

## Supplementary Appendix 1

This appendix has been provided by the authors to give readers additional information about their work.

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## **SUPPORTING APPENDIX ONLINE MATERIAL**

### **Methods**

#### **Study populations**

The Icelandic discovery sample set comprised 5,085 women and 776 men who had dual-energy X-ray absorptiometry (DEXA, Hologic QDR4500A) BMD measurements at the lumbar spine (L2-L4) and the hip (combined values at the femoral neck, trochanter and intertrochanter region). There were 5,715 (4,951 women) with hip measurement and 5,858 (5,083 women) with spine measurement. Of this group, 1,200 women had been selected for IlluminaHap300K genotyping because of their low BMD ( $< -1.2$  SD of age and weight corrected BMD) as a part of our osteoporosis genetic program. All others were genotyped on Illumina Hap300k through other disease projects. The Icelandic replication group comprised 3,189 women and 983 men. Information on diseases that influence BMD or medications that have an effect on BMD (e.g. Hormone Replacement Therapy or Corticosteroids use) was only available for 2,500 of the original discovery individuals and for 1,800 of the replication samples. The rs9594738 HapMap SNP didn't have any data in the discovery sample set and was subsequently genotyped in 2099 individuals in the discovery set, in addition to the Icelandic replication sample set. Osteoporotic fractures were defined as low impact fractures, self-reported. Fractures of fingers, hands, toes, or feet were not included. Hip fracture cases were from individuals undergoing femoral neck fractures surgery at Reykjavik's University Hospital or the General Hospital, Akureyri. Of the hip fracture cases used in this study (n=1087) only 308 (28%) had BMD measurement, whereas of all other fractures (assessed by questionnaire) 71% also had a BMD measurement. The control group used in the fracture case control analysis (n= 35,400) were genotyped on Illumina Hap300k through other projects at deCODE. A summary of the Icelandic

study populations' characteristics is given in Appendix Table 1A and 1B. All participants gave informed consent and the study was approved by the Data Protection Commission of Iceland (DPC) and the National Bioethics Committee of Iceland.

The Danish samples were derived from the Prospective Epidemiological Risk Factor (PERF study)<sup>1,2</sup>. These are postmenopausal women (n = 2,269), in the age range 55–86 years, taking part in a prospective epidemiological study and in various clinical trials for osteoporosis at the Center for Clinical and Basic Research, Copenhagen. Baseline DEXA- measurement (Hologic QDR2000) at the hip (total hip) and lumbar spine (L2–L4) was used for 2,269 with spine measure and for 2,244 with hip measure.

Osteoporotic fractures included self-reported low trauma fractures and vertebral fractures assessed by digital measurements of morphologic changes. 64% of the fracture cases also had a BMD measurement. A summary of the Danish study population's characteristics is given in Appendix Tables 1A and 1B. The study was approved by the Ethical Committee of Copenhagen County and was in accordance with the principles of the Helsinki.

The Australian cohort in this study is from the Dubbo Osteoporosis Epidemiology Study (DOES)<sup>3</sup>, including 571 males and 920 females in the age range 60-99 years. All are of Caucasian ethnicity. Bone mineral density was measured at the lumbar spine and the hip femoral neck (FNBMD) by DEXA (LUNAR DPX-L). Osteoporotic fractures included low trauma fractures assessed by questionnaire and ascertained by reviewing all radiography reports. All fracture cases also had a BMD measurement. The study was approved by the St. Vincent's Ethics Review Committee (Sydney), and all subjects gave written informed consent. A summary of the Australian study population's characteristics is given in Appendix Table 1A and 1B.

## **Illumina Genotyping**

Samples for the genome-wide association study were assayed with the Infinium humanHap300 or humanCNV370 SNP chips (Illumina). Three different versions of the chips were used, humanHap300, humanHap300-duo and humanCNV370. The analysis was restricted to SNPs that had a call rate of 97% on each of the chip types, a combined call rate of 98% and did not deviate from Hardy Weinberg equilibrium ( $p > 10^{-7}$ ) on any chip type. Thus, the final analyses are based on 301,019 SNPs.

## **Single SNP Genotyping**

All single-SNP genotyping was carried out at deCODE Genetics on the Centaurus (Nanogen) platform<sup>4</sup>. The quality of each Centaurus SNP assay was evaluated by genotyping each assay in the CEU HapMap samples and comparing the results with the HapMap data. The Icelandic replication set contained 300 individuals that were also genotyped on the humanCNV370 chip and used for genotype comparisons. Assays with a mismatch rate  $> 1.5\%$  were not used, and a linkage disequilibrium (LD) test was used for markers known to be in LD.

## **Association analysis**

Age and weight corrected BMD was computed for each sex and population separately to have a mean 0 and standard deviation 1 (commonly known as weight corrected Z-scores in the bone field<sup>5</sup>). BMD increased linearly with weight in both genders. For women we modelled BMD to decrease linearly after the age of 45 while for men we modelled BMD to decrease linearly in all age ranges. For the Icelandic and Danish populations regression was done against a randomly recruited reference group<sup>2,6</sup>. In the Australian cohort correction was done against the whole cohort, which consists of majority of individuals 60 years and older in Dubbo, Australia<sup>3</sup>. For each SNP, a

linear regression, using the genotype as an additive covariate and standardized BMD as a response, was fitted to test for association. We tested the additive model against the full model (i.e. treating the genotype as a categorical variable) and no significant deviation from the additive model was detected ( $p > 0.1$  for all SNPs in Table 1, 2 and 3).

For the Icelandic discovery sample, the method of genomic control<sup>7</sup> was used to adjust for the relatedness of the subjects. To do that, we transformed the (unadjusted) P values, based on the t-tests, to 1-df chi-square statistics. The inflation factor  $\lambda$  for the chi-square statistics was estimated as 1.18 for hip BMD and 1.22 for spine BMD. The unadjusted chi-square statistics were divided by  $\lambda$  to obtain the adjusted test statistics. For the combined analysis an inflation factor for the test statistics was computed using simulations using our genealogical database: We create simulated genotypes by choosing uniformly at random a minor allele frequency as a multiple of 5% in the range 5% to 50%. We then randomly assign alleles to individuals born in the year 1700 or earlier. Individuals born after year 1700 were randomly assigned one of their parents' genotypes. The P values obtained from associating the BMD to these genotypes, assuming that the patients are unrelated, was converted to a corresponding 1 df chi<sup>2</sup> statistic that gives the same p value. This chi<sup>2</sup> statistic was then divided by the inflation factor to obtain the adjusted chi<sup>2</sup> statistic and the adjusted p value. This inflation factor was estimated as  $\lambda = 1.21$  (hip) and 1.22 (spine). For comparison purposes we also simulated inflation factor for the original population, these were estimated as  $\lambda = 1.15$  (hip) and 1.13 (spine). The actual sample size divided by this inflation factor was used as an estimate of the effective sample size. An overall Z -score was calculated by summing the Z -scores weighted by the square root of the effective sample size, over all populations, and dividing by the square root of the sum of the sample sizes. An overall estimate of the effect per allele was calculated by weighting together the effects in each population by the population's effective sample size.

For comparison we also applied the EIGENSTRAT method<sup>8</sup>, which relies on patterns of correlation between individuals to detect stratification, to our Icelandic discovery sample. Due to computational constraints we restricted our analysis to approximately one third of the available SNPs (n=103,516). No evidence of substantial stratification was detected, with the largest principal component estimated to explain 0.1% of the overall variation of the genotype data. Consequently, accounting for the 30 largest principal components identified by EIGENSTRAT had a miniscule effect on significance. The largest correction, for the SNPs in this report, was for rs9479055 and corresponded to dividing its  $\chi^2$ -statistic by 1.003. Thus, we concluded that correction based on the EIGENSTRAT method would not improve the quality of our analysis.

For association analysis of osteoporotic fractures a standard likelihood ratio statistics was used, as implemented in the NEMO software created at deCODE, to calculate two-sided P values and odds ratio (OR) for each individual allele, assuming a multiplicative model for risk, i.e., that the risk of the two alleles a person carries multiply. Allelic frequencies, rather than carrier frequencies are presented for the markers. The haplotype frequencies were estimated using their maximum likelihood estimates and a test of differences between groups was carried out using a generalized likelihood ratio test. When testing for risk of a variant given the risk of a previously reported variant or a set of previously reported variants the likelihood of the model that included a risk contribution from any of the previously reported markers and the new marker was tested versus the likelihood of the model that only included only a risk contribution from any of the previously reported markers. Our program, NEMO, was used for all haplotype analysis, for evaluating the measures of LD between individual markers and for linear regression analysis of haplotypes.

Results from multiple case-control groups were combined using a Mantel-Haenszel model in which the groups were allowed to have different population

frequencies for alleles, haplotypes and genotypes but were assumed to have a common relative risk <sup>9</sup>.

To test for possible interactions between different loci found we selected one SNP from each of our associated loci. For each pair of markers we then tested a model that included an additive effect from both loci as well as a multiplicative interaction term for the number of risk alleles at each locus against a model that included only the two additive terms. No significant interaction between loci was detected ( $p > 0.05$  for all pairs).

#### **Refinement of associated signals:**

Chr13q14: We considered all SNPs within 250 kb in either direction from rs954759, corresponding approximately to two haplotype blocks in either direction. We found that conditional on the association with the most highly associated marker in the region, rs9594759, a significant association was found to the marker rs10507508 ( $p = 1.96 \times 10^{-5}$ , 0.0011 when correcting for 59 markers in region). Further, we computed associations with a linear combination of haplotypes chosen to act as surrogates to HapMap markers in the region. Surrogate to the two equivalent markers, rs9533090 and rs9594738, was the most significantly associated marker with spine BMD ( $p = 9.56 \times 10^{-12}$ ).

Chr6q25: Two markers were genome-wide significant in the upstream region of *ESR1*; rs2504063 ( $p = 5.68 \times 10^{-8}$ ) and rs851982 ( $p = 1.56 \times 10^{-7}$ ). These markers are highly correlated, but not equivalent ( $d_{\text{prime}} = 1$ ,  $r_2 = 0.47$ ). 16 other markers, within 100 kb of these two, were selected for further study. None of these 18 markers were equivalent and the highest  $r_2$  between a pair of markers was 0.79. No surrogate for a

HapMap marker was found that showed a significantly higher level of association than rs2504063. Conditioned on the association with the most highly associated marker a significant association was still found to 14 of the remaining 17 markers in the region. Conditioned on the association from two markers in the region a significant association was still found to other markers in the region. We reconsidered this analysis for the five markers that replicated in our replication cohort and were genome-wide significant in the combined analysis. Given the association from any two of these markers a significant association was still observed from one of the three remaining markers. Conditioned on an association observed at rs1038304, rs1999805 and rs4870044 no residual association was found to the other two markers.

### **Suggestive loci:**

Some of the loci that did not reach genome-wide significance in our analysis replicated or showed evidence of association with osteoporotic fractures.

A SNP, rs11898505, in the *SPTBNI* (spectrin beta non-erythrocytic 1) gene on 2p16 was nearly genome-wide significant in the combined Icelandic samples ( $P = 2.0 \times 10^{-7}$ ) but did not replicate consistently in the other populations (Table 3). However, this SNP associated with osteoporotic fractures in all sample sets with an OR 1.11 and  $P = 1.8 \times 10^{-4}$  in the combined overall analysis (Table 4). Vertebral fractures were individually the most associated ones with OR 1.29 and  $P$  value of  $1.5 \times 10^{-4}$  in the overall analysis (Appendix Table 5). The *SPTBNI* gene encodes a major cytoskeletal scaffolding protein and has not, to our knowledge, been considered to play a specific role in bone biology or BMD regulation (Appendix Figure 1G). The gene has a wide tissue expression, including bone and bone marrow (Unigene Hs.503178, Hs.705692).



Another region that showed only a modest association with BMD but associated with fractures was around the *LRP4* (low density lipoprotein receptor-related protein 4) gene on 11p11. We chose to follow this region, not only because of overrepresentation of markers in the region, but also because the sequence and domain organization of *LRP4* shows significant similarities to those of members of the LDL receptor family, including the *LRP5* and *LRP6* (low density lipoprotein receptor-related protein 6) genes, both of which have been reported to associate with BMD or osteoporosis <sup>10</sup>. The SNP rs2306033, resulting in the conservative change of alanine to valine at codon 1203 in exon 26 of the *LRP4* gene, associated modestly with hip BMD with an overall *P* value  $4.0 \times 10^{-5}$  (Table 3), but associated also with osteoporotic fractures in the overall combined analysis with OR 1.11 and *P* value  $7.4 \times 10^{-3}$  (Table 4). Three other SNPs in the region replicated in the combined Danish and Australian sample sets for BMD and were associated with osteoporotic fractures, although the overall *P* values of these SNPs were only in the range of  $P 10^{-3}$  to  $P 10^{-4}$  in the BMD association analysis (Appendix Table 3, 5, Figure 1H).

Other regions of interest included the *Osx* (*Osterix*, also known as *SP7*) gene on 12q13, with SNPs that ranked as the 6<sup>th</sup> and 7<sup>th</sup> markers in the spine genome-scan (Appendix Table 1A). This is a transcription factor that is essential to osteoblast differentiation <sup>11</sup> and therefore a strong candidate gene for influencing bone density. The SNP, rs10876432, replicated well in the Icelandic sample set and showed similar effect in the other populations, although these were not individually significant (Appendix Table 3A, Appendix Figure 1I). No association was observed with fractures for this SNP.

#### **References:**

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**SUPPLEMENTARY TABLES:**

**Supplementary Table 1A Study Population Characteristics**

	Iceland discovery		Iceland Replication		Denmark	Australia	
	Men	Women	Men	Women	Women	Men	Women
#	776	5085	982	3183	2269	571	920
Age (SD), y	66.2 (14.3)	59.4 (14.1)	56.6 (16.7)	58.1 (14.3)	72.4 (5.7)	85.6 (5.5)	76.1 (6.3)
Age-range, y	18-96	18-98	18-88	18-92	55-86	61-90	60-99
BMI (SD)	26.7 (4.1)	26.1 (4.7)	26.4 (3.8)	25.8 (4.4)	25.7 (3.5)	26.7 (4.0)	26.2 (5.0)
Height (SD), cm	176.4 (6.6)	164.2 (7.0)	178.2 (6.6)	164.3 (7.3)	160.5 (5.8)	171.3 (6.4)	157.9 (6.2)
Weight (SD), kg	83.4 (14.6)	70.5 (13.2)	83.4 (13.8)	69.9 (12.5)	65.8 (9.9)	78.4 (13.1)	65.4 (13.3)
raw HipBMD (SD), g/cm <sup>2</sup>	0.931 (0.161)	0.820 (0.161)	0.970 (0.172)	0.878 (0.158)	0.788 (0.134)	0.899 (0.162)	0.750 (0.126)
HipBMDcorr. (SD)	-0.303 (1.062)	-0.493 (1.032)	-0.125 (1.216)	-0.004 (1.161)	-0.048 (1.022)	0.000 (1.000)	0.000 (1.000)
raw SpineBMD (SD), g/cm <sup>2</sup>	1.015 (0.179)	0.944 (0.171)	1.022 (0.195)	1.011 (0.190)	0.875 (0.166)	1.276 (0.233)	1.031 (0.203)
SpineBMDcorr. (SD)	-0.381 (1.194)	-0.403 (1.085)	-0.410 (1.373)	0.061 (1.209)	-0.055 (1.066)	0.000 (1.000)	0.000 (1.000)

**Supplementary Table 1B Osteoporotic fractures in study populations**

Fracture Type	Iceland	Denmark	Australia
Any Low Trauma	2986	905	550
Vertebral	263	203	251
Hip	1087	101	156
Forearm	1057	515	125

