779	rs12708490
15q13.3	30,780,036	rs8035130
15q13.3	30,780,403	rs16969681
15q13.3	30,780,937	rs16969816
15q13.3	30,781,293	rs16969862
15q13.3	30,781,348	rs12591992
15q13.3	30,781,704	rs12592056
15q13.3	30,781,917	rs12594722
15q13.3	30,782,048	rs4779584
15q13.3	30,782,135	rs9888701
15q13.3	30,782,198	rs7172208
15q13.3	30,782,590	rs16970016
15q13.3	30,782,673	rs7166282
15q13.3	30,784,442	rs3861195
15q13.3	30,784,874	rs11853552
15q13.3	30,785,128	rs11857997
15q13.3	30,787,098	rs1554865
15q13.3	30,788,001	rs1881538
15q13.3	30,788,556	rs12914734
15q13.3	30,788,858	rs7182252
15q13.3	30,791,354	rs11638007
15q13.3	30,791,539	rs11632715
15q13.3	30,793,167	rs1534594
15q13.3	30,793,800	rs12592288
15q13.3	30,796,770	rs1406389
15q13.3	30,798,028	rs2293581
15q13.3	30,802,498	rs1528734
15q13.3	30,802,694	rs7497354
15q13.3	30,802,752	rs9920024
15q13.3	30,803,446	rs11630554
15q13.3	30,803,770	rs10519738
15q13.3	30,808,220	rs16973303
15q13.3	30,809,874	rs11854391
15q13.3	30,810,390	rs2280738
15q13.3	30,810,778	rs12915554
15q13.3	30,811,243	rs3743105
15q13.3	30,811,747	rs7162202
15q13.3	30,811,859	rs17525764
15q13.3	30,811,859	rs17816279
15q13.3	30,812,919	rs3743103
15q13.3	30,813,271	rs10318
15q13.3	30,813,959	rs1129456
15q13.3	30,814,471	rs7176378
15q13.3	30,816,842	rs11071936
15q13.3	30,820,130	rs4453446
15q13.3	30,820,399	rs7175986
15q13.3	30,824,409	rs12905295
15q13.3	30,825,787	rs7496435
15q13.3	30,826,590	rs17816285
15q13.3	30,827,888	rs10519739
15q13.3	30,828,074	rs10519740
15q13.3	30,828,286	rs12439770
15q13.3	30,829,630	rs16958114
15q13.3	30,830,125	rs12904470
15q13.3	30,830,747	rs1919360
15q13.3	30,830,949	rs1919362
15q13.3	30,835,148	rs11633236

15q13.3	30,837,715	rs1258763
15q13.3	30,839,102	rs1258756
15q13.3	30,840,760	rs12050872
15q13.3	30,841,293	rs2697937
15q13.3	30,842,858	rs3108628
15q13.3	30,843,196	rs2141438
15q13.3	30,843,508	rs2053939
15q13.3	30,843,508	rs4482251
15q13.3	30,844,649	rs1258721
15q13.3	30,845,067	rs3817591
15q13.3	30,845,815	rs12148620
15q13.3	30,846,355	rs3812929
15q13.3	30,847,699	rs2840190
15q13.3	30,847,893	rs1020561
15q13.3	30,848,487	rs1258724
15q13.3	30,848,692	rs11853746
15q13.3	30,849,208	rs1258726
15q13.3	30,849,631	rs3110558
15q13.3	30,849,653	rs12442768
15q13.3	30,849,684	rs16958617
15q13.3	30,850,170	rs1979167
15q13.3	30,850,518	rs1979168
15q13.3	30,851,101	rs3743106
15q13.3	30,851,408	rs3743108
15q13.3	30,851,440	rs3825862
15q13.3	30,851,589	rs17816333
15q13.3	30,852,083	rs1258731
15q13.3	30,852,603	rs1258732
15q13.3	30,852,937	rs2037844
15q13.3	30,853,102	rs16958702
15q13.3	30,854,631	rs17816345
15q13.3	30,854,948	rs1258734
15q13.3	30,855,275	rs1258735
15q13.3	30,855,315	rs1258736
15q13.3	30,855,341	rs12594522
15q13.3	30,855,573	rs896507
15q13.3	30,861,143	rs2077680

<b>CHR</b>	<b>BP</b>	<b>SNP</b>
14q22.2	52,555,108	rs4901334
14q22.2	52,558,141	rs12433730
14q22.2	52,563,324	rs10137117
14q22.2	52,563,872	rs10139750
14q22.2	52,563,901	rs8021587
14q22.2	52,569,647	rs17126068
14q22.2	52,572,713	rs12897244
14q22.2	52,575,641	rs2150541
14q22.2	52,577,434	rs17126072
14q22.2	52,595,177	rs12882412
14q22.2	52,612,077	rs2152492
14q22.2	52,695,157	rs8005652
14q22.2	52,701,283	rs10483621
14q22.2	52,701,921	rs4901357
14q22.2	52,711,951	rs7160009
14q22.2	52,730,313	rs2552400
14q22.2	52,735,601	rs2254182
14q22.2	52,752,572	rs4901365
14q22.2	52,758,455	rs6572885
14q22.2	52,763,499	rs1270515
14q22.2	52,770,091	rs11157957
14q22.2	52,772,120	rs1424832
14q22.2	52,776,759	rs763328
14q22.2	52,801,683	rs7146135
14q22.2	52,810,756	rs7151631
14q22.2	52,814,615	rs1364597
14q22.2	52,823,675	rs8013473

14q22.2 52,830,063	rs2161944
14q22.2 52,830,264	rs12434333
14q22.2 52,831,455	rs11626176
14q22.2 52,833,496	rs4901392
14q22.2 52,840,394	rs10132541
14q22.2 52,862,629	rs4901403
14q22.2 52,867,043	rs17126346
14q22.2 52,867,898	rs1424838
14q22.2 52,871,996	rs17126349
14q22.2 52,873,879	rs4901408
14q22.2 52,874,082	rs8023182
14q22.2 52,881,770	rs17126361
14q22.2 52,883,170	rs1255329
14q22.2 52,886,214	rs17126390
14q22.2 52,889,307	rs1255311
14q22.2 52,889,727	rs1255309
14q22.2 52,892,776	rs877018
14q22.2 52,896,997	rs1255288
14q22.2 52,903,676	rs1255277
14q22.2 52,908,879	rs17126432
14q22.2 52,912,225	rs17831927
14q22.2 52,913,714	rs6572905
14q22.2 52,918,686	rs4901416
14q22.2 52,919,582	rs1959839
14q22.2 52,929,105	rs3951266
14q22.2 52,931,563	rs2185823
14q22.2 52,931,636	rs7145276
14q22.2 52,936,440	rs7152432
14q22.2 52,938,344	rs1954329
14q22.2 52,938,563	rs12881359
14q22.2 52,941,665	rs1959844
14q22.2 52,942,144	rs12147371
14q22.2 52,942,157	rs10137772
14q22.2 52,943,242	rs7140955
14q22.2 52,943,591	rs10141685
14q22.2 52,945,697	rs8016132
14q22.2 52,945,741	rs8020203
14q22.2 52,946,599	rs12896513
14q22.2 52,947,864	rs11622595
14q22.2 52,949,420	rs12588025
14q22.2 52,949,813	rs1959846
14q22.2 52,956,528	rs11157969
14q22.2 52,958,888	rs1954332
14q22.2 52,976,589	rs11846138
14q22.2 52,977,625	rs2358222
14q22.2 52,978,083	rs1891552
14q22.2 52,981,315	rs17253256
14q22.2 52,982,078	rs11623604
14q22.2 52,982,584	rs1954333
14q22.2 52,989,059	rs1954303
14q22.2 52,989,928	rs11849931
14q22.2 52,992,995	rs7146329
14q22.2 53,008,870	rs4901426
14q22.2 53,012,538	rs17126556
14q22.2 53,012,683	rs17126559
14q22.2 53,020,233	rs1954313
14q22.2 53,021,754	rs12437319
14q22.2 53,028,619	rs2358227
14q22.2 53,029,970	rs12433690
14q22.2 53,049,564	rs4901431
14q22.2 53,050,472	rs17093060
14q22.2 53,053,482	rs12896283
14q22.2 53,054,715	rs11157973
14q22.2 53,056,970	rs2000224
14q22.2 53,061,954	rs2251492
14q22.2 53,070,047	rs1891550
14q22.2 53,076,776	rs2245007