## Supplementary Table 2A

## Top 50 signals in Spine-QTL analysis

SNP	P-value	Chr.	Position*	Freq.	Effect on Z score+	Close to Gene
T rs9594759	1.17E-08	chr13	41930593	0.632	-0.133 (-0.179, -0.087)	RANKL, AKAP11
G rs2504063	5.68E-08	chr6	152132400	0.615	0.125 (0.080, 0.170)	ESR1
T rs851982	1.56E-07	chr6	152066678	0.609	-0.119 (-0.164, -0.075)	ESR1
T rs2504070	4.62E-07	chr6	152126666	0.309	-0.123 (-0.171, -0.075)	ESR1
G rs7992970	8.50E-07	chr13	41843463	0.216	0.134 (0.081, 0.188)	RANKL, AKAP11
G rs10876432	1.01E-06	chr12	52018158	0.273	0.123 (0.074, 0.172)	Osx (SP7)
G rs2016266	1.04E-06	chr12	52014222	0.316	0.117 (0.070, 0.164)	Osx (SP7)
G rs11898505	1.73E-06	chr2	54538061	0.689	-0.116 (-0.164, -0.069)	SPTBN1
T rs1999805	2.27E-06	chr6	152110057	0.563	0.107 (0.063, 0.152)	ESR1
T rs3020331	3.41E-06	chr6	152050473	0.438	0.103 (0.060, 0.146)	ESR1
T rs4870044	4.09E-06	chr6	151943102	0.284	-0.114 (-0.163, -0.066)	ESR1, C6orf97
G rs1377172	5.21E-06	chr18	57447361	0.672	0.109 (0.062, 0.156)	CDH20, RNF152
G rs1286077	5.85E-06	chr14	90516137	0.127	0.151 (0.085, 0.216)	RPS6KA5
T rs4810077	6.77E-06	chr20	55477509	0.646	0.106 (0.060, 0.152)	HMG1L1, CTCFL
G rs7752591	6.94E-06	chr6	151988761	0.519	0.101 (0.057, 0.145)	ESR1, C6orf97
T rs3780674	7.21E-06	chr9	122206740	0.146	0.142 (0.080, 0.203)	CDK5RAP2
G rs10125592	8.07E-06	chr9	122201556	0.146	0.141 (0.079, 0.203)	CDK5RAP2
T rs1286147	8.08E-06	chr14	90537320	0.873	-0.148 (-0.213, -0.083)	RPS6KA5
G rs1038304	8.25E-06	chr6	151974868	0.472	-0.100 (-0.144, -0.056)	ESR1, C6orf97
G rs6469804	8.53E-06	chr8	120114010	0.482	0.100 (0.056, 0.144)	OPG, COLEC10
T rs2244352	8.95E-06	chr21	39679843	0.340	-0.105 (-0.151, -0.059)	WRB
T rs4315567	9.65E-06	chr2	54509448	0.301	0.109 (0.061, 0.157)	SPTBN1
C rs2872375	1.24E-05	chr3	78378354	0.690	-0.106 (-0.154, -0.059)	
G rs10505328	1.28E-05	chr8	119219639	0.496	0.099 (0.054, 0.143)	SAMD12,EXT1, RANK
T rs3851406	1.30E-05	chr3	169807659	0.909	-0.169 (-0.246, -0.093)	
T rs12273926	1.32E-05	chr11	83346437	0.852	0.138 (0.076, 0.200)	DLG2
T rs10507507	1.60E-05	chr13	41867646	0.823	-0.126 (-0.184, -0.069)	RANKL, AKAP11
G rs12479765	1.68E-05	chr20	33288794	0.838	-0.129 (-0.188, -0.07)	MMP24
G rs1917098	1.76E-05	chr3	78386915	0.285	0.107 (0.058, 0.155)	
T rs4391370	1.91E-05	chr7	84105660	0.181	-0.124 (-0.181, -0.067)	BX647900, SEMA3D
G rs2504065	1.97E-05	chr6	152136860	0.493	-0.096 (-0.140, -0.052)	ESR1
G rs3783833	2.02E-05	chr14	90505343	0.141	0.135 (0.073, 0.198)	RPS6KA5
T rs713485	2.15E-05	chr18	57421905	0.666	0.101 (0.055, 0.148)	CDH20, RNF152
T rs7028896	2.19E-05	chr9	132521981	0.064	0.196 (0.105, 0.286)	PRDM12, FUBP3
G rs10403583	2.46E-05	chr19	43983611	0.800	-0.118 (-0.173, -0.063)	LGALS4, LGALS7
T rs4830487	7.64E-05	chrX	13040405	0.606	-0.086 (-0.129, -0.044)	
T rs7595929	2.78E-05	chr2	54479744	0.347	0.099 (0.053, 0.145)	SPTBN1
G rs4147528	2.82E-05	chr8	119202598	0.507	-0.095 (-0.139, -0.05)	SAMD12,EXT1, RANK
G rs6929137	3.00E-05	chr6	151978370	0.703	0.101 (0.054, 0.149)	ESR1, C6orf97
T rs1350929	3.08E-05	chr3	111951197	0.446	0.093 (0.049, 0.137)	
T rs11246386	3.26E-05	chr11	1034938	0.231	0.111 (0.059, 0.163)	MUC2
T rs1401207	3.30E-05	chr16	78919303	0.762	-0.111 (-0.164, -0.059)	
T rs1398330	3.36E-05	chr3	78405572	0.224	0.110 (0.058, 0.162)	
G rs6942152	3.53E-05	chr6	155469316	0.204	-0.116 (-0.171, -0.061)	TIAM2
T rs6993813	3.59E-05	chr8	120121419	0.495	0.093 (0.049, 0.137)	OPG, COLEC10
G rs7753676	3.62E-05	chr6	151918508	0.373	-0.095 (-0.140, -0.050)	ESR1, C6orf97
T rs6899351	3.80E-05	chr6	123150805	0.695	0.099 (0.052, 0.146)	SMPDL3A
G rs1006899	3.87E-05	chr21	14766923	0.153	0.128 (0.067, 0.189)	SAMSN1
T rs9306419	3.97E-05	chr22	24699358	0.117	0.144 (0.075, 0.212)	MYO18B
T rs9375185	4.13E-05	chr6	123160199	0.827	0.121 (0.063, 0.179)	SMPDL3A

\* Build 36 position

+ Effect on each allele of the SNP on standardized BMD, given as SD units, with 95% confidence intervals

Supplementary Table 2B

Top 50 signals in Hip-QTL analysis

SNP	P-value	Chr.	Position*	Freq.	Effect on Z score+	Close to Gene
T rs6696981	1.15E-06	chr1	22575445	0.138	0.149 (0.089,0.208)	ZBTB40, WNT4
G rs7752591	2.16E-06	chr6	151988761	0.519	0.100 (0.059,0.141)	ESR1, C6orf97
G rs7524102	2.58E-06	chr1	22571034	0.177	0.130 (0.076,0.184)	ZBTB40, WNT4
G rs7676236	3.94E-06	chr4	102793390	0.321	-0.105 (-0.150,-0.061)	BANK1
G rs907580	4.54E-06	chr9	99662418	0.713	0.107 (0.061,0.152)	FOXE1
G rs1007738	7.10E-06	chr11	46805936	0.231	0.113 (0.064,0.162)	CKAP5, LRP4
G rs2892966	7.86E-06	chr4	122864017	0.380	0.097 (0.055,0.140)	ANXA5, TMEM155
G rs2037957	8.03E-06	chr8	134528403	0.666	-0.101 (-0.145,-0.057)	ST3GAL1
T rs3020331	8.15E-06	chr6	152050473	0.437	0.093 (0.052,0.134)	ESR1
G rs10497621	9.82E-06	chr2	183705688	0.086	0.164 (0.092,0.237)	NUP35
T rs4692511	9.86E-06	chr4	30973757	0.146	0.132 (0.074,0.191)	PCDH7
G rs7024345	1.14E-05	chr9	99635059	0.710	0.102 (0.056,0.148)	FOXE1
G rs8100029	1.27E-05	chr19	7354832	0.044	-0.228 (-0.330,-0.125)	ARHGEF18
G rs1038304	1.42E-05	chr6	151974868	0.472	-0.092 (-0.133,-0.050)	ESR1, C6orf97
T rs851982	1.59E-05	chr6	152066678	0.609	-0.092 (-0.134,-0.050)	ESR1
T rs4516411	1.62E-05	chr2	39322180	0.930	0.180 (0.098,0.262)	MAP4K3, CDKL4
T rs6900157	1.63E-05	chr6	151995820	0.684	0.097 (0.053,0.141)	ESR1, C6orf97
G rs6929137	1.84E-05	chr6	151978370	0.702	0.098 (0.053,0.143)	ESR1, C6orf97
G rs12437971	2.14E-05	chr15	98662088	0.438	-0.091 (-0.133,-0.049)	ADAMTS17
G rs4075039	2.22E-05	chr3	118645474	0.856	-0.129 (-0.188,-0.069)	
T rs12775433	2.82E-05	chr10	101824082	0.340	0.094 (0.050,0.139)	CPN1
T rs2451255	3.04E-05	chr6	159430804	0.557	-0.089 (-0.130,-0.047)	TAGAP
T rs2847351	3.14E-05	chr18	10437041	0.657	-0.093 (-0.137,-0.049)	APCDD1
T rs1332498	3.33E-05	chr1	150957072	0.592	0.088 (0.047,0.130)	LCE4A
T rs884013	3.62E-05	chr18	44710128	0.070	0.169 (0.089,0.250)	SMAD7
G rs10137819	3.91E-05	chr14	100464694	0.434	-0.088 (-0.131,-0.046)	
T rs873775	4.02E-05	chr1	150959096	0.592	0.087 (0.046,0.129)	LCE4A
T rs4482635	4.10E-05	chr3	25045902	0.878	-0.133 (-0.196,-0.069)	
C rs7524281	4.10E-05	chr1	151049879	0.599	0.088 (0.046,0.130)	LCE1B
G rs3018362	4.25E-05	chr18	58233073	0.637	0.090 (0.047,0.133)	RANK
G rs10838635	4.70E-05	chr11	46901803	0.240	0.101 (0.052,0.150)	LRP4
G rs7543680	4.75E-05	chr1	22603856	0.763	-0.102 (-0.151,-0.053)	ZBTB40
T rs7645105	4.79E-05	chr3	118808141	0.590	0.087 (0.045,0.129)	
T rs11600292	5.09E-05	chr11	46915274	0.760	-0.101 (-0.150,-0.052)	C11orf49, LRP4
T rs6485702	5.74E-05	chr11	46855347	0.357	0.088 (0.045,0.131)	LRP4
G rs7751941	5.98E-05	chr6	151988351	0.788	0.102 (0.052,0.152)	ESR1, C6orf97
T rs2043644	6.07E-05	chr4	148959669	0.090	-0.147 (-0.219,-0.075)	ARHGAP10
G rs6485690	6.36E-05	chr11	46755207	0.643	-0.088 (-0.131,-0.045)	CKAP5, LRP4
G rs2232965	6.55E-05	chr19	18287950	0.795	0.106 (0.054,0.159)	LSM4
T rs524410	6.56E-05	chr6	159418118	0.442	0.085 (0.043,0.127)	TAGAP
C rs10008779	6.91E-05	chr4	168473476	0.507	-0.084 (-0.126,-0.043)	SPOCK3, CR614646 MSH3, DHFR, RASGRF2
G rs33013	6.96E-05	chr5	80095772	0.601	-0.086 (-0.129,-0.044)	
T rs5896	7.20E-05	chr11	46701579	0.151	0.117 (0.059,0.175)	F2, LRP4
T rs5936694	7.42E-05	chrX	68612237	0.710	0.086 (0.044,0.129)	TMEM28
T rs12143926	7.46E-05	chr1	88276958	0.606	-0.086 (-0.128,-0.043)	
G rs7753676	7.48E-05	chr6	151918508	0.374	-0.086 (-0.128,-0.043)	ESR1, C6orf97
G rs7622520	7.71E-05	chr3	67279910	0.441	0.085 (0.043,0.127)	KBTBD8, SUCLG2 FLJ42408, ZNF330, IL15
T rs10003871	7.92E-05	chr4	142479872	0.641	-0.087 (-0.130,-0.044)	
T rs4507007	7.95E-05	chr18	57537499	0.868	0.123 (0.062,0.185)	CDH20, RNF152
T rs10510248	8.12E-05	chr3	3023519	0.757	0.096 (0.048,0.144)	CNTN4, IL5RA

\* Build 36 position

+ Effect on each allele of the SNP on standardized BMD, given as SD units, with 95% confidence intervals

Supplementary Table 3A

## Spine BMD association analysis for all SNPs in replication effort

SNP	Pos.*	Freq.	Iceland effect	<i>P</i> Iceland	Denmark effect	Australia effect	DK and AUS combined effect	DK and AUS <i>P</i> value	Overall combined effect	<i>P</i> value
A rs7524102	C1_22571034	0.817	-0.13 (-0.17, -0.08)	1.78E-07	-0.12 (-0.21, -0.02)	-0.04 (-0.14, 0.07)	-0.09 (-0.15, -0.02)	0.012	-0.11 (-0.15, -0.07)	9.22E-09
G rs6696981	C1_22575445	0.858	-0.14 (-0.19, -0.08)	2.85E-07	-0.11 (-0.22, 0.00)	-0.01 (-0.14, 0.12)	-0.07 (-0.15, 0.01)	0.083	-0.12 (-0.16, -0.07)	1.69E-07
T rs4516411	C2_39322180	0.930	0.05 (-0.02, 0.12)	0.20	0.01 (-0.12, 0.13)	-0.01 (-0.15, 0.13)	-0.00 (-0.06, 0.06)	0.97	0.03 (-0.03, 0.09)	0.29
C rs7595929	C2_54479744	0.640	-0.09 (-0.13, -0.05)	5.64E-06	0.02 (-0.05, 0.10)	0.01 (-0.08, 0.10)	0.02 (-0.03, 0.07)	0.46	-0.06 (-0.09, -0.02)	0.00073
G rs4315567	C2_54509448	0.685	-0.10 (-0.14, -0.06)	6.38E-07	0.04 (-0.03, 0.11)	-0.02 (-0.11, 0.06)	0.02 (-0.04, 0.07)	0.54	-0.06 (-0.10, -0.03)	0.00014
G rs11898505	C2_54538061	0.674	-0.10 (-0.14, -0.06)	2.03E-07	-0.02 (-0.09, 0.06)	-0.04 (-0.13, 0.04)	-0.03 (-0.08, 0.02)	0.28	-0.08 (-0.11, -0.05)	8.4E-07
G rs10497621	C2_183705688	0.087	0.08 (0.01, 0.14)	0.021	-0.04 (-0.17, 0.09)	0.04 (-0.13, 0.21)	-0.01 (-0.11, 0.09)	0.86	0.05 (-0.00, 0.10)	0.067
T rs10510248	C3_3023519	0.767	0.02 (-0.03, 0.06)	0.45	0.02 (-0.10, 0.07)	-0.04 (-0.15, 0.08)	-0.02 (-0.08, 0.04)	0.51	0.01 (-0.03, 0.05)	0.77
C rs2872375	C3_78378354	0.683	-0.07 (-0.11, -0.03)	0.00022	-0.02 (-0.09, 0.06)	-0.04 (-0.13, 0.05)	-0.03 (-0.08, 0.02)	0.30	-0.06 (-0.09, -0.03)	0.00026
G rs1398330	C3_78405572	0.767	-0.09 (-0.13, -0.05)	0.000036	-0.03 (-0.11, 0.05)	-0.06 (-0.16, 0.04)	-0.04 (-0.10, 0.02)	0.16	-0.08 (-0.11, -0.04)	0.000025
G rs1350929	C3_111951197	0.557	-0.04 (-0.08, -0.00)	0.040	-0.04 (-0.11, 0.03)	-0.05 (-0.13, 0.03)	-0.04 (-0.09, 0.00)	0.073	-0.04 (-0.07, -0.01)	0.0069
T rs3851406	C3_169807659	0.907	-0.12 (-0.18, -0.06)	0.00017	-0.02 (-0.12, 0.09)	-0.02 (-0.16, 0.12)	-0.02 (-0.09, 0.06)	0.66	-0.09 (-0.14, -0.04)	0.00071
T rs4692511	C4_30973757	0.147	0.03 (-0.02, 0.08)	0.22	0.05 (-0.05, 0.15)	0.06 (-0.06, 0.17)	0.05 (-0.02, 0.12)	0.14	0.04 (-0.00, 0.08)	0.068
G rs7676236	C4_102793390	0.323	-0.05 (-0.09, -0.01)	0.0071	-0.02 (-0.10, 0.05)	-0.02 (-0.11, 0.07)	-0.02 (-0.07, 0.03)	0.46	-0.04 (-0.08, -0.01)	0.0078
T rs2043644	C4_148959669	0.086	-0.09 (-0.15, -0.02)	0.0085	-0.00 (-0.11, 0.11)	0.06 (-0.12, 0.24)	0.02 (-0.07, 0.11)	0.67	-0.06 (-0.12, -0.00)	0.040
C rs1265159	C6_31248026	0.803	-0.07 (-0.12, -0.03)	0.0019	-0.07 (-0.15, 0.02)	-0.02 (-0.11, 0.07)	-0.05 (-0.11, 0.01)	0.11	-0.07 (-0.10, -0.03)	0.00050
A rs3132453	C6_31712023	0.106	-0.10 (-0.16, -0.04)	0.00090	0.02 (-0.10, 0.14)	0.00 (-0.14, 0.14)	0.01 (-0.07, 0.09)	0.79	-0.06 (-0.11, -0.02)	0.0090
G rs12198173	C6_32134786	0.922	-0.10 (-0.17, -0.03)	0.0058	-0.02 (-0.16, 0.11)	-0.17 (-0.35, 0.01)	-0.07 (-0.16, 0.03)	0.16	-0.09 (-0.15, -0.03)	0.0020
C rs13199524	C6_32174743	0.922	-0.10 (-0.17, -0.03)	0.0038	-0.03 (-0.17, 0.11)	-0.14 (-0.29, 0.02)	-0.07 (-0.16, 0.02)	0.12	-0.09 (-0.15, -0.04)	0.0011
T rs3130340	C6_32352605	0.787	-0.10 (-0.14, -0.05)	0.000014	-0.12 (-0.20, -0.04)	-0.04 (-0.14, 0.05)	-0.09 (-0.15, -0.03)	0.0024	-0.10 (-0.13, -0.06)	1.17E-07
T rs6899351	C6_123150805	0.699	0.06 (0.02, 0.10)	0.0036	-0.04 (-0.12, 0.04)	-0.08 (-0.17, 0.01)	-0.05 (-0.11, -0.00)	0.041	0.02 (-0.01, 0.06)	0.20
C rs9479055	C6_151889660	0.348	-0.08 (-0.12, -0.04)	0.000023	-0.06 (-0.13, 0.01)	-0.07 (-0.16, 0.01)	-0.07 (-0.11, -0.02)	0.0086	-0.08 (-0.11, -0.05)	6.22E-07
T rs4463269	C6_151903921	0.245	-0.06 (-0.10, -0.01)	0.010	-0.05 (-0.13, 0.02)	-0.15 (-0.24, -0.06)	-0.09 (-0.14, -0.04)	0.00053	-0.07 (-0.10, -0.03)	0.000050
A rs3734803	C6_151911338	0.158	-0.07 (-0.12, -0.03)	0.0030	-0.15 (-0.25, -0.06)	-0.11 (-0.21, -0.00)	-0.13 (-0.20, -0.07)	0.000030	-0.09 (-0.13, -0.06)	1.68E-06
T rs4869738	C6_151933844	0.181	-0.08 (-0.13, -0.04)	0.00034	-0.03 (-0.12, 0.06)	-0.13 (-0.23, -0.04)	-0.07 (-0.13, -0.02)	0.013	-0.08 (-0.12, -0.04)	0.000013
T rs4870044	C6_151943102	0.281	-0.12 (-0.16, -0.08)	8.07E-09	-0.11 (-0.19, -0.03)	-0.07 (-0.16, 0.02)	-0.10 (-0.15, -0.04)	0.00048	-0.11 (-0.14, -0.08)	1.62E-11
G rs1038304	C6_151974868	0.469	-0.12 (-0.16, -0.08)	6.67E-11	-0.05 (-0.12, 0.02)	-0.06 (-0.14, 0.03)	-0.05 (-0.10, -0.00)	0.035	-0.10 (-0.13, -0.07)	3.97E-11
A rs6929137	C6_151978370	0.298	-0.12 (-0.16, -0.08)	6.54E-09	-0.08 (-0.15, -0.00)	-0.06 (-0.14, 0.03)	-0.07 (-0.12, -0.02)	0.0066	-0.10 (-0.13, -0.07)	2.45E-10
A rs7751941	C6_151988351	0.214	-0.13 (-0.17, -0.08)	2.12E-08	-0.06 (-0.14, 0.03)	-0.03 (-0.13, 0.07)	-0.05 (-0.10, 0.01)	0.11	-0.10 (-0.14, -0.07)	2.72E-08
A rs852003	C6_152003895	0.560	-0.10 (-0.13, -0.06)	3.29E-07	-0.03 (-0.10, 0.04)	-0.04 (-0.12, 0.05)	-0.03 (-0.08, 0.01)	0.16	-0.08 (-0.11, -0.05)	4.68E-07
G rs712219	C6_152020132	0.597	-0.10 (-0.13, -0.06)	4.25E-07	-0.02 (-0.09, 0.05)	-0.04 (-0.13, 0.04)	-0.03 (-0.08, 0.02)	0.24	-0.08 (-0.11, -0.05)	9.95E-07
T rs851993	C6_152047704	0.612	-0.09 (-0.13, -0.06)	1.14E-06	-0.03 (-0.10, 0.04)	0.01 (-0.08, 0.09)	-0.01 (-0.06, 0.04)	0.63	-0.07 (-0.10, -0.04)	0.000015
C rs3020331	C6_152050473	0.555	-0.12 (-0.16, -0.09)	3.12E-11	-0.01 (-0.08, 0.06)	-0.01 (-0.09, 0.08)	-0.01 (-0.06, 0.04)	0.74	-0.09 (-0.12, -0.06)	1.05E-08
T rs851982	C6_152066678	0.602	-0.13 (-0.17, -0.09)	7.23E-12	-0.00 (-0.08, 0.07)	0.01 (-0.08, 0.09)	0.00 (-0.04, 0.04)	0.96	-0.09 (-0.12, -0.06)	1.46E-08
G rs1159327	C6_152089715	0.714	-0.09 (-0.13, -0.05)	0.000025	0.04 (-0.04, 0.12)	-0.05 (-0.15, 0.04)	0.00 (-0.07, 0.08)	0.92	-0.06 (-0.09, -0.03)	0.00058
C rs1999805	C6_152110057	0.437	-0.10 (-0.13, -0.06)	3.78E-07	-0.06 (-0.13, 0.01)	-0.07 (-0.16, 0.02)	-0.06 (-0.11, -0.01)	0.015	-0.09 (-0.12, -0.06)	2.22E-08
T rs2504070	C6_152126666	0.316	-0.09 (-0.13, -0.05)	0.000013	0.04 (-0.04, 0.12)	0.00 (-0.09, 0.10)	0.03 (-0.03, 0.08)	0.34	-0.05 (-0.09, -0.02)	0.0019