14q22.2 53,082,853	rs11157975
14q22.2 53,090,485	rs10145210
14q22.2 53,097,749	rs4584745
14q22.2 53,097,749	rs7493781
14q22.2 53,111,705	rs1999345
14q22.2 53,116,516	rs17705765
14q22.2 53,117,621	rs2810061
14q22.2 53,118,724	rs1984025
14q22.2 53,120,826	rs7152946
14q22.2 53,125,087	rs7156227
14q22.2 53,126,377	rs1001161
14q22.2 53,126,732	rs2776514
14q22.2 53,138,531	rs210327
14q22.2 53,140,662	rs210326
14q22.2 53,142,608	rs1380131
14q22.2 53,159,106	rs10873073
14q22.2 53,159,356	rs10483624
14q22.2 53,159,827	rs10483623
14q22.2 53,161,879	rs4901434
14q22.2 53,165,583	rs210375
14q22.2 53,169,450	rs210388
14q22.2 53,171,619	rs8020341
14q22.2 53,171,759	rs210386
14q22.2 53,172,763	rs6572916
14q22.2 53,177,541	rs210381
14q22.2 53,188,522	rs210321
14q22.2 53,193,102	rs210313
14q22.2 53,193,501	rs210311
14q22.2 53,202,404	rs10141869
14q22.2 53,212,776	rs7154592
14q22.2 53,214,603	rs7140911
14q22.2 53,215,067	rs7146962
14q22.2 53,218,192	rs17126761
14q22.2 53,223,746	rs210302
14q22.2 53,227,716	rs210370
14q22.2 53,231,830	rs210363
14q22.2 53,233,786	rs210361
14q22.2 53,234,456	rs210360
14q22.2 53,237,222	rs210359
14q22.2 53,237,867	rs964254
14q22.2 53,239,490	rs210357
14q22.2 53,242,605	rs7151053
14q22.2 53,243,289	rs210352
14q22.2 53,245,589	rs12885035
14q22.2 53,247,211	rs1026487
14q22.2 53,248,640	rs17635121
14q22.2 53,248,686	rs8005983
14q22.2 53,250,349	rs210343
14q22.2 53,255,833	rs169748
14q22.2 53,256,814	rs7155858
14q22.2 53,256,878	rs17126825
14q22.2 53,262,222	rs210332
14q22.2 53,272,873	rs10143898
14q22.2 53,274,830	rs1380124
14q22.2 53,275,362	rs12895682
14q22.2 53,275,921	rs12586452
14q22.2 53,276,387	rs11621375
14q22.2 53,280,536	rs9323246
14q22.2 53,281,917	rs8009949
14q22.2 53,286,519	rs11623166
14q22.2 53,292,038	rs12590186
14q22.2 53,294,303	rs6572922
14q22.2 53,295,858	rs4901444
14q22.2 53,296,123	rs12894060
14q22.2 53,296,438	rs12184995
14q22.2 53,298,267	rs1958654
14q22.2 53,298,796	rs8015573

14q22.2 53,304,503	rs10147611
14q22.2 53,308,392	rs10498453
14q22.2 53,308,747	rs10498454
14q22.2 53,313,634	rs4901450
14q22.2 53,313,634	rs7401585
14q22.2 53,316,103	rs12589674
14q22.2 53,317,833	rs17126895
14q22.2 53,321,945	rs7154006
14q22.2 53,322,290	rs883519
14q22.2 53,327,510	rs17126903
14q22.2 53,329,348	rs8017615
14q22.2 53,333,601	rs8009420
14q22.2 53,340,961	rs8004644
14q22.2 53,343,338	rs2150279
14q22.2 53,344,193	rs8020936
14q22.2 53,347,739	rs17126953
14q22.2 53,352,059	rs11849392
14q22.2 53,360,138	rs2884439
14q22.2 53,360,547	rs12434693
14q22.2 53,360,580	rs12431733
14q22.2 53,361,132	rs4898812
14q22.2 53,362,407	rs883219
14q22.2 53,365,399	rs1958636
14q22.2 53,371,277	rs7154026
14q22.2 53,372,596	rs4901454
14q22.2 53,380,347	rs11157980
14q22.2 53,380,675	rs1952748
14q22.2 53,380,777	rs2150276
14q22.2 53,386,357	rs7148896
14q22.2 53,390,192	rs1958643
14q22.2 53,391,034	rs1958644
14q22.2 53,391,156	rs1958645
14q22.2 53,398,432	rs1888344
14q22.2 53,400,045	rs4901458
14q22.2 53,409,243	rs7160860
14q22.2 53,410,376	rs7156353
14q22.2 53,415,547	rs17127017
14q22.2 53,427,887	rs17127035
14q22.2 53,437,350	rs12435627
14q22.2 53,438,622	rs2181733
14q22.2 53,440,346	rs8018146
14q22.2 53,441,332	rs10498464
14q22.2 53,442,591	rs1951865
14q22.2 53,444,978	rs12879252
14q22.2 53,445,204	rs11625439
14q22.2 53,453,695	rs11157990
14q22.2 53,461,563	rs10498466
14q22.2 53,475,815	rs2147105
14q22.2 53,480,669	rs4444235
14q22.2 53,487,272	rs17563
14q22.2 53,488,161	rs2071047
14q22.2 53,492,803	rs762642
14q22.2 53,497,352	rs12434228
14q22.2 53,499,105	rs1957860
14q22.2 53,501,325	rs8014363
14q22.2 53,503,283	rs10873077
14q22.2 53,507,352	rs6572929
14q22.2 53,513,874	rs12892252
14q22.2 53,521,052	rs11157994
14q22.2 53,526,981	rs7160450
14q22.2 53,527,828	rs1957844
14q22.2 53,531,911	rs17253452
14q22.2 53,533,084	rs7141833
14q22.2 53,539,487	rs4901474
14q22.2 53,543,549	rs7149949
14q22.2 53,576,486	rs17708795
14q22.2 53,583,027	rs1983786

14q22.2 53,588,576	rs11158001
14q22.2 53,589,723	rs1951659
14q22.2 53,592,607	rs1033823
14q22.2 53,597,817	rs11621185
14q22.2 53,616,199	rs8007000
14q22.2 53,619,256	rs12878931
14q22.2 53,629,768	rs1957636
14q22.2 53,643,881	rs12587564
14q22.2 53,651,669	rs713423
14q22.2 53,660,900	rs10483627
14q22.2 53,664,028	rs996041
14q22.2 53,669,837	rs4898828
14q22.2 53,674,026	rs17127321
14q22.2 53,677,386	rs2358477
14q22.2 53,677,512	rs811165
14q22.2 53,689,066	rs811153
14q22.2 53,699,691	rs932683
14q22.2 53,710,314	rs8012016
14q22.2 53,716,500	rs10131289
14q22.2 53,722,229	rs1953743
14q22.2 53,728,957	rs8008441
14q22.2 53,738,263	rs4901494
14q22.2 53,753,737	rs10134051
14q22.2 53,763,218	rs1187428
14q22.2 53,766,489	rs10133577
14q22.2 53,766,574	rs11627070
14q22.2 53,766,956	rs1187430
14q22.2 53,769,416	rs1187432
14q22.2 53,769,745	rs11629285
14q22.2 53,793,804	rs2358483
14q22.2 53,800,017	rs4901501
14q22.2 53,804,500	rs1008499
14q22.2 53,822,058	rs10143156
14q22.2 53,825,276	rs2179897
14q22.2 53,826,585	rs4287470
14q22.2 53,827,247	rs7359097
14q22.2 53,830,397	rs6572944
14q22.2 53,831,209	rs1950208
14q22.2 53,835,243	rs11845885
14q22.2 53,838,647	rs12432299
14q22.2 53,838,761	rs12432843
14q22.2 53,839,589	rs6572946
14q22.2 53,842,379	rs1884015
14q22.2 53,843,761	rs1950210
14q22.2 53,844,684	rs9323260
14q22.2 53,845,109	rs2143968
14q22.2 53,845,573	rs2143969
14q22.2 53,846,318	rs2143972
14q22.2 53,846,722	rs12147623
14q22.2 53,847,452	rs17127455
14q22.2 53,847,495	rs7147119
14q22.2 53,854,287	rs1007141
14q22.2 53,857,291	rs10143482
14q22.2 53,862,606	rs10142602
14q22.2 53,862,815	rs7149808
14q22.2 53,863,964	rs9323262
14q22.2 53,864,913	rs10151748
14q22.2 53,866,651	rs17093094
14q22.2 53,866,718	rs10483632
14q22.2 53,868,345	rs10483633
14q22.2 53,869,789	rs10483634
14q22.2 53,870,267	rs17127477
14q22.2 53,870,595	rs10483636
14q22.2 53,871,337	rs12431978
14q22.2 53,872,350	rs9646153
14q22.2 53,872,594	rs4561356
14q22.2 53,873,515	rs10150369