A rs2504063	C6_152132400	0.381	-0.11 (-0.15, -0.07)	3.59E-09	-0.04 (-0.11, 0.03)	-0.04 (-0.12, 0.04)	-0.04 (-0.09, 0.01)	0.10	-0.09 (-0.12, -0.06)	6.05E-09
G rs2504065	C6_152136860	0.489	-0.10 (-0.13, -0.06)	2.27E-07	-0.03 (-0.10, 0.04)	-0.03 (-0.11, 0.04)	-0.03 (-0.08, 0.01)	0.17	-0.08 (-0.11, -0.05)	4.11E-07
A rs10505328	C8_119219639	0.506	-0.09 (-0.12, -0.05)	2.37E-06	0.04 (-0.03, 0.11)	0.02 (-0.08, 0.11)	0.03 (-0.02, 0.08)	0.22	-0.05 (-0.08, -0.02)	0.00093
A rs6469804	C8_120114010	0.510	-0.14 (-0.17, -0.10)	3.19E-13	-0.07 (-0.14, -0.00)	-0.08 (-0.16, 0.00)	-0.07 (-0.12, -0.03)	0.0020	-0.12 (-0.15, -0.09)	7.42E-15
C rs6993813	C8_120121419	0.496	-0.14 (-0.17, -0.10)	1.71E-13	-0.08 (-0.14, -0.01)	-0.05 (-0.14, 0.03)	-0.07 (-0.12, -0.02)	0.0062	-0.12 (-0.15, -0.09)	1.78E-14
G rs7024345	C9_99635059	0.716	0.02 (-0.02, 0.06)	0.31	0.00 (-0.11, 0.11)	0.04 (-0.05, 0.13)	0.02 (-0.04, 0.07)	0.52	0.02 (-0.01, 0.05)	0.23
A rs10125592	C9_122201556	0.851	-0.11 (-0.16, -0.06)	0.000021	0.00 (-0.10, 0.10)	-0.04 (-0.16, 0.08)	-0.03 (-0.11, 0.06)	0.53	-0.09 (-0.14, -0.05)	0.000042
C rs3780674	C9_122206740	0.851	-0.11 (-0.16, -0.06)	0.000016	-0.02 (-0.11, 0.08)	-0.02 (-0.13, 0.10)	-0.02 (-0.08, 0.05)	0.66	-0.08 (-0.12, -0.04)	0.00012
C rs7028896	C9_132521981	0.937	-0.13 (-0.20, -0.05)	0.00066	0.01 (-0.11, 0.14)	-0.09 (-0.23, 0.05)	-0.03 (-0.10, 0.05)	0.52	-0.10 (-0.16, -0.04)	0.0014
C rs11246386	C11_1034938	0.768	-0.11 (-0.15, -0.06)	9.68E-07	0.01 (-0.07, 0.09)	-0.06 (-0.16, 0.04)	-0.02 (-0.07, 0.04)	0.59	-0.08 (-0.12, -0.04)	9.91E-06
T rs5896	C11_46701579	0.151	0.01 (-0.04, 0.06)	0.65	-0.02 (-0.12, 0.08)	0.07 (-0.06, 0.19)	0.02 (-0.05, 0.09)	0.67	0.01 (-0.03, 0.05)	0.54
G rs2306033	C11_46854022	0.854	-0.02 (-0.08, 0.03)	0.36	0.01 (-0.09, 0.11)	-0.09 (-0.22, 0.04)	-0.03 (-0.10, 0.04)	0.42	-0.03 (-0.07, 0.02)	0.23
T rs11039024	C11_46879744	0.159	0.01 (-0.04, 0.06)	0.69	-0.04 (-0.14, 0.06)	0.06 (-0.06, 0.17)	-0.00 (-0.16, 0.16)	0.98	0.01 (-0.03, 0.05)	0.75
G rs10838635	C11_46901803	0.240	0.03 (-0.01, 0.07)	0.15	-0.01 (-0.10, 0.07)	0.08 (-0.01, 0.18)	0.02 (-0.03, 0.08)	0.40	0.03 (-0.00, 0.06)	0.094
T rs11600292	C11_46915274	0.760	-0.03 (-0.07, 0.02)	0.24	0.01 (-0.07, 0.10)	-0.09 (-0.18, 0.01)	-0.02 (-0.08, 0.03)	0.37	-0.03 (-0.06, 0.01)	0.14
G rs7935346	C11_46964955	0.769	-0.02 (-0.07, 0.02)	0.32	-0.02 (-0.10, 0.07)	-0.08 (-0.19, 0.02)	-0.04 (-0.10, 0.01)	0.14	-0.03 (-0.06, 0.01)	0.10
G rs7121418	C11_47121682	0.349	0.01 (-0.03, 0.05)	0.54	0.02 (-0.06, 0.09)	0.02 (-0.07, 0.11)	0.02 (-0.03, 0.07)	0.48	0.01 (-0.02, 0.04)	0.37
G rs2279439	C11_47153558	0.754	-0.02 (-0.06, 0.02)	0.41	-0.02 (-0.11, 0.06)	-0.08 (-0.18, 0.02)	-0.04 (-0.10, 0.01)	0.13	-0.03 (-0.06, 0.01)	0.13
A rs2016266	C12_52014222	0.685	-0.08 (-0.12, -0.04)	0.000026	-0.08 (-0.17, 0.02)	- (-,-)	-0.08 (-0.16, 0.01)	0.069	-0.08 (-0.12, -0.05)	4.66E-06
A rs10876432	C12_52018158	0.726	-0.12 (-0.16, -0.07)	4.00E-07	-0.04 (-0.12, 0.04)	-0.04 (-0.13, 0.06)	-0.04 (-0.10, 0.02)	0.19	-0.09 (-0.13, -0.06)	9.33E-07
A rs7992970	C13_41843463	0.779	-0.14 (-0.19, -0.10)	2.30E-10	-0.04 (-0.13, 0.04)	-0.07 (-0.16, 0.03)	-0.05 (-0.11, 0.00)	0.062	-0.11 (-0.15, -0.08)	2.71E-10
4 rs9594738	C13_41850145	0.562	-0.19 (-0.24, -0.14)	1.45E-14	-0.18 (-0.25, -0.11)	-0.09 (-0.17, -0.00)	-0.14 (-0.19, -0.09)	1.81E-08	-0.17 (-0.21, -0.14)	1.96E-21
A rs10507508	C13_41867782	0.947	-0.18 (-0.26, -0.10)	0.000012	-0.15 (-0.31, 0.01)	-0.15 (-0.35, 0.05)	-0.15 (-0.26, -0.04)	0.0092	-0.17 (-0.24, -0.11)	3.64E-07
T rs9594759	C13_41930593	0.624	-0.14 (-0.17, -0.10)	2.17E-12	-0.14 (-0.21, -0.07)	-0.07 (-0.15, 0.01)	-0.11 (-0.16, -0.06)	9.70E-06	-0.13 (-0.16, -0.10)	1.07E-16
A rs3783833	C14_90505343	0.853	-0.10 (-0.15, -0.05)	0.000088	0.02 (-0.07, 0.11)	-0.08 (-0.19, 0.02)	-0.02 (-0.08, 0.04)	0.47	-0.08 (-0.12, -0.04)	0.00024
A rs1286077	C14_90516137	0.866	-0.11 (-0.17, -0.06)	0.000030	0.04 (-0.05, 0.13)	-0.05 (-0.16, 0.06)	0.00 (-0.05, 0.05)	0.89	-0.08 (-0.12, -0.03)	0.00063
C rs884013	C18_44710128	0.925	-0.08 (-0.15, -0.00)	0.036	0.04 (-0.10, 0.18)	-0.13 (-0.30, 0.04)	-0.03 (-0.12, 0.07)	0.60	-0.06 (-0.12, -0.00)	0.042
C rs713485	C18_57421905	0.331	-0.09 (-0.13, -0.05)	2.22E-06	-0.00 (-0.09, 0.09)	-0.00 (-0.12, 0.11)	-0.00 (-0.07, 0.06)	0.95	-0.07 (-0.10, -0.03)	0.000071
A rs1377172	C18_57447361	0.327	-0.09 (-0.13, -0.05)	3.26E-06	0.01 (-0.09, 0.11)	- (-,-)	0.01 (-0.08, 0.10)	0.82	-0.08 (-0.12, -0.04)	0.000017
C rs4507007	C18_57537499	0.123	-0.12 (-0.17, -0.07)	0.000016	-0.03 (-0.13, 0.08)	-0.05 (-0.18, 0.08)	-0.04 (-0.11, 0.04)	0.34	-0.09 (-0.14, -0.05)	0.000034
A rs3018362	C18_58233073	0.354	-0.07 (-0.11, -0.04)	0.00014	-0.03 (-0.10, 0.05)	-0.07 (-0.15, 0.02)	-0.04 (-0.09, 0.01)	0.097	-0.06 (-0.09, -0.03)	0.000044
A rs2232965	C19_18287950	0.198	-0.06 (-0.11, -0.02)	0.0068	-0.03 (-0.12, 0.05)	0.07 (-0.04, 0.17)	0.00 (-0.04, 0.04)	0.86	-0.04 (-0.08, -0.00)	0.031
T rs209956	C20_52156263	0.723	0.05 (0.01, 0.09)	0.020	-0.02 (-0.10, 0.06)	-0.02 (-0.11, 0.07)	-0.02 (-0.07, 0.04)	0.50	0.03 (-0.01, 0.06)	0.12
C rs4810077	C20_55477509	0.351	-0.07 (-0.11, -0.03)	0.00034	-0.00 (-0.08, 0.07)	0.08 (-0.01, 0.17)	0.03 (-0.02, 0.08)	0.25	-0.04 (-0.07, -0.01)	0.017
A rs1006899	C21_14766923	0.838	-0.13 (-0.18, -0.08)	5.35E-07	-0.02 (-0.11, 0.07)	0.00 (-0.12, 0.12)	-0.01 (-0.07, 0.05)	0.77	-0.09 (-0.13, -0.05)	0.000014
T rs2244352	C21_39679843	0.332	-0.06 (-0.10, -0.03)	0.0012	-0.01 (-0.09, 0.06)	-0.01 (-0.11, 0.09)	-0.01 (-0.07, 0.04)	0.66	-0.05 (-0.08, -0.02)	0.0030
C rs9306419	C22_24699358	0.873	-0.12 (-0.17, -0.06)	0.000040	-0.07 (-0.18, 0.05)	-0.08 (-0.25, 0.09)	-0.07 (-0.16, 0.02)	0.12	-0.11 (-0.15, -0.06)	0.000013

\* Positions are Build36 coordinates; Allele frequencies are shown and effect on BMD as standard deviations. All P values are two-sided.