14q22.2	53,873,913	rs11625167
14q22.2	53,873,970	rs10450919
14q22.2	53,875,348	rs17127485
14q22.2	53,875,469	rs17726338
14q22.2	53,875,613	rs10144925
14q22.2	53,876,666	rs11627953
14q22.2	53,877,291	rs2358662
14q22.2	53,878,203	rs7143704
14q22.2	53,880,016	rs1950198
14q22.2	53,883,773	rs8009858
14q22.2	53,885,533	rs8017164
14q22.2	53,890,332	rs761509
14q22.2	53,891,017	rs10138778
14q22.2	53,892,038	rs1950199
14q22.2	53,897,274	rs1955458
14q22.2	53,900,363	rs1955459
14q22.2	53,901,582	rs7144936
14q22.2	53,902,742	rs8018632
14q22.2	53,903,695	rs12893789
14q22.2	53,905,692	rs7147950
14q22.2	53,906,583	rs4901511
14q22.2	53,909,646	rs1950202
14q22.2	53,910,865	rs10146310
14q22.2	53,911,548	rs12888951
14q22.2	53,927,036	rs4293296
14q22.2	53,931,558	rs8007223
14q22.2	53,945,264	rs2179896
14q22.2	53,945,934	rs4251631

<b>CHR</b>	<b>BP</b>	<b>SNP</b>
20p12.3	6,023,178	rs2232068
20p12.3	6,031,493	rs4142219
20p12.3	6,033,006	rs11700048
20p12.3	6,033,216	rs11700084
20p12.3	6,034,772	rs6053908
20p12.3	6,037,552	rs6085405
20p12.3	6,037,797	rs6085406
20p12.3	6,041,090	rs2326719
20p12.3	6,041,177	rs16991866
20p12.3	6,044,695	rs2295435
20p12.3	6,059,569	rs6038366
20p12.3	6,062,257	rs6053925
20p12.3	6,063,581	rs6053929
20p12.3	6,066,980	rs2144936
20p12.3	6,072,113	rs1774885
20p12.3	6,074,302	rs11087720
20p12.3	6,076,201	rs947465
20p12.3	6,076,223	rs1774886
20p12.3	6,076,868	rs1778777
20p12.3	6,076,868	rs6053941
20p12.3	6,078,025	rs3897509
20p12.3	6,078,577	rs1342347
20p12.3	6,085,310	rs6076954
20p12.3	6,091,379	rs3844457
20p12.3	6,092,454	rs3852936
20p12.3	6,104,745	rs7270088
20p12.3	6,110,015	rs6085425
20p12.3	6,114,488	rs6133296
20p12.3	6,124,595	rs6053959
20p12.3	6,124,793	rs6053961
20p12.3	6,128,089	rs6085432
20p12.3	6,129,863	rs6053968
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20p12.3	6,130,577	rs3747923
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*Supplemental Table 5. Additional BMP pathway genes around which tagSNP associations with CRC were analysed.*

BMPR1A  
BMPR1B  
BMPR2  
GREM1  
GREM2  
NOG  
CER1  
DAND5/GREM3  
NBL1  
CHRD  
FST  
FSTL1  
FSTL3  
FSTL4  
FSTL5  
BMP2  
BMP3  
BMP4  
BMP5  
BMP6  
BMP7  
BMP8A  
BMP8B  
BMP9/GDF2  
BMP10  
BMP11/GDF11  
SMAD1  
SMAD5  
SMAD9 (SMAD8)  
SMAD4  
SMAD6  
SMAD7  
BAMBI  
SMURF1  
SYCP1  
SYCP2  
SYCP3

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