Supplementary Table 3B

## Hip BMD association analysis for all SNPs in replication effort

SNP	Pos.*	Freq.	Iceland effect	P Iceland	Denmark effect	Australia effect	DK and AUS combined effect	DK and AUS P value	Overall combined effect	P value
A rs7524102	C1_22571034	0.817	-0.15 (-0.20, -0.11)	7.45E-12	-0.14 (-0.23, -0.04)	-0.15 (-0.25, -0.04)	-0.14 (-0.20, -0.08)	0.000014	-0.15 (-0.19, -0.11)	4.97E-16
G rs6696981	C1_22575445	0.858	-0.16 (-0.21, -0.11)	2.79E-10	-0.12 (-0.23, -0.02)	-0.10 (-0.23, 0.02)	-0.11 (-0.19, -0.04)	0.0023	-0.14 (-0.19, -0.10)	3.82E-12
G rs4516411	C2_39322180	0.070	-0.09 (-0.16, -0.03)	0.0064	0.00 (-0.16, 0.17)	0.06 (-0.08, 0.19)	0.02 (-0.05, 0.10)	0.55	-0.06 (-0.12, -0.00)	0.049
T rs7595929	C2_54479744	0.360	0.04 (0.01, 0.08)	0.019	-0.06 (-0.13, 0.01)	0.05 (-0.04, 0.13)	-0.02 (-0.07, 0.03)	0.51	0.02 (-0.01, 0.06)	0.11
G rs4315567	C2_54509448	0.685	-0.06 (-0.10, -0.02)	0.0019	0.04 (-0.03, 0.11)	-0.10 (-0.19, -0.02)	-0.01 (-0.06, 0.03)	0.53	-0.05 (-0.08, -0.02)	0.0033
G rs11898505	C2_54538061	0.674	-0.05 (-0.09, -0.01)	0.0086	-0.03 (-0.10, 0.04)	-0.10 (-0.18, -0.01)	-0.05 (-0.10, 0.01)	0.029	-0.04 (-0.07, -0.01)	0.00069
A rs10497621	C2_183705688	0.913	-0.11 (-0.17, -0.05)	0.00024	0.05 (-0.08, 0.17)	-0.11 (-0.28, 0.05)	-0.01 (-0.11, 0.08)	0.80	-0.08 (-0.13, -0.03)	0.0013
C rs10510248	C3_3023519	0.233	-0.06 (-0.10, -0.02)	0.0015	-0.02 (-0.10, 0.06)	0.03 (-0.09, 0.15)	-0.00 (-0.05, 0.05)	0.94	-0.05 (-0.08, -0.01)	0.0060
C rs2872375	C3_78378354	0.683	-0.03 (-0.06, 0.01)	0.17	0.00 (-0.07, 0.07)	0.03 (-0.06, 0.11)	0.01 (-0.04, 0.06)	0.69	-0.01 (-0.05, 0.02)	0.36
T rs1398330	C3_78405572	0.233	0.03 (-0.01, 0.07)	0.14	0.01 (-0.07, 0.09)	-0.01 (-0.11, 0.09)	0.00 (-0.05, 0.06)	0.96	0.02 (-0.01, 0.06)	0.21
T rs1350929	C3_111951197	0.443	-0.00 (-0.04, 0.03)	0.96	0.04 (-0.03, 0.10)	0.04 (-0.04, 0.12)	0.04 (-0.01, 0.08)	0.11	0.01 (-0.01, 0.04)	0.41
T rs3851406	C3_169807659	0.907	-0.07 (-0.13, -0.01)	0.029	-0.01 (-0.12, 0.09)	0.11 (-0.03, 0.24)	0.04 (-0.04, 0.11)	0.38	-0.04 (-0.09, 0.02)	0.18
C rs4692511	C4_30973757	0.853	-0.10 (-0.15, -0.05)	0.000057	-0.03 (-0.13, 0.07)	-0.04 (-0.15, 0.08)	-0.03 (-0.10, 0.04)	0.36	-0.08 (-0.12, -0.04)	0.00011
G rs7676236	C4_102793390	0.323	-0.07 (-0.10, -0.03)	0.00033	-0.00 (-0.08, 0.07)	-0.02 (-0.11, 0.07)	-0.01 (-0.06, 0.04)	0.67	-0.05 (-0.08, -0.02)	0.0012
T rs2043644	C4_148959669	0.086	-0.10 (-0.16, -0.04)	0.0016	0.00 (-0.11, 0.11)	0.13 (-0.04, 0.30)	0.05 (-0.05, 0.14)	0.33	-0.06 (-0.11, -0.01)	0.025
C rs1265159	C6_31248026	0.803	-0.07 (-0.11, -0.03)	0.0015	-0.08 (-0.16, 0.00)	-0.01 (-0.10, 0.09)	-0.05 (-0.11, 0.01)	0.082	-0.06 (-0.10, -0.03)	0.00031
A rs3132453	C6_31712023	0.106	-0.07 (-0.12, -0.02)	0.011	0.00 (-0.12, 0.13)	-0.06 (-0.19, 0.08)	-0.02 (-0.10, 0.06)	0.59	-0.06 (-0.10, -0.01)	0.016
G rs12198173	C6_32134786	0.922	-0.08 (-0.15, -0.02)	0.015	-0.08 (-0.21, 0.05)	0.05 (-0.13, 0.24)	-0.04 (-0.14, 0.06)	0.47	-0.07 (-0.13, -0.01)	0.014
C rs13199524	C6_32174743	0.922	-0.09 (-0.15, -0.02)	0.011	-0.07 (-0.20, 0.06)	0.03 (-0.13, 0.18)	-0.03 (-0.13, 0.06)	0.50	-0.07 (-0.13, -0.02)	0.012
T rs3130340	C6_32352605	0.787	-0.06 (-0.10, -0.01)	0.010	-0.06 (-0.14, 0.02)	0.01 (-0.09, 0.11)	-0.03 (-0.09, 0.03)	0.30	-0.05 (-0.08, -0.01)	0.0065
T rs6899351	C6_123150805	0.699	0.04 (0.01, 0.08)	0.019	-0.06 (-0.13, 0.02)	-0.04 (-0.13, 0.05)	-0.05 (-0.10, 0.00)	0.060	0.02 (-0.02, 0.05)	0.35
C rs9479055	C6_151889660	0.348	-0.09 (-0.12, -0.05)	1.74E-06	-0.06 (-0.13, 0.01)	-0.08 (-0.17, -0.00)	-0.07 (-0.12, -0.02)	0.0050	-0.08 (-0.11, -0.05)	3.05E-08
T rs4463269	C6_151903921	0.245	-0.09 (-0.13, -0.05)	0.000022	-0.03 (-0.10, 0.05)	-0.13 (-0.21, -0.04)	-0.07 (-0.12, -0.02)	0.0095	-0.08 (-0.11, -0.05)	6.76E-07
A rs3734803	C6_151911338	0.158	-0.09 (-0.13, -0.04)	0.00027	-0.11 (-0.20, -0.02)	-0.07 (-0.17, 0.03)	-0.09 (-0.16, -0.03)	0.0032	-0.09 (-0.13, -0.05)	3.16E-06
T rs4869738	C6_151933844	0.181	-0.09 (-0.13, -0.05)	0.000053	-0.00 (-0.08, 0.08)	-0.15 (-0.25, -0.06)	-0.06 (-0.12, -0.01)	0.030	-0.08 (-0.12, -0.05)	4.74E-06
T rs4870044	C6_151943102	0.281	-0.08 (-0.12, -0.05)	0.000014	-0.11 (-0.19, -0.04)	-0.03 (-0.11, 0.06)	-0.08 (-0.13, -0.03)	0.0032	-0.08 (-0.11, -0.05)	1.56E-07
G rs1038304	C6_151974868	0.469	-0.11 (-0.14, -0.07)	6.72E-10	-0.04 (-0.11, 0.02)	-0.01 (-0.09, 0.07)	-0.03 (-0.08, 0.02)	0.21	-0.08 (-0.11, -0.06)	5.26E-09
A rs6929137	C6_151978370	0.298	-0.10 (-0.14, -0.07)	3.05E-08	-0.04 (-0.11, 0.03)	-0.02 (-0.11, 0.06)	-0.03 (-0.08, 0.02)	0.20	-0.08 (-0.11, -0.05)	1.03E-07
A rs7751941	C6_151988351	0.214	-0.11 (-0.15, -0.06)	5.18E-07	-0.07 (-0.15, 0.01)	-0.01 (-0.11, 0.09)	-0.05 (-0.11, 0.01)	0.085	-0.09 (-0.12, -0.06)	2.67E-07
A rs852003	C6_152003895	0.560	-0.10 (-0.13, -0.06)	2.63E-08	-0.02 (-0.08, 0.05)	0.02 (-0.06, 0.10)	-0.00 (-0.05, 0.05)	0.94	-0.07 (-0.10, -0.04)	2.59E-06
G rs712219	C6_152020132	0.597	-0.10 (-0.14, -0.07)	7.87E-09	-0.01 (-0.08, 0.06)	0.01 (-0.07, 0.10)	0.00 (-0.01, 0.01)	1.00	-0.07 (-0.10, -0.04)	1.04E-06
T rs851993	C6_152047704	0.612	-0.09 (-0.13, -0.06)	2.22E-07	-0.02 (-0.08, 0.05)	0.02 (-0.06, 0.11)	-0.00 (-0.05, 0.05)	0.98	-0.06 (-0.09, -0.04)	0.000014
C rs3020331	C6_152050473	0.555	-0.11 (-0.15, -0.08)	3.79E-11	-0.01 (-0.08, 0.06)	-0.00 (-0.09, 0.09)	-0.01 (-0.06, 0.04)	0.73	-0.08 (-0.11, -0.05)	1.06E-08
T rs851982	C6_152066678	0.602	-0.11 (-0.15, -0.08)	8.81E-11	-0.01 (-0.08, 0.06)	-0.01 (-0.09, 0.08)	-0.01 (-0.06, 0.04)	0.72	-0.08 (-0.11, -0.05)	2.10E-08
G rs1159327	C6_152089715	0.714	-0.07 (-0.11, -0.04)	0.00014	0.03 (-0.04, 0.11)	0.00 (-0.08, 0.08)	0.02 (-0.04, 0.07)	0.50	-0.05 (-0.08, -0.01)	0.0051
C rs199805	C6_152110057	0.437	-0.07 (-0.11, -0.04)	0.000048	-0.01 (-0.08, 0.06)	-0.03 (-0.12, 0.06)	-0.02 (-0.07, 0.03)	0.45	-0.06 (-0.09, -0.03)	0.00012
T rs2504070	C6_152126666	0.316	-0.04 (-0.07, 0.00)	0.061	0.02 (-0.06, 0.09)	-0.01 (-0.10, 0.08)	0.01 (-0.05, 0.06)	0.80	-0.02 (-0.05, 0.01)	0.15



A rs2504063	C6_152132400	0.381	-0.07 (-0.11, -0.04)	0.000046	-0.03 (-0.10, 0.04)	-0.02 (-0.10, 0.06)	-0.02 (-0.07, 0.02)	0.32	-0.06 (-0.09, -0.03)	0.000079
G rs2504065	C6_152136860	0.489	-0.06 (-0.09, -0.02)	0.000078	-0.01 (-0.08, 0.06)	-0.04 (-0.12, 0.04)	-0.02 (-0.07, 0.03)	0.39	-0.05 (-0.07, -0.02)	0.0010
G rs10505328	C8_119219639	0.494	0.04 (0.00, 0.07)	0.042	-0.02 (-0.09, 0.05)	-0.08 (-0.17, 0.01)	-0.04 (-0.09, 0.01)	0.10	0.01 (-0.02, 0.05)	0.40
A rs6469804	C8_120114010	0.510	-0.09 (-0.13, -0.06)	1.99E-07	-0.06 (-0.12, 0.00)	-0.08 (-0.16, -0.00)	-0.07 (-0.12, -0.02)	0.0032	-0.08 (-0.11, -0.06)	2.45E-09
C rs6993813	C8_120121419	0.496	-0.10 (-0.13, -0.06)	2.06E-08	-0.09 (-0.15, -0.02)	-0.08 (-0.17, 0.00)	-0.09 (-0.13, -0.04)	0.00039	-0.09 (-0.12, -0.07)	3.29E-11
A rs10125592	C9_122201556	0.851	-0.07 (-0.12, -0.03)	0.0024	0.03 (-0.15, 0.20)	-0.01 (-0.13, 0.11)	0.00 (-0.15, 0.15)	0.99	-0.06 (-0.10, -0.02)	0.0064
C rs3780674	C9_122206740	0.851	-0.08 (-0.12, -0.03)	0.0016	-0.00 (-0.10, 0.10)	-0.03 (-0.14, 0.09)	-0.01 (-0.08, 0.05)	0.70	-0.06 (-0.10, -0.02)	0.0043
C rs7028896	C9_132521981	0.937	-0.09 (-0.16, -0.02)	0.0089	-0.08 (-0.20, 0.04)	-0.10 (-0.24, 0.04)	-0.09 (-0.17, -0.01)	0.034	-0.09 (-0.14, -0.04)	0.00080
A rs7024345	C9_99635059	0.284	-0.09 (-0.13, -0.05)	3.04E-06	-0.02 (-0.10, 0.06)	0.00 (-0.10, 0.11)	-0.01 (-0.07, 0.04)	0.65	-0.07 (-0.10, -0.04)	0.000032
C rs11246386	C11_1034938	0.768	-0.07 (-0.11, -0.03)	0.0011	0.04 (-0.04, 0.12)	0.01 (-0.09, 0.11)	0.03 (-0.03, 0.08)	0.32	-0.04 (-0.08, -0.00)	0.026
C rs5896	C11_46701579	0.849	-0.09 (-0.13, -0.04)	0.00051	-0.05 (-0.15, 0.04)	-0.02 (-0.15, 0.10)	-0.04 (-0.11, 0.03)	0.25	-0.07 (-0.11, -0.03)	0.00039
G rs2306033	C11_46854022	0.854	-0.10 (-0.15, -0.05)	0.000092	-0.04 (-0.13, 0.06)	-0.09 (-0.21, 0.03)	-0.06 (-0.12, 0.01)	0.11	-0.08 (-0.12, -0.04)	0.000034
C rs11039024	C11_46879744	0.841	-0.07 (-0.12, -0.03)	0.0019	-0.01 (-0.10, 0.08)	-0.03 (-0.15, 0.09)	-0.02 (-0.08, 0.05)	0.61	-0.06 (-0.10, -0.02)	0.0040
A rs10838635	C11_46901803	0.760	-0.07 (-0.11, -0.03)	0.00043	-0.03 (-0.10, 0.05)	-0.04 (-0.14, 0.05)	-0.03 (-0.09, 0.02)	0.26	-0.06 (-0.09, -0.03)	0.00038
T rs11600292	C11_46915274	0.760	-0.07 (-0.11, -0.03)	0.0012	-0.05 (-0.12, 0.03)	-0.05 (-0.14, 0.05)	-0.05 (-0.10, 0.01)	0.11	-0.06 (-0.09, -0.03)	0.00032
G rs7935346	C11_46964955	0.769	-0.06 (-0.10, -0.02)	0.0027	-0.06 (-0.14, 0.02)	-0.06 (-0.16, 0.04)	-0.06 (-0.12, -0.00)	0.036	-0.06 (-0.10, -0.03)	0.00026
A rs7121418	C11_47121682	0.651	-0.04 (-0.08, -0.01)	0.020	-0.07 (-0.14, -0.00)	-0.02 (-0.10, 0.07)	-0.05 (-0.10, -0.00)	0.042	-0.05 (-0.07, -0.02)	0.0022
G rs2279439	C11_47153558	0.754	-0.05 (-0.09, -0.01)	0.011	-0.06 (-0.14, 0.02)	-0.06 (-0.16, 0.04)	-0.06 (-0.11, 0.00)	0.059	-0.05 (-0.09, -0.02)	0.0016
A rs2016266	C12_52014222	0.685	-0.04 (-0.08, -0.01)	0.021	-0.05 (-0.14, 0.03)	-	-0.05 (-0.13, 0.03)	0.21	-0.04 (-0.08, -0.01)	0.0088
A rs10876432	C12_52018158	0.726	-0.06 (-0.10, -0.02)	0.0053	-0.05 (-0.13, 0.03)	-0.01 (-0.11, 0.10)	-0.03 (-0.09, 0.03)	0.27	-0.05 (-0.08, -0.02)	0.0035
A rs7992970	C13_41843463	0.779	-0.10 (-0.14, -0.05)	4.83E-06	-0.04 (-0.11, 0.04)	-0.03 (-0.12, 0.07)	-0.03 (-0.09, 0.02)	0.25	-0.08 (-0.11, -0.04)	8.17E-06
T rs9594738	C13_41850145	0.562	-0.14 (-0.18, -0.09)	8.24E-09	-0.08 (-0.15, -0.01)	0.00 (-0.10, 0.11)	-0.05 (-0.10, 0.00)	0.063	-0.10 (-0.13, -0.06)	1.94E-08
A rs10507508	C13_41867782	0.947	-0.13 (-0.20, -0.05)	0.0011	-0.08 (-0.23, 0.08)	-0.23 (-0.42, -0.03)	-0.14 (-0.25, -0.03)	0.016	-0.13 (-0.19, -0.07)	0.000053
T rs9594759	C13_41930593	0.624	-0.09 (-0.12, -0.05)	1.64E-06	-0.07 (-0.14, -0.01)	0.03 (-0.05, 0.11)	-0.03 (-0.08, 0.02)	0.17	-0.07 (-0.10, -0.04)	2.07E-06
A rs3783833	C14_90505343	0.853	-0.09 (-0.14, -0.04)	0.00028	0.02 (-0.06, 0.11)	-0.05 (-0.15, 0.06)	-0.01 (-0.07, 0.06)	0.86	-0.06 (-0.10, -0.02)	0.0017
A rs1286077	C14_90516137	0.866	-0.09 (-0.14, -0.04)	0.00031	0.05 (-0.03, 0.14)	-0.02 (-0.13, 0.10)	0.03 (-0.04, 0.09)	0.41	-0.06 (-0.10, -0.01)	0.0099
C rs884013	C18_44710128	0.925	-0.12 (-0.19, -0.06)	0.00024	0.01 (-0.13, 0.15)	-0.20 (-0.37, -0.03)	-0.07 (-0.17, 0.02)	0.14	-0.11 (-0.16, -0.05)	0.00010
C rs713485	C18_57421905	0.331	-0.07 (-0.10, -0.03)	0.00034	0.01 (-0.06, 0.09)	0.00 (-0.09, 0.10)	0.01 (-0.04, 0.06)	0.68	-0.04 (-0.07, -0.01)	0.0057
A rs1377172	C18_57447361	0.327	-0.06 (-0.10, -0.03)	0.00078	-0.01 (-0.11, 0.09)	-	-0.01 (-0.10, 0.08)	0.79	-0.06 (-0.09, -0.02)	0.0011
C rs4507007	C18_57537499	0.123	-0.12 (-0.17, -0.07)	6.69E-06	0.00 (-0.11, 0.11)	0.11 (-0.02, 0.24)	0.04 (-0.03, 0.12)	0.23	-0.07 (-0.11, -0.03)	0.0016
A rs3018362	C18_58233073	0.354	-0.08 (-0.11, -0.04)	0.000024	-0.08 (-0.15, -0.01)	-0.03 (-0.12, 0.05)	-0.06 (-0.11, -0.01)	0.013	-0.07 (-0.10, -0.04)	9.85E-07
A rs2232965	C19_18287950	0.198	-0.09 (-0.14, -0.05)	0.000016	-0.04 (-0.12, 0.04)	-0.00 (-0.12, 0.11)	-0.03 (-0.09, 0.04)	0.41	-0.07 (-0.11, -0.04)	0.000049
C rs209956	C20_52156263	0.277	-0.07 (-0.11, -0.03)	0.00025	0.03 (-0.04, 0.11)	0.04 (-0.05, 0.13)	0.04 (-0.02, 0.09)	0.19	-0.04 (-0.07, -0.01)	0.019
T rs4810077	C20_55477509	0.649	0.04 (0.01, 0.08)	0.022	-0.02 (-0.09, 0.05)	-0.07 (-0.15, 0.01)	-0.04 (-0.09, 0.01)	0.14	0.02 (-0.01, 0.05)	0.25
A rs1006899	C21_14766923	0.838	-0.06 (-0.11, -0.01)	0.0099	0.00 (-0.09, 0.09)	0.02 (-0.09, 0.12)	0.01 (-0.05, 0.07)	0.78	-0.04 (-0.08, -0.00)	0.045
T rs2244352	C21_39679843	0.332	-0.02 (-0.06, 0.01)	0.22	-0.03 (-0.10, 0.04)	-0.00 (-0.08, 0.08)	-0.02 (-0.08, 0.04)	0.48	-0.02 (-0.05, 0.01)	0.16
C rs9306419	C22_24699358	0.873	-0.11 (-0.16, -0.06)	0.000053	-0.08 (-0.19, 0.04)	-0.05 (-0.22, 0.11)	-0.07 (-0.16, 0.02)	0.11	-0.10 (-0.14, -0.05)	0.000016

\* Positions are Build36 coordinates; Allele frequencies are shown and effect on BMD as standard deviations. All P values are two-sided.

Supplementary Table 4

## SNP association by gender (for overall combined analysis)

SNP	Position	Freq*	HipFemale effect	P value	HipMale effect	P value	SpineFemale effect	P value	SpineMale effect	P value
A rs7524102	C1_22571034	0.817	-0.16 (-0.20, -0.12)	1.4E-15	-0.10 (-0.18, -0.01)	0.034	-0.12 (-0.16, -0.07)	6.6E-08	-0.10 (-0.19, -0.00)	0.043
G rs6696981	C1_22575445	0.858	-0.16 (-0.20, -0.11)	5.6E-12	-0.09 (-0.19, 0.01)	0.083	-0.12 (-0.16, -0.07)	1.2E-06	-0.11 (-0.23, 0.00)	0.056
T rs4516411	C2_39322180	0.930	0.07 (0.01, 0.14)	0.029	0.01 (-0.11, 0.13)	0.89	0.05 (-0.01, 0.12)	0.100	-0.07 (-0.22, 0.07)	0.33
C rs7595929	C2_54479744	0.640	-0.01 (-0.05, 0.03)	0.64	-0.10 (-0.17, -0.03)	0.004	-0.05 (-0.09, -0.02)	0.0040	-0.08 (-0.16, 0.01)	0.078
G rs4315567	C2_54509448	0.685	-0.03 (-0.07, 0.00)	0.074	-0.11 (-0.18, -0.04)	0.002	-0.06 (-0.09, -0.02)	0.0019	-0.11 (-0.19, -0.02)	0.016
G rs11898505	C2_54538061	0.674	-0.03 (-0.06, 0.00)	0.082	-0.09 (-0.17, -0.02)	0.010	-0.07 (-0.10, -0.03)	0.00018	-0.11 (-0.20, -0.02)	0.012
G rs10497621	C2_183705688	0.087	0.10 (0.04, 0.15)	0.00041	0.00 (-0.12, 0.13)	0.94	0.06 (0.00, 0.12)	0.038	-0.01 (-0.16, 0.14)	0.87
T rs10510248	C3_3023519	0.767	0.05 (0.02, 0.09)	0.0035	0.01 (-0.06, 0.08)	0.82	0.01 (-0.03, 0.05)	0.69	-0.01 (-0.10, 0.08)	0.83
C rs2872375	C3_78378354	0.683	-0.02 (-0.05, 0.01)	0.24	0.01 (-0.07, 0.09)	0.77	-0.07 (-0.10, -0.03)	0.00017	-0.03 (-0.12, 0.06)	0.50
G rs1398330	C3_78405572	0.767	-0.02 (-0.06, 0.01)	0.23	-0.01 (-0.09, 0.06)	0.69	-0.08 (-0.11, -0.04)	8.6E-05	-0.07 (-0.17, 0.02)	0.12
G rs1350929	C3_111951197	0.557	-0.01 (-0.04, 0.02)	0.64	-0.03 (-0.09, 0.03)	0.33	-0.05 (-0.08, -0.02)	0.0025	0.00 (-0.12, 0.13)	0.97
T rs3851406	C3_169807659	0.907	-0.03 (-0.09, 0.02)	0.28	-0.06 (-0.20, 0.08)	0.40	-0.08 (-0.14, -0.03)	0.0032	-0.12 (-0.26, 0.02)	0.084
T rs4692511	C4_30973757	0.147	0.08 (0.04, 0.13)	0.00023	0.06 (-0.04, 0.16)	0.21	0.06 (0.01, 0.10)	0.015	-0.04 (-0.15, 0.07)	0.46
G rs7676236	C4_102793390	0.323	-0.05 (-0.08, -0.02)	0.0041	-0.06 (-0.13, 0.01)	0.12	-0.04 (-0.07, -0.00)	0.035	-0.07 (-0.15, 0.01)	0.092
T rs2043644	C4_148959669	0.086	-0.07 (-0.13, -0.01)	0.015	-0.00 (-0.01, 0.01)	0.98	-0.06 (-0.12, -0.00)	0.043	-0.06 (-0.22, 0.11)	0.52
C rs1265159	C6_31248026	0.803	-0.07 (-0.11, -0.03)	0.00030	-0.04 (-0.12, 0.05)	0.39	-0.06 (-0.10, -0.02)	0.0029	-0.09 (-0.19, 0.01)	0.085
A rs3132453	C6_31712023	0.106	-0.05 (-0.10, -0.00)	0.031	-0.06 (-0.17, 0.05)	0.30	-0.07 (-0.12, -0.01)	0.013	-0.06 (-0.19, 0.06)	0.33
G rs12198173	C6_32134786	0.922	-0.09 (-0.15, -0.03)	0.0054	0.01 (-0.08, 0.09)	0.88	-0.09 (-0.15, -0.02)	0.0065	-0.10 (-0.24, 0.04)	0.16
C rs13199524	C6_32174743	0.922	-0.09 (-0.15, -0.03)	0.0047	0.00 (-0.03, 0.04)	0.93	-0.09 (-0.15, -0.03)	0.0038	-0.10 (-0.24, 0.03)	0.14
T rs3130340	C6_32352605	0.787	-0.05 (-0.09, -0.02)	0.0049	-0.02 (-0.12, 0.08)	0.65	-0.10 (-0.14, -0.07)	1.2E-07	-0.06 (-0.16, 0.04)	0.26
T rs6899351	C6_123150805	0.699	0.02 (-0.02, 0.05)	0.38	0.01 (-0.06, 0.08)	0.74	0.02 (-0.01, 0.06)	0.22	0.02 (-0.06, 0.11)	0.61
C rs9479055	C6_151889660	0.348	-0.07 (-0.10, -0.04)	6.2E-06	-0.12 (-0.19, -0.05)	0.00075	-0.08 (-0.11, -0.04)	3.5E-06	-0.08 (-0.15, -0.00)	0.046
T rs4463269	C6_151903921	0.245	-0.07 (-0.10, -0.03)	0.00015	-0.14 (-0.22, -0.06)	0.00034	-0.06 (-0.09, -0.02)	0.00095	-0.10 (-0.18, -0.03)	0.0085
A rs3734803	C6_151911338	0.158	-0.08 (-0.12, -0.03)	0.00032	-0.15 (-0.24, -0.06)	0.00110	-0.09 (-0.13, -0.05)	3.2E-05	-0.11 (-0.20, -0.02)	0.021
T rs4869738	C6_151933844	0.181	-0.06 (-0.10, -0.03)	0.0011	-0.16 (-0.24, -0.08)	0.00014	-0.07 (-0.11, -0.03)	0.00101	-0.15 (-0.24, -0.06)	0.00084
T rs4870044	C6_151943102	0.281	-0.07 (-0.11, -0.04)	3.9E-05	-0.14 (-0.21, -0.06)	0.00042	-0.11 (-0.14, -0.07)	2.4E-09	-0.13 (-0.21, -0.05)	0.0016
G rs1038304	C6_151974868	0.469	-0.07 (-0.11, -0.04)	1.9E-06	-0.13 (-0.20, -0.06)	0.00025	-0.09 (-0.12, -0.06)	6.9E-08	-0.16 (-0.24, -0.08)	7.9E-05
A rs6929137	C6_151978370	0.298	-0.07 (-0.10, -0.04)	2.3E-05	-0.14 (-0.21, -0.06)	0.00032	-0.09 (-0.13, -0.06)	1.1E-07	-0.14 (-0.22, -0.06)	0.0010
A rs7751941	C6_151988351	0.214	-0.08 (-0.12, -0.04)	1.5E-05	-0.13 (-0.21, -0.04)	0.004	-0.09 (-0.13, -0.05)	2.3E-06	-0.14 (-0.23, -0.04)	0.0046
A rs852003	C6_152003895	0.560	-0.06 (-0.09, -0.03)	0.00028	-0.12 (-0.20, -0.05)	0.00087	-0.07 (-0.10, -0.04)	4.0E-05	-0.12 (-0.20, -0.04)	0.0024
G rs712219	C6_152020132	0.597	-0.07 (-0.10, -0.04)	4.0E-05	-0.10 (-0.18, -0.03)	0.007	-0.07 (-0.10, -0.04)	3.2E-05	-0.11 (-0.19, -0.03)	0.0084
T rs851993	C6_152047704	0.612	-0.05 (-0.09, -0.02)	0.00067	-0.11 (-0.19, -0.04)	0.003	-0.06 (-0.10, -0.03)	0.00020	-0.09 (-0.17, -0.01)	0.030
C rs3020331	C6_152050473	0.555	-0.08 (-0.11, -0.05)	1.1E-06	-0.11 (-0.19, -0.04)	0.002	-0.08 (-0.12, -0.05)	3.6E-07	-0.11 (-0.19, -0.03)	0.0066
T rs851982	C6_152066678	0.602	-0.08 (-0.11, -0.05)	6.4E-07	-0.10 (-0.17, -0.02)	0.010	-0.08 (-0.12, -0.05)	4.3E-07	-0.11 (-0.20, -0.03)	0.0084
G rs1159327	C6_152089715	0.714	-0.05 (-0.08, -0.02)	0.0046	-0.02 (-0.10, 0.06)	0.59	-0.07 (-0.10, -0.03)	0.00034	-0.02 (-0.11, 0.06)	0.57
C rs1999805	C6_152110057	0.437	-0.05 (-0.08, -0.02)	0.0018	-0.09 (-0.16, -0.02)	0.015	-0.08 (-0.11, -0.05)	6.6E-07	-0.11 (-0.18, -0.03)	0.0086
T rs2504070	C6_152126666	0.316	-0.03 (-0.06, 0.01)	0.13	-0.01 (-0.07, 0.06)	0.85	-0.06 (-0.10, -0.03)	0.00083	-0.01 (-0.12, 0.10)	0.84
A rs2504063	C6_152132400	0.381	-0.07 (-0.10, -0.04)	1.7E-05	-0.01 (-0.07, 0.06)	0.82	-0.09 (-0.12, -0.06)	4.7E-08	-0.08 (-0.16, -0.00)	0.048
G rs2504065	C6_152136860	0.489	-0.05 (-0.08, -0.02)	0.0012	-0.03 (-0.10, 0.04)	0.37	-0.07 (-0.10, -0.04)	2.0E-05	-0.11 (-0.18, -0.03)	0.0057

A rs10505328	C8_119219639	0.506	-0.01 (-0.05, 0.02)	0.39	-0.01 (-0.12, 0.10)	0.86	-0.04 (-0.07, -0.01)	0.023	-0.12 (-0.20, -0.04)	0.0043
A rs6469804	C8_120114010	0.510	-0.07 (-0.10, -0.04)	2.8E-06	-0.14 (-0.21, -0.07)	4.3E-05	-0.10 (-0.13, -0.07)	5.8E-10	-0.19 (-0.26, -0.11)	9.0E-07
C rs6993813	C8_120121419	0.496	-0.08 (-0.11, -0.05)	9.9E-08	-0.15 (-0.22, -0.08)	2.0E-05	-0.10 (-0.13, -0.07)	7.3E-10	-0.19 (-0.27, -0.11)	2.1E-06
G rs7024345	C9_99635059	0.716	0.07 (0.03, 0.10)	0.00010	0.06 (-0.02, 0.14)	0.13	0.02 (-0.02, 0.05)	0.28	0.03 (-0.06, 0.11)	0.55
A rs10125592	C9_122201556	0.851	-0.06 (-0.11, -0.01)	0.017	-0.07 (-0.17, 0.03)	0.19	-0.10 (-0.14, -0.05)	0.00011	-0.08 (-0.20, 0.03)	0.15
C rs3780674	C9_122206740	0.851	-0.06 (-0.10, -0.01)	0.011	-0.07 (-0.17, 0.03)	0.20	-0.08 (-0.13, -0.04)	0.00029	-0.08 (-0.19, 0.04)	0.18
C rs7028896	C9_132521981	0.937	-0.10 (-0.15, -0.04)	0.0016	-0.07 (-0.19, 0.06)	0.29	-0.10 (-0.17, -0.03)	0.0031	-0.09 (-0.21, 0.03)	0.12
C rs11246386	C11_1034938	0.768	-0.03 (-0.07, 0.01)	0.096	-0.08 (-0.17, 0.01)	0.089	-0.06 (-0.10, -0.02)	0.0036	-0.19 (-0.28, -0.10)	5.6E-05
T rs5896	C11_46701579	0.151	0.08 (0.04, 0.13)	0.00024	0.03 (-0.08, 0.14)	0.59	0.01 (-0.04, 0.06)	0.64	0.02 (-0.08, 0.12)	0.67
G rs2306033	C11_46854022	0.854	-0.08 (-0.13, -0.04)	0.00020	-0.09 (-0.20, 0.01)	0.068	-0.02 (-0.06, 0.03)	0.43	-0.06 (-0.17, 0.04)	0.26
T rs11039024	C11_46879744	0.159	0.06 (0.02, 0.10)	0.0047	0.04 (-0.06, 0.14)	0.45	0.00 (-0.04, 0.04)	0.97	0.03 (-0.07, 0.13)	0.52
G rs10838635	C11_46901803	0.240	0.06 (0.02, 0.10)	0.00094	0.06 (-0.03, 0.14)	0.18	0.03 (-0.01, 0.07)	0.10	0.02 (-0.05, 0.08)	0.59
T rs11600292	C11_46915274	0.760	-0.06 (-0.10, -0.03)	0.00052	-0.05 (-0.13, 0.04)	0.28	-0.03 (-0.07, 0.01)	0.15	-0.01 (-0.08, 0.05)	0.65
G rs7935346	C11_46964955	0.769	-0.06 (-0.10, -0.03)	0.00066	-0.06 (-0.15, 0.03)	0.18	-0.03 (-0.07, 0.01)	0.11	-0.02 (-0.10, 0.06)	0.62
G rs7121418	C11_47121682	0.349	0.04 (0.01, 0.07)	0.0078	0.06 (-0.02, 0.13)	0.14	0.02 (-0.01, 0.05)	0.25	-0.01 (-0.15, 0.13)	0.85
G rs2279439	C11_47153558	0.754	-0.06 (-0.09, -0.02)	0.0012	-0.02 (-0.11, 0.06)	0.59	-0.03 (-0.07, 0.00)	0.075	0.01 (-0.17, 0.18)	0.92
A rs2016266	C12_52014222	0.685	-0.04 (-0.07, -0.00)	0.031	-0.07 (-0.16, 0.02)	0.12	-0.08 (-0.12, -0.04)	5.4E-05	-0.12 (-0.22, -0.02)	0.022
A rs10876432	C12_52018158	0.726	-0.05 (-0.09, -0.02)	0.0038	-0.03 (-0.11, 0.06)	0.55	-0.09 (-0.13, -0.05)	4.5E-06	-0.10 (-0.20, 0.01)	0.073
A rs7992970	C13_41843463	0.779	-0.07 (-0.11, -0.03)	0.00018	-0.11 (-0.19, -0.03)	0.011	-0.10 (-0.14, -0.06)	2.2E-07	-0.17 (-0.26, -0.08)	0.00021
T rs9594738	C13_41850145	0.562	-0.11 (-0.15, -0.07)	3.0E-08	-0.07 (-0.14, 0.01)	0.108	-0.18 (-0.22, -0.14)	1.5E-19	-0.13 (-0.21, -0.05)	0.0019
A rs10507508	C13_41867782	0.947	-0.12 (-0.18, -0.05)	0.00093	-0.21 (-0.36, -0.05)	0.011	-0.17 (-0.24, -0.10)	3.6E-06	-0.18 (-0.35, -0.01)	0.042
T rs9594759	C13_41930593	0.624	-0.08 (-0.11, -0.05)	3.1E-07	-0.02 (-0.11, 0.08)	0.74	-0.13 (-0.16, -0.10)	3.9E-15	-0.11 (-0.19, -0.03)	0.0070
A rs3783833	C14_90505343	0.853	-0.05 (-0.10, -0.01)	0.018	-0.11 (-0.20, -0.02)	0.019	-0.07 (-0.12, -0.03)	0.0012	-0.10 (-0.20, 0.00)	0.061
A rs1286077	C14_90516137	0.866	-0.04 (-0.09, 0.01)	0.13	-0.15 (-0.25, -0.05)	0.004	-0.07 (-0.12, -0.02)	0.0032	-0.10 (-0.21, 0.01)	0.067
C rs884013	C18_44710128	0.925	-0.12 (-0.18, -0.06)	9.03E-05	-0.05 (-0.18, 0.09)	0.50	-0.07 (-0.13, -0.01)	0.030	-0.02 (-0.17, 0.12)	0.73
C rs713485	C18_57421905	0.331	-0.04 (-0.07, -0.00)	0.036	-0.08 (-0.16, -0.00)	0.045	-0.06 (-0.09, -0.02)	0.0011	-0.11 (-0.20, -0.02)	0.016
A rs1377172	C18_57447361	0.327	-0.05 (-0.08, -0.01)	0.014	-0.11 (-0.20, -0.02)	0.014	-0.07 (-0.11, -0.03)	0.00050	-0.14 (-0.23, -0.04)	0.0074
C rs4507007	C18_57537499	0.123	-0.09 (-0.13, -0.04)	0.00033	0.01 (-0.06, 0.07)	0.87	-0.08 (-0.13, -0.04)	0.00060	-0.13 (-0.25, -0.02)	0.024
A rs3018362	C18_58233073	0.354	-0.08 (-0.11, -0.05)	1.3E-06	-0.05 (-0.12, 0.03)	0.22	-0.07 (-0.10, -0.03)	5.6E-05	-0.05 (-0.13, 0.04)	0.30
A rs2232965	C19_18287950	0.198	-0.07 (-0.11, -0.03)	0.00021	-0.08 (-0.17, 0.01)	0.084	-0.03 (-0.08, 0.01)	0.10	-0.07 (-0.18, 0.03)	0.17
T rs209956	C20_52156263	0.723	0.04 (0.01, 0.08)	0.021	0.03 (-0.05, 0.11)	0.50	0.03 (-0.01, 0.07)	0.13	0.02 (-0.07, 0.11)	0.67
C rs4810077	C20_55477509	0.351	-0.02 (-0.06, 0.01)	0.15	0.01 (-0.03, 0.05)	0.65	-0.04 (-0.08, -0.01)	0.013	-0.03 (-0.16, 0.10)	0.65
A rs1006899	C21_14766923	0.838	-0.02 (-0.07, 0.02)	0.33	-0.14 (-0.23, -0.04)	0.007	-0.09 (-0.13, -0.04)	7.6E-05	-0.10 (-0.23, 0.02)	0.099
T rs2244352	C21_39679843	0.332	-0.02 (-0.06, 0.01)	0.19	-0.02 (-0.09, 0.06)	0.65	-0.06 (-0.09, -0.02)	0.0016	-0.02 (-0.09, 0.06)	0.65
C rs9306419	C22_24699358	0.873	-0.11 (-0.16, -0.06)	8.1E-06	-0.04 (-0.17, 0.08)	0.48	-0.12 (-0.17, -0.07)	2.0E-06	-0.00 (-0.04, 0.04)	0.94

Data is shown for the overall combined analysis.

**Supplementary Table 5. Osteoporotic fracture analysis.** The numbers of cases of any low trauma fractures, forearm fractures, hip fractures and vertebral fractures are: 2986, 617, 1087 and 263 for Iceland; 905, 515, 101 and 203 for Denmark and 550, 125, 156 and 251 for Australia.

	Iceland				Denmark				Australia				Overall Combined	
	OFx frq (n=2986)	Ctrl frq (n=35400)	OR	P value	OFx frq (n=870)	Ctrl frq (n=1040)	OR	P value	OFx frq (n=550)	Ctrl frq (N=345)	OR	P value	OR	P value
<b>1p36 - A rs7524102</b>														
Any fracture	0.829	0.817	1.09	0.025	0.861	0.834	1.23	0.024	0.846	0.811	1.29	0.059	1.12 (1.05,1.20)	0.00084
Forearm fracture	0.832	0.817	1.11	0.11	0.868	0.834	1.31	0.014	0.841	0.811	1.24	0.31	1.16 (1.05,1.29)	0.0053
Hip fracture	0.828	0.817	1.08	0.24	0.875	0.834	1.39	0.13	0.901	0.811	2.12	0.00053	1.15 (1.03,1.29)	0.016
Vertebral fracture	0.834	0.817	1.12	0.37	0.869	0.834	1.32	0.082	0.845	0.811	1.28	0.15	1.22 (1.03,1.44)	0.022
<b>1p36 - G rs6696981</b>														
Any fracture	0.872	0.858	1.13	0.0041	0.902	0.879	1.27	0.024	0.897	0.880	1.18	0.28	1.15 (1.07,1.25)	0.00024
Forearm fracture	0.875	0.858	1.15	0.049	0.904	0.879	1.30	0.038	0.883	0.880	1.02	0.93	1.17 (1.04,1.32)	0.0076
Hip fracture	0.871	0.858	1.11	0.14	0.911	0.879	1.41	0.17	0.936	0.880	1.99	0.0085	1.17 (1.03,1.33)	0.016
Vertebral fracture	0.878	0.859	1.18	0.24	0.918	0.879	1.54	0.020	0.908	0.880	1.34	0.15	1.31 (1.08,1.59)	0.0059
<b>6p21 - MHC -T rs3130340</b>														
Any fracture	0.800	0.786	1.09	0.0180	0.782	0.761	1.13	0.12	0.775	0.777	0.98	0.89	1.09 (1.02,1.16)	0.0077
Forearm fracture	0.805	0.787	1.12	0.0661	0.776	0.761	1.09	0.38	0.811	0.777	1.23	0.29	1.11 (1.01,1.23)	0.026
Hip fracture	0.801	0.787	1.09	0.15	0.809	0.761	1.33	0.13	0.803	0.777	1.17	0.39	1.11 (1.00,1.24)	0.044
Vertebral fracture	0.809	0.787	1.15	0.25	0.794	0.761	1.21	0.16	0.774	0.777	0.98	0.90	1.12 (0.96,1.30)	0.14
<b>6q25 - ESR1 -C rs9479055</b>														
Any fracture	0.355	0.348	1.03	0.29	0.390	0.356	1.16	0.030	0.413	0.406	1.03	0.77	1.05 (1.00,1.11)	0.061
Forearm fracture	0.361	0.348	1.06	0.25	0.389	0.356	1.15	0.077	0.450	0.406	1.20	0.25	1.09 (1.01,1.19)	0.031
Hip fracture	0.324	0.349	0.89	0.026	0.414	0.356	1.28	0.116	0.441	0.406	1.16	0.33	0.94 (0.86,1.03)	0.21
Vertebral fracture	0.372	0.348	1.11	0.30	0.393	0.356	1.17	0.17	0.369	0.406	0.86	0.23	1.06 (0.93,1.20)	0.40
<b>6q25 - ESR1 - T rs4870044</b>														
Any fracture	0.281	0.281	1.00	1.00	0.277	0.252	1.14	0.082	0.302	0.300	1.01	0.95	1.02 (0.97,1.09)	0.14
Forearm fracture	0.284	0.281	1.01	0.79	0.281	0.252	1.16	0.093	0.330	0.300	1.15	0.41	1.06 (0.97,1.15)	0.20
Hip fracture	0.254	0.282	0.87	0.0087	0.291	0.252	1.22	0.25	0.312	0.300	1.05	0.74	0.91 (0.83,1.00)	0.051
Vertebral fracture	0.298	0.281	1.08	0.45	0.295	0.252	1.24	0.085	0.282	0.300	0.91	0.51	1.08 (0.94,1.24)	0.26
<b>6q25 - ESR1 - G rs1038304</b>														
Any fracture	0.472	0.469	1.01	0.72	0.511	0.476	1.15	0.030	0.524	0.485	1.17	0.12	1.04 (0.99,1.10)	0.11
Forearm fracture	0.480	0.469	1.05	0.34	0.517	0.476	1.18	0.032	0.509	0.485	1.10	0.53	1.08 (1.00,1.17)	0.041
Hip fracture	0.457	0.470	0.95	0.30	0.474	0.476	0.99	0.96	0.500	0.485	1.06	0.68	0.96 (0.89,1.05)	0.40
Vertebral fracture	0.487	0.469	1.07	0.46	0.513	0.476	1.16	0.18	0.549	0.485	1.29	0.041	1.15 (1.02,1.30)	0.024
<b>6q25 - ESR1 - A rs6929137</b>														
Any fracture	0.299	0.298	1.00	0.90	0.323	0.288	1.18	0.019	0.361	0.317	1.22	0.054	1.05 (0.99,1.10)	0.12
Forearm fracture	0.300	0.298	1.01	0.86	0.326	0.288	1.19	0.033	0.338	0.317	1.10	0.55	1.06 (0.98,1.16)	0.16

Hip fracture	0.294	0.299	0.98	0.67	0.286	0.288	0.99	0.95	0.349	0.317	1.16	0.33	1.00 (0.91,1.09)	0.92
Vertebral fracture	0.317	0.298	1.09	0.40	0.326	0.288	1.20	0.14	0.388	0.317	1.37	0.016	1.19 (1.05,1.36)	0.0086
<b>6q25 - ESR1 - C rs1999805</b>														
Any fracture	0.440	0.437	1.01	0.72	0.413	0.401	1.05	0.47	0.471	0.434	1.16	0.17	1.03 (0.97,1.08)	0.35
Forearm fracture	0.452	0.437	1.06	0.21	0.410	0.401	1.04	0.63	0.505	0.434	1.33	0.089	1.07 (0.99,1.16)	0.093
Hip fracture	0.428	0.438	0.96	0.39	0.431	0.401	1.13	0.43	0.477	0.434	1.19	0.28	0.99 (0.91,1.08)	0.80
Vertebral fracture	0.412	0.437	0.90	0.29	0.431	0.401	1.13	0.28	0.429	0.434	0.98	0.87	0.99 (0.87,1.12)	0.87
<b>8q24 - OPG - C rs6993813</b>														
Any fracture	0.508	0.496	1.05	0.086	0.532	0.517	1.06	0.36	0.539	0.519	1.08	0.44	1.06 (1.00,1.11)	0.039
Forearm fracture	0.523	0.496	1.12	0.024	0.539	0.517	1.09	0.26	0.519	0.519	1.00	1.00	1.11 (1.02,1.20)	0.012
Hip fracture	0.497	0.497	1.00	1.00	0.567	0.517	1.22	0.18	0.553	0.519	1.15	0.38	1.19 (0.96,1.47)	0.12
Vertebral fracture	0.536	0.496	1.17	0.10	0.573	0.517	1.25	0.045	0.529	0.519	1.04	0.75	1.17 (1.03,1.32)	0.017
<b>8q24 - OPG - A rs6469804</b>														
Any fracture	0.521	0.510	1.05	0.13	0.551	0.540	1.04	0.51	0.574	0.540	1.15	0.17	1.05 (1.00,1.11)	0.052
Forearm fracture	0.536	0.510	1.11	0.032	0.552	0.540	1.05	0.54	0.561	0.540	1.09	0.58	1.09 (1.01,1.18)	0.027
Hip fracture	0.511	0.511	1.00	0.99	0.558	0.540	1.08	0.63	0.592	0.540	1.24	0.15	1.03 (0.94,1.13)	0.53
Vertebral fracture	0.539	0.511	1.12	0.25	0.593	0.540	1.24	0.052	0.564	0.540	1.10	0.44	1.15 (1.02,1.30)	0.024
<b>13q14 - RANKL - T rs9594738</b>														
Any fracture	0.575	0.559	1.07	0.085	0.488	0.486	1.01	0.90	0.466	0.486	0.92	0.42	1.04 (0.98,1.11)	0.23
Forearm fracture	0.584	0.562	1.10	0.10	0.477	0.486	0.97	0.67	0.491	0.486	1.02	0.90	1.05 (0.96,1.14)	0.29
Hip fracture	0.569	0.564	1.02	0.75	0.511	0.486	1.10	0.51	0.454	0.486	0.88	0.38	1.01 (0.91,1.11)	0.84
Vertebral fracture	0.585	0.564	1.09	0.40	0.511	0.486	1.11	0.37	0.466	0.486	0.92	0.53	1.05 (0.92,1.19)	0.47
<b>13q14 - RANKL - T rs9594759</b>														
Any fracture	0.631	0.624	1.03	0.33	0.551	0.559	0.97	0.65	0.531	0.533	0.99	0.94	1.02 (0.97,1.07)	0.52
Forearm fracture	0.647	0.624	1.11	0.044	0.536	0.559	0.91	0.24	0.588	0.533	1.25	0.14	1.06 (0.98,1.15)	0.16
Hip fracture	0.619	0.625	0.98	0.62	0.622	0.559	1.30	0.083	0.500	0.533	0.88	0.36	0.99 (0.91,1.08)	0.82
Vertebral fracture	0.643	0.624	1.08	0.42	0.579	0.559	1.09	0.45	0.519	0.533	0.95	0.65	1.05 (0.92,1.19)	0.48
<b>2p16 - G rs11898505</b>														
Any fracture	0.693	0.673	1.10	0.0041	0.663	0.635	1.13	0.076	0.663	0.616	1.22	0.054	1.11 (1.05,1.17)	0.00018
Forearm fracture	0.708	0.674	1.17	0.0025	0.660	0.635	1.12	0.17	0.615	0.616	1.00	0.99	1.15 (1.05,1.25)	0.0014
Hip fracture	0.678	0.675	1.02	0.76	0.652	0.635	1.07	0.65	0.629	0.616	1.06	0.72	1.02 (0.94,1.12)	0.60
Vertebral fracture	0.744	0.675	1.40	0.0015	0.676	0.635	1.20	0.12	0.669	0.616	1.26	0.083	1.29 (1.13,1.48)	0.00015
<b>2p16 - G rs4315567</b>														
Any fracture	0.702	0.685	1.08	0.013	0.662	0.643	1.09	0.22	0.675	0.638	1.18	0.12	1.09 (1.03,1.15)	0.0021
Forearm fracture	0.710	0.685	1.12	0.029	0.668	0.643	1.12	0.18	0.612	0.638	0.89	0.48	1.10 (1.01,1.20)	0.023
Hip fracture	0.689	0.686	1.02	0.77	0.642	0.643	0.99	0.97	0.679	0.638	1.20	0.24	1.03 (0.94,1.13)	0.54
Vertebral fracture	0.761	0.685	1.46	0.00047	0.681	0.643	1.18	0.16	0.680	0.638	1.21	0.16	1.29 (1.13,1.48)	0.00018
<b>18q21 - RANK - A rs3018362</b>														
Any fracture	0.365	0.353	1.06	0.0815	0.382	0.342	1.18	0.012	0.349	0.324	1.12	0.29	1.08 (1.02,1.14)	0.0050
Forearm fracture	0.370	0.354	1.08	0.15	0.362	0.342	1.09	0.30	0.345	0.324	1.10	0.56	1.08 (1.00,1.17)	0.062
Hip fracture	0.356	0.354	1.01	0.88	0.346	0.342	1.01	0.93	0.336	0.324	1.06	0.72	1.01 (0.93,1.11)	0.79
Vertebral fracture	0.352	0.354	0.99	0.94	0.405	0.342	1.31	0.019	0.339	0.324	1.07	0.60	1.11 (0.97,1.26)	0.12

**11p11 - LRP4 - G rs2306033**

Any fracture	0.865	0.854	1.10	0.029	0.874	0.860	1.13	0.21	0.877	0.859	1.17	0.31	1.11 (1.03,1.19)	0.0074
Forearm fracture	0.868	0.854	1.13	0.093	0.875	0.860	1.14	0.25	0.883	0.859	1.24	0.39	1.14 (1.01,1.27)	0.030
Hip fracture	0.867	0.854	1.11	0.12	0.846	0.860	0.90	0.61	0.876	0.859	1.16	0.51	1.10 (0.97,1.24)	0.15
Vertebral fracture	0.860	0.855	1.05	0.74	0.880	0.860	1.20	0.28	0.896	0.859	1.42	0.081	1.17 (0.97,1.4)	0.10

**G rs7935346**

Any fracture	0.776	0.768	1.05	0.21	0.783	0.756	1.16	0.053	0.792	0.750	1.27	0.055	1.08 (1.01,1.14)	0.019
Forearm fracture	0.777	0.769	1.05	0.42	0.784	0.756	1.17	0.092	0.797	0.750	1.31	0.19	1.09 (0.99,1.20)	0.067
Hip fracture	0.776	0.769	1.04	0.50	0.772	0.756	1.10	0.62	0.760	0.750	1.06	0.76	1.05 (0.94,1.16)	0.40
Vertebral fracture	0.779	0.769	1.06	0.63	0.791	0.756	1.22	0.14	0.799	0.750	1.33	0.071	1.17 (1.01,1.36)	0.041

**A rs7121418**

Any fracture	0.660	0.651	1.04	0.17	0.690	0.660	1.15	0.042	0.695	0.682	1.06	0.59	1.06 (1.01,1.12)	0.030
Forearm fracture	0.660	0.651	1.04	0.43	0.688	0.660	1.14	0.12	0.740	0.682	1.33	0.115	1.08 (0.99,1.17)	0.068
Hip fracture	0.654	0.651	1.01	0.85	0.668	0.660	1.04	0.80	0.669	0.682	0.94	0.72	1.01 (0.92,1.10)	0.89
Vertebral fracture	0.672	0.651	1.10	0.36	0.694	0.660	1.17	0.18	0.678	0.682	0.98	0.90	1.09 (0.96,1.25)	0.19

**G rs2279439**

Any fracture	0.757	0.754	1.02	0.59	0.777	0.750	1.17	0.060	0.791	0.744	1.31	0.034	1.05 (0.99,1.12)	0.086
Forearm fracture	0.760	0.754	1.03	0.57	0.776	0.750	1.16	0.14	0.787	0.744	1.27	0.23	1.07 (0.98,1.18)	0.14
Hip fracture	0.752	0.754	0.99	0.85	0.763	0.750	1.08	0.68	0.770	0.744	1.15	0.44	1.01 (0.91,1.11)	0.88
Vertebral fracture	0.771	0.754	1.10	0.40	0.784	0.750	1.21	0.19	0.796	0.744	1.35	0.061	1.19 (1.02,1.38)	0.028

**12q13 - OSX - A rs10876432**

Any fracture	0.727	0.726	1.01	0.88	0.732	0.705	1.14	0.096	0.700	0.713	0.94	0.60	1.02 (0.96,1.10)	0.48
Forearm fracture	0.739	0.726	1.07	0.32	0.724	0.705	1.10	0.35	0.679	0.713	0.85	0.39	1.06 (0.95,1.18)	0.29
Hip fracture	0.726	0.726	1.00	1.00	0.719	0.705	1.07	0.71	0.665	0.713	0.80	0.21	0.92 (0.72,1.18)	0.52
Vertebral fracture	0.732	0.726	1.03	0.80	0.719	0.705	1.07	0.58	0.721	0.713	1.04	0.81	1.05 (0.90,1.22)	0.54

**Supplementary Table 6A**

**Ranking of Candidate genes in list of top 5000 SNPs associated with the spine BMD**

SNP	Allele	Chr.	Position Build36	rank	effect	p	Candidate gene(s)*
rs9594759	T	chr13	41930593	1	-0.13 (-0.18, -0.09)	1.17E-08	RANKL
rs2504063	A	chr6	152132400	2	-0.12 (-0.17, -0.08)	5.68E-08	ESR1
rs851982	T	chr6	152066678	3	-0.12 (-0.16, -0.07)	1.56E-07	ESR1
rs2504070	T	chr6	152126666	4	-0.12 (-0.17, -0.08)	4.62E-07	ESR1
rs7992970	A	chr13	41843463	5	-0.13 (-0.19, -0.08)	8.50E-07	RANKL
rs1999805	C	chr6	152110057	9	-0.11 (-0.15, -0.06)	2.27E-06	ESR1
rs3020331	C	chr6	152050473	10	-0.10 (-0.15, -0.06)	3.41E-06	ESR1
rs4870044	T	chr6	151943102	11	-0.11 (-0.16, -0.07)	4.09E-06	ESR1
rs7752591	A	chr6	151988761	15	-0.10 (-0.14, -0.06)	6.94E-06	ESR1
rs1038304	G	chr6	151974868	19	-0.10 (-0.14, -0.06)	8.25E-06	ESR1
rs6469804	A	chr8	120114010	20	-0.10 (-0.14, -0.06)	8.53E-06	OPG
rs10507507	T	chr13	41867646	27	-0.13 (-0.18, -0.07)	1.60E-05	RANKL
rs2504065	G	chr6	152136860	31	-0.10 (-0.14, -0.05)	1.97E-05	ESR1
rs6929137	A	chr6	151978370	39	-0.10 (-0.15, -0.05)	3.00E-05	ESR1
rs6993813	C	chr8	120121419	45	-0.09 (-0.14, -0.05)	3.59E-05	OPG
rs7753676	G	chr6	151918508	46	-0.09 (-0.14, -0.05)	3.62E-05	ESR1
rs1159327	G	chr6	152089715	51	-0.10 (-0.15, -0.05)	4.33E-05	ESR1
rs6469792	C	chr8	120077552	56	-0.09 (-0.13, -0.05)	6.19E-05	OPG
rs6900157	C	chr6	151995820	68	-0.09 (-0.14, -0.05)	8.49E-05	ESR1
rs7316953	C	chr13	41915470	69	-0.11 (-0.16, -0.05)	8.65E-05	RANKL
rs4355801	A	chr8	119993054	88	-0.09 (-0.13, -0.04)	0.00013	OPG
rs7999869	C	chr13	33160060	103	-0.09 (-0.14, -0.04)	0.00016	RANKL
rs9478223	C	chr6	151941931	121	-0.14 (-0.21, -0.07)	0.00020	ESR1
rs7751941	A	chr6	151988351	178	-0.10 (-0.15, -0.04)	0.00032	ESR1
rs4898457	G	chrX	152811550	198	-0.09 (-0.15, -0.04)	0.00038	IRAK1
rs238256	T	chr13	41821675	202	-0.09 (-0.14, -0.04)	0.00039	RANKL
rs9533093	T	chr13	41859597	229	-0.10 (-0.16, -0.04)	0.00046	RANKL
rs1924097	A	chr13	42207550	248	-0.08 (-0.13, -0.04)	0.00053	RANKL
rs9479055	C	chr6	151889660	252	-0.08 (-0.13, -0.03)	0.00053	ESR1
rs12549314	C	chr8	25516796	253	-0.10 (-0.15, -0.04)	0.00054	GnRH
rs1564860	T	chr8	120044851	273	-0.08 (-0.13, -0.04)	0.00059	OPG
rs12150965	A	chr19	59156210	292	-0.11 (-0.18, -0.05)	0.00068	OSCAR
rs3018362	A	chr18	58233073	309	-0.08 (-0.13, -0.03)	0.00072	RANK
rs9898	C	chr3	187873321	327	-0.08 (-0.13, -0.03)	0.00076	AHSG
rs4876876	C	chr8	120055416	444	-0.07 (-0.12, -0.03)	0.00114	OPG
rs6933660	A	chr6	151845447	485	-0.08 (-0.13, -0.03)	0.00123	ESR1
rs3132453	A	chr6	31712023	504	-0.11 (-0.18, -0.04)	0.00129	TNF
rs990909	A	chr13	38188569	536	-0.08 (-0.13, -0.03)	0.00140	RANKL
rs1555587	T	chr13	42189413	540	-0.09 (-0.14, -0.03)	0.00141	RANKL
rs923346	C	chr11	67938951	547	-0.10 (-0.15, -0.04)	0.00143	LRP5
rs376999	G	chr13	41984646	570	-0.08 (-0.12, -0.03)	0.00149	RANKL
rs2306862	T	chr11	67934086	618	-0.09 (-0.15, -0.04)	0.00161	LRP5
rs2276108	A	chr11	102152746	622	-0.10 (-0.17, -0.04)	0.00163	MMP-1
rs4803455	A	chr19	46543349	632	-0.07 (-0.12, -0.03)	0.00165	TGFb1
rs5945361	A	chrX	152799594	651	-0.09 (-0.14, -0.03)	0.00171	IRAK1
rs2734647	C	chrX	152945374	653	-0.11 (-0.18, -0.04)	0.00171	IRAK1
rs2055101	G	chr8	119956104	664	-0.07 (-0.11, -0.03)	0.00175	OPG
rs4869738	T	chr6	151933844	677	-0.09 (-0.14, -0.03)	0.00179	ESR1
rs665657	T	chr13	41987378	694	-0.07 (-0.12, -0.03)	0.00184	RANKL
rs6571303	C	chrX	152901148	746	-0.10 (-0.17, -0.04)	0.00198	IRAK1
rs10507508	A	chr13	41867782	765	-0.16 (-0.25, -0.06)	0.00202	RANKL
rs3736228	T	chr11	67957871	766	-0.09 (-0.15, -0.03)	0.00202	LRP5
rs4806674	T	chr19	59153350	798	-0.07 (-0.11, -0.02)	0.00211	OSCAR
rs2523674	T	chr6	31544768	854	-0.07 (-0.11, -0.03)	0.00226	TNF
rs3734803	A	chr6	151911338	865	-0.09 (-0.15, -0.03)	0.00231	ESR1
rs2224191	A	chr20	6755276	871	-0.12 (-0.20, -0.04)	0.00234	BMP2
rs7322806	G	chr13	41944397	878	-0.09 (-0.15, -0.03)	0.00236	RANKL

rs10505338	T	chr8	119824671	885	-0.07 (-0.12, -0.03)	0.00238	OPG
rs17774945	C	chr5	58238687	913	-0.14 (-0.23, -0.05)	0.00246	PDE4D
rs2239464	G	chrX	153001625	984	-0.09 (-0.16, -0.03)	0.00265	IRAK1
rs238280	A	chr13	41836474	1054	-0.08 (-0.13, -0.03)	0.00287	RANKL
rs2957128	A	chr18	58211715	1091	-0.07 (-0.11, -0.02)	0.00297	RANK
rs1468772	C	chr1	154383112	1141	-0.07 (-0.12, -0.02)	0.00314	BGLAP
rs1557501	C	chrX	152850324	1155	-0.10 (-0.16, -0.03)	0.00320	IRAK1
rs8076149	G	chr17	4453303	1215	-0.07 (-0.11, -0.02)	0.00338	ALOX15
rs13098911	T	chr3	46210205	1246	-0.11 (-0.19, -0.04)	0.00347	CCR2 CCR3
rs2269368	C	chrX	152843013	1250	-0.11 (-0.19, -0.04)	0.00347	IRAK1
rs6444147	C	chr3	187799894	1319	-0.09 (-0.15, -0.03)	0.00371	AHSG
rs11569864	C	chr1	12091110	1328	-0.11 (-0.19, -0.04)	0.00374	PLOD1 TNFR2
rs10505346	T	chr8	120033024	1345	-0.08 (-0.13, -0.03)	0.00379	OPG
rs608343	G	chr11	67953406	1374	-0.07 (-0.12, -0.02)	0.00387	LRP5
rs2266888	G	chrX	152892914	1454	-0.10 (-0.16, -0.03)	0.00413	IRAK1
rs4941417	T	chr13	41612711	1456	-0.08 (-0.13, -0.03)	0.00413	RANKL
rs1264695	T	chr6	30175871	1522	-0.08 (-0.13, -0.02)	0.00437	HLA-A
rs7837123	G	chr8	120048430	1550	-0.10 (-0.17, -0.03)	0.00443	OPG
rs555722	T	chr13	25979152	1554	-0.08 (-0.14, -0.03)	0.00445	RANKL
rs35760	G	chr12	101474348	1560	-0.08 (-0.14, -0.03)	0.00447	IGF1
rs11841247	A	chr13	41642049	1612	-0.08 (-0.13, -0.02)	0.00465	RANKL
rs7631551	A	chr3	46161314	1634	-0.11 (-0.18, -0.03)	0.00471	CCR3
rs4576968	A	chr13	40969635	1637	-0.06 (-0.11, -0.02)	0.00472	RANKL
rs1905786	C	chr8	120020873	1663	-0.06 (-0.11, -0.02)	0.00477	OPG
rs17793693	C	chr3	12320971	1679	-0.11 (-0.19, -0.03)	0.00483	PPARG
rs1059702	C	chrX	152937386	1696	-0.11 (-0.18, -0.03)	0.00487	IRAK1
rs9285148	G	chr13	41602669	1700	-0.07 (-0.13, -0.02)	0.00488	RANKL
rs853165	C	chr5	142530444	1771	-0.06 (-0.11, -0.02)	0.00507	NR3C1
rs247632	G	chr5	142982770	1880	-0.06 (-0.11, -0.02)	0.00544	NR3C1
rs6763361	A	chr3	187793068	1923	-0.07 (-0.12, -0.02)	0.00556	AHSG
rs4661037	T	chr1	154505103	1943	-0.08 (-0.13, -0.02)	0.00562	BGLAP
rs2844505	G	chr6	31547042	1949	-0.07 (-0.11, -0.02)	0.00564	TNF
rs2044732	G	chr13	41731400	2061	-0.07 (-0.12, -0.02)	0.00602	RANKL
rs266743	A	chr3	187958485	2069	-0.07 (-0.12, -0.02)	0.00604	AHSG
rs1015390	T	chr12	46630305	2109	-0.09 (-0.15, -0.03)	0.00619	VDR
rs1037272	A	chr13	41688458	2112	-0.08 (-0.13, -0.02)	0.00620	RANKL
rs3130617	C	chr6	31735502	2150	-0.07 (-0.11, -0.02)	0.00632	TNF
rs1409032	C	chr13	23584133	2220	-0.07 (-0.11, -0.02)	0.00655	RANKL
rs152225	A	chr5	142971358	2223	-0.06 (-0.11, -0.02)	0.00656	NR3C1
rs9891712	C	chr17	39096330	2279	-0.11 (-0.18, -0.03)	0.00674	SOST
rs9547011	C	chr13	30377640	2376	-0.07 (-0.11, -0.02)	0.00710	RANKL
rs9510894	T	chr13	23321447	2386	-0.07 (-0.12, -0.02)	0.00714	RANKL
rs9315903	G	chr13	41736604	2402	-0.09 (-0.16, -0.03)	0.00718	RANKL
rs9548463	T	chr13	31119841	2453	-0.12 (-0.20, -0.03)	0.00733	RANKL
rs6441961	T	chr3	46327388	2461	-0.07 (-0.12, -0.02)	0.00736	CCR2 CCR3
rs4770482	C	chr13	23194067	2485	-0.08 (-0.14, -0.02)	0.00746	RANKL
rs7566418	A	chr2	161555483	2490	-0.06 (-0.11, -0.02)	0.00749	TANK
rs1485303	A	chr8	120045437	2502	-0.06 (-0.10, -0.02)	0.00753	OPG
rs852003	A	chr6	152003895	2574	-0.06 (-0.10, -0.02)	0.00778	ESR1
rs442277	G	chr22	18432566	2584	-0.06 (-0.11, -0.02)	0.00782	COMT
rs7324038	T	chr13	19453812	2590	-0.11 (-0.19, -0.03)	0.00785	RANKL
rs4463269	T	chr6	151903921	2610	-0.07 (-0.12, -0.02)	0.00791	ESR1
rs13336428	A	chr16	1472464	2659	-0.06 (-0.11, -0.02)	0.00808	CLCN7
rs6054529	C	chr20	6746495	2773	-0.06 (-0.10, -0.02)	0.00841	BMP2
rs4764702	A	chr12	101461236	2775	-0.08 (-0.14, -0.02)	0.00842	IGF1
rs624003	T	chr11	67987816	2802	-0.06 (-0.11, -0.02)	0.00849	LRP5
rs1457596	G	chr12	101486637	2814	-0.09 (-0.16, -0.02)	0.00853	IGF1
rs7331220	C	chr13	42192055	2826	-0.07 (-0.12, -0.02)	0.00857	RANKL
rs6214	G	chr12	101317699	2831	-0.06 (-0.10, -0.02)	0.00859	IGF1
rs2321566	G	chr13	33169418	2848	-0.06 (-0.10, -0.02)	0.00863	RANKL
rs4870024	C	chr6	151872462	2861	-0.08 (-0.14, -0.02)	0.00866	ESR1
rs1264702	A	chr6	30173554	2944	-0.07 (-0.13, -0.02)	0.00892	HLA-A



rs10492440	T	chr13	41660106	2994	-0.09 (-0.15, -0.02)	0.00908	RANKL
rs3134058	A	chr8	120023289	3018	-0.06 (-0.10, -0.01)	0.00914	OPG
rs916570	T	chr6	30174010	3083	-0.07 (-0.12, -0.02)	0.00932	HLA-A
rs1157106	T	chr4	55056149	3144	-0.06 (-0.11, -0.01)	0.00949	KIT
rs17077384	C	chr13	31757048	3181	-0.11 (-0.19, -0.03)	0.00964	RANKL
rs851993	T	chr6	152047704	3187	-0.06 (-0.10, -0.01)	0.00967	ESR1
rs4526865	G	chr13	28788283	3194	-0.06 (-0.11, -0.01)	0.00968	RANKL
rs2321480	C	chr13	33162201	3219	-0.06 (-0.10, -0.01)	0.00973	RANKL
rs1530641	G	chr3	187718601	3235	-0.06 (-0.11, -0.01)	0.00979	AHSG
rs397701	T	chr22	18412327	3262	-0.06 (-0.10, -0.01)	0.00987	COMT
rs712219	G	chr6	152020132	3363	-0.06 (-0.10, -0.01)	0.010	ESR1
rs3917498	C	chr7	94784191	3381	-0.06 (-0.11, -0.01)	0.010	PON1
rs12489988	G	chr3	123206390	3384	-0.10 (-0.17, -0.02)	0.010	CASR
rs1002036	C	chr13	30405727	3409	-0.07 (-0.12, -0.02)	0.010	RANKL
rs1485302	A	chr8	120045325	3549	-0.06 (-0.10, -0.01)	0.011	OPG
rs9397066	A	chr6	151961629	3563	-0.07 (-0.12, -0.02)	0.011	ESR1
rs546803	C	chr11	67942968	3623	-0.06 (-0.11, -0.01)	0.011	LRP5
rs2559836	T	chr12	101459392	3661	-0.08 (-0.14, -0.02)	0.011	IGF1
rs4686428	G	chr3	187730067	3676	-0.07 (-0.12, -0.02)	0.011	AHSG
rs8097062	G	chr18	58236020	3678	-0.06 (-0.10, -0.01)	0.011	RANK
rs1564858	A	chr8	120014347	3693	-0.08 (-0.14, -0.02)	0.011	OPG
rs10507496	T	chr13	41207828	3732	-0.08 (-0.15, -0.02)	0.011	RANKL
rs1037254	C	chr13	38218761	3762	-0.06 (-0.11, -0.01)	0.011	RANKL
rs4569113	G	chr13	26215232	3776	-0.06 (-0.10, -0.01)	0.011	RANKL
rs1516116	T	chr2	161508360	3795	-0.06 (-0.10, -0.01)	0.011	TANK
rs3733159	A	chr3	187843103	3827	-0.06 (-0.11, -0.01)	0.011	AHSG
rs693633	G	chr13	25598764	3850	-0.14 (-0.26, -0.03)	0.012	RANKL
rs9545074	T	chr13	35171871	3885	-0.06 (-0.11, -0.01)	0.012	RANKL
rs628780	G	chr13	25721979	3906	-0.06 (-0.10, -0.01)	0.012	RANKL
rs6066502	T	chr20	45911998	4038	-0.09 (-0.16, -0.02)	0.012	NCOA3
rs6490694	T	chr13	21559666	4061	-0.07 (-0.12, -0.01)	0.012	RANKL
rs9576606	A	chr13	38208746	4079	-0.11 (-0.20, -0.02)	0.012	RANKL
rs2763028	A	chr6	152573915	4153	-0.07 (-0.13, -0.02)	0.012	ESR1
rs12959396	T	chr18	58190289	4165	-0.06 (-0.10, -0.01)	0.013	RANK
rs374225	T	chr22	18409878	4187	-0.06 (-0.10, -0.01)	0.013	COMT
rs115063	T	chr7	24144360	4210	-0.06 (-0.10, -0.01)	0.013	NPY
rs1722659	A	chr2	161533247	4298	-0.06 (-0.12, -0.01)	0.013	TANK
rs2166019	T	chr4	55053122	4306	-0.06 (-0.10, -0.01)	0.013	KIT
rs4917	T	chr3	187820407	4308	-0.06 (-0.10, -0.01)	0.013	AHSG
rs3134036	A	chr8	119891041	4318	-0.05 (-0.10, -0.01)	0.013	OPG
rs9510743	T	chr13	22922344	4381	-0.06 (-0.11, -0.01)	0.013	RANKL
rs400288	G	chr13	41759772	4410	-0.06 (-0.11, -0.01)	0.013	RANKL
rs43054	G	chr7	94917358	4429	-0.06 (-0.11, -0.01)	0.013	PON1
rs1538225	C	chr13	33725602	4450	-0.07 (-0.13, -0.02)	0.014	RANKL
rs854561	T	chr7	94784953	4498	-0.06 (-0.11, -0.01)	0.014	PON1
rs2035979	T	chr8	119941620	4608	-0.06 (-0.10, -0.01)	0.014	OPG
rs2073741	G	chr22	18369890	4651	-0.07 (-0.13, -0.01)	0.014	COMT
rs3742303	A	chr13	30119106	4687	-0.17 (-0.30, -0.03)	0.014	RANKL
rs43065	T	chr7	94949227	4693	-0.07 (-0.12, -0.01)	0.014	PON1
rs7997603	T	chr13	30847809	4741	-0.11 (-0.20, -0.02)	0.014	RANKL
rs3133585	A	chr8	119906332	4777	-0.05 (-0.10, -0.01)	0.015	OPG
rs3826838	G	chr19	53875096	4881	-0.08 (-0.15, -0.02)	0.015	DBP
rs7220711	A	chr17	39145491	4942	-0.06 (-0.10, -0.01)	0.015	SOST
rs1639	T	chr7	94881786	4950	-0.07 (-0.13, -0.01)	0.015	PON1
rs6942710	T	chr7	16556831	4952	-0.06 (-0.10, -0.01)	0.015	SOSTDC1

\* 200 kb in either direction of the gene was included in the analysis

## Supplementary Table 6B

### Ranking of Candidate genes in list of top 5000 SNPs associated with the hip BMD

SNP	Allele	Chr.	Position Build36	rank	effect	p	Candidate gene(s)*
rs7752591	A	chr6	151988761	2	-0.10 (-0.14, -0.06)	2.16E-06	ESR1
rs3020331	C	chr6	152050473	9	-0.09 (-0.13, -0.05)	8.15E-06	ESR1
rs1038304	G	chr6	151974868	14	-0.09 (-0.13, -0.05)	1.42E-05	ESR1
rs851982	T	chr6	152066678	15	-0.09 (-0.13, -0.05)	1.59E-05	ESR1
rs6900157	C	chr6	151995820	17	-0.10 (-0.14, -0.05)	1.63E-05	ESR1
rs6929137	A	chr6	151978370	18	-0.10 (-0.14, -0.05)	1.84E-05	ESR1
rs3018362	A	chr18	58233073	30	-0.09 (-0.13, -0.05)	4.25E-05	RANK
rs7751941	A	chr6	151988351	36	-0.10 (-0.15, -0.05)	5.98E-05	ESR1
rs7753676	G	chr6	151918508	46	-0.09 (-0.13, -0.04)	7.48E-05	ESR1
rs712219	G	chr6	152020132	53	-0.08 (-0.13, -0.04)	9.07E-05	ESR1
rs1107748	T	chr17	39129340	61	-0.08 (-0.13, -0.04)	0.00011	SOST
rs4870044	T	chr6	151943102	75	-0.09 (-0.14, -0.04)	0.00012	ESR1
rs9315903	G	chr13	41736604	88	-0.13 (-0.19, -0.06)	0.00015	RANKL
rs258799	T	chr5	142510153	108	-0.08 (-0.12, -0.04)	0.00019	NR3C1
rs9478223	C	chr6	151941931	111	-0.13 (-0.20, -0.06)	0.00020	ESR1
rs3734803	A	chr6	151911338	151	-0.10 (-0.16, -0.05)	0.00028	ESR1
rs9594759	T	chr13	41930593	163	-0.08 (-0.12, -0.04)	0.00031	RANKL
rs7220711	A	chr17	39145491	175	-0.08 (-0.12, -0.04)	0.00035	SOST
rs2504063	A	chr6	152132400	180	-0.08 (-0.12, -0.03)	0.00036	ESR1
rs8097062	G	chr18	58236020	184	-0.08 (-0.12, -0.03)	0.00037	RANK
rs4390539	G	chr15	48189160	192	-0.09 (-0.14, -0.04)	0.00039	HDC
rs851993	T	chr6	152047704	219	-0.07 (-0.12, -0.03)	0.00046	ESR1
rs9315908	G	chr13	41788109	222	-0.11 (-0.17, -0.05)	0.00047	RANKL
rs852003	A	chr6	152003895	234	-0.07 (-0.12, -0.03)	0.00049	ESR1
rs9315909	A	chr13	41799736	250	-0.11 (-0.17, -0.05)	0.00054	RANKL
rs1513670	A	chr17	39162857	252	-0.08 (-0.12, -0.03)	0.00054	SOST
rs9479055	C	chr6	151889660	287	-0.07 (-0.12, -0.03)	0.00065	ESR1
rs4793017	A	chr17	39136506	300	-0.08 (-0.12, -0.03)	0.00069	SOST
rs9547011	C	chr13	30377640	304	-0.08 (-0.12, -0.03)	0.0007	RANKL
rs4463269	T	chr6	151903921	343	-0.08 (-0.13, -0.03)	0.0008	ESR1
rs1159327	G	chr6	152089715	347	-0.08 (-0.12, -0.03)	0.0008	ESR1
rs1001854	G	chr13	31459356	351	-0.07 (-0.12, -0.03)	0.0008	RANKL
rs4869738	T	chr6	151933844	390	-0.09 (-0.14, -0.04)	0.0010	ESR1
rs1924097	A	chr13	42207550	438	-0.07 (-0.12, -0.03)	0.0011	RANKL
rs12549314	C	chr8	25516796	488	-0.09 (-0.14, -0.03)	0.0012	GnRH
rs10507507	T	chr13	41867646	532	-0.09 (-0.14, -0.03)	0.0013	RANKL
rs853165	C	chr5	142530444	545	-0.07 (-0.11, -0.03)	0.0014	NR3C1
rs12956925	A	chr18	58164620	551	-0.09 (-0.15, -0.04)	0.0014	RANK
rs2665833	G	chr17	59260578	679	-0.07 (-0.11, -0.03)	0.0017	GH1
rs9552503	C	chr13	21258110	701	-0.07 (-0.11, -0.03)	0.0018	RANKL
rs6933660	A	chr6	151845447	721	-0.08 (-0.12, -0.03)	0.0019	ESR1
rs7132324	C	chr12	46593576	722	-0.07 (-0.11, -0.03)	0.0019	VDR
rs4531631	A	chr13	42033131	731	-0.08 (-0.13, -0.03)	0.0019	RANKL
rs213599	A	chr13	30352611	754	-0.07 (-0.11, -0.02)	0.0020	RANKL
rs2040718	T	chr13	30366980	867	-0.07 (-0.12, -0.03)	0.0023	RANKL
rs7997427	G	chr13	41189130	892	-0.09 (-0.15, -0.03)	0.0024	RANKL
rs4760670	G	chr12	46605880	916	-0.07 (-0.11, -0.02)	0.0024	VDR
rs12479669	A	chr20	44341442	925	-0.07 (-0.12, -0.03)	0.0025	CD40
rs168312	G	chr13	42019760	961	-0.08 (-0.13, -0.03)	0.0026	RANKL
rs232581	A	chr2	38280657	990	-0.07 (-0.12, -0.03)	0.0026	CYP1B1
rs1999805	C	chr6	152110057	1062	-0.06 (-0.11, -0.02)	0.0028	ESR1
rs12489988	G	chr3	123206390	1073	-0.11 (-0.18, -0.04)	0.0028	CASR
rs3093662	A	chr6	31652168	1100	-0.14 (-0.24, -0.05)	0.0029	TNF
rs7319920	A	chr13	34765044	1115	-0.08 (-0.13, -0.03)	0.0029	RANKL
rs4941139	T	chr18	58313771	1132	-0.06 (-0.11, -0.02)	0.0030	RANK
rs4522364	T	chr15	48129516	1179	-0.07 (-0.11, -0.02)	0.0031	HDC
rs4941815	C	chr13	35207635	1202	-0.06 (-0.11, -0.02)	0.0031	RANKL

rs9837111	C	chr3	69686775	1273	-0.13 (-0.22, -0.04)	0.0034	MITF
rs2225621	T	chr13	22926215	1275	-0.06 (-0.11, -0.02)	0.0034	RANKL
rs2504070	T	chr6	152126666	1278	-0.07 (-0.11, -0.02)	0.0034	ESR1
rs2290547	G	chr3	47036187	1305	-0.09 (-0.14, -0.03)	0.0035	PTHR1
rs4898457	G	chrX	152811550	1362	-0.07 (-0.12, -0.02)	0.0036	IRAK1
rs2160532	G	chr12	15124762	1443	-0.06 (-0.10, -0.02)	0.0039	MGP
rs5031002	A	chrX	66859350	1455	-0.18 (-0.30, -0.06)	0.0039	AR
rs7156	T	chr7	16606140	1490	-0.06 (-0.10, -0.02)	0.0040	SOSTDC1
rs2853564	C	chr12	46564754	1515	-0.06 (-0.10, -0.02)	0.0041	VDR
rs5945361	A	chrX	152799594	1530	-0.07 (-0.12, -0.02)	0.0041	IRAK1
rs9898	C	chr3	187873321	1573	-0.07 (-0.11, -0.02)	0.0042	AHSG
rs3848731	G	chr20	44354555	1607	-0.07 (-0.12, -0.02)	0.0044	CD40
rs1547347	G	chr13	39542540	1653	-0.11 (-0.18, -0.03)	0.0045	RANKL
rs9512755	C	chr13	27056229	1715	-0.09 (-0.15, -0.03)	0.0047	RANKL
rs1639	T	chr7	94881786	1731	-0.08 (-0.13, -0.02)	0.0047	PON1
rs213615	G	chr13	30347156	1733	-0.06 (-0.10, -0.02)	0.0047	RANKL
rs11538677	A	chr13	35100269	1879	-0.09 (-0.16, -0.03)	0.0052	RANKL
rs9324918	G	chr5	142747353	1883	-0.08 (-0.14, -0.02)	0.0052	NR3C1
rs2584608	G	chr17	59290442	1891	-0.06 (-0.10, -0.02)	0.0052	GH1
rs851995	A	chr6	152047227	1909	-0.06 (-0.10, -0.02)	0.0053	ESR1
rs4670788	C	chr2	37965730	1949	-0.13 (-0.23, -0.04)	0.0054	CYP1B1
rs258790	A	chr5	142522170	2009	-0.06 (-0.10, -0.02)	0.0056	NR3C1
rs9544915	T	chr13	35128485	2027	-0.09 (-0.15, -0.03)	0.0056	RANKL
rs1053275	G	chr7	94839491	2088	-0.06 (-0.10, -0.02)	0.0059	PON1
rs68352	C	chr2	38261470	2097	-0.06 (-0.10, -0.02)	0.0059	CYP1B1
rs4770748	A	chr13	18557081	2107	-0.12 (-0.20, -0.03)	0.0059	RANKL
rs1886490	A	chr13	25494562	2139	-0.08 (-0.14, -0.02)	0.0061	RANKL
rs4760648	C	chr12	46566932	2172	-0.06 (-0.10, -0.02)	0.0061	VDR
rs4302546	G	chr5	59558262	2176	-0.07 (-0.12, -0.02)	0.0061	PDE4D
rs258820	G	chr5	142574714	2213	-0.06 (-0.10, -0.02)	0.0062	NR3C1
rs4870024	C	chr6	151872462	2233	-0.08 (-0.14, -0.02)	0.0063	ESR1
rs1859121	T	chr7	94814903	2395	-0.06 (-0.10, -0.02)	0.0067	PON1
rs9510743	T	chr13	22922344	2426	-0.06 (-0.11, -0.02)	0.0068	RANKL
rs617753	C	chr18	58336658	2447	-0.07 (-0.12, -0.02)	0.0068	RANK
rs6567287	C	chr18	58345824	2495	-0.07 (-0.12, -0.02)	0.0070	RANK
rs3818314	C	chr13	20965681	2500	-0.08 (-0.14, -0.02)	0.0070	RANKL
rs7904252	G	chr10	104446715	2526	-0.06 (-0.11, -0.02)	0.0071	CYP17
rs978903	A	chr7	94842103	2653	-0.06 (-0.10, -0.02)	0.0075	PON1
rs1340874	A	chr6	151962465	2689	-0.07 (-0.13, -0.02)	0.0077	ESR1
rs846489	A	chr13	29740355	2737	-0.10 (-0.18, -0.03)	0.0078	RANKL
rs3890733	T	chr12	46575640	2747	-0.06 (-0.10, -0.02)	0.0078	VDR
rs11208756	C	chr1	66041899	2775	-0.13 (-0.22, -0.03)	0.0079	LEPR
rs6469792	C	chr8	120077552	2797	-0.06 (-0.10, -0.01)	0.0079	OPG
rs9566949	C	chr13	31463539	2802	-0.06 (-0.11, -0.02)	0.0080	RANKL
rs2957128	A	chr18	58211715	2818	-0.06 (-0.10, -0.01)	0.0080	RANK
rs7168944	C	chr15	48192536	2845	-0.06 (-0.11, -0.02)	0.0080	HDC
rs10493387	C	chr1	65994521	2851	-0.09 (-0.16, -0.02)	0.0081	LEPR
rs4428857	G	chr1	65996109	2863	-0.09 (-0.16, -0.02)	0.0081	LEPR
rs7999869	C	chr13	33160060	2963	-0.06 (-0.10, -0.02)	0.0085	RANKL
rs4341514	C	chr11	2098179	2968	-0.06 (-0.10, -0.01)	0.0085	IGF2
rs3917498	C	chr7	94784191	3036	-0.06 (-0.10, -0.02)	0.0087	PON1
rs2261	G	chr2	38283267	3154	-0.05 (-0.10, -0.01)	0.0091	CYP1B1
rs1002036	C	chr13	30405727	3181	-0.07 (-0.12, -0.02)	0.0092	RANKL
rs151474	T	chr13	41806680	3223	-0.06 (-0.10, -0.01)	0.0094	RANKL
rs482983	C	chr13	29593606	3340	-0.06 (-0.10, -0.01)	0.0097	RANKL
rs13090187	C	chr3	69790275	3393	-0.06 (-0.10, -0.01)	0.0099	MITF
rs12416759	A	chr11	14893519	3399	-0.10 (-0.17, -0.02)	0.0099	CALCA
rs10405617	A	chr19	10613968	3412	-0.06 (-0.11, -0.01)	0.0100	PDE4A
rs9315391	C	chr13	35629309	3423	-0.07 (-0.12, -0.02)	0.0100	RANKL
rs7316953	C	chr13	41915470	3492	-0.07 (-0.12, -0.02)	0.010	RANKL
rs6490797	A	chr13	22958289	3547	-0.07 (-0.12, -0.02)	0.010	RANKL
rs6032754	C	chr20	44352166	3601	-0.06 (-0.10, -0.01)	0.011	CD40

rs846491	C	chr13	29743131	3718	-0.09 (-0.16, -0.02)	0.011	RANKL
rs10498514	C	chr14	63968808	3731	-0.17 (-0.30, -0.04)	0.011	ESR2
rs9533215	A	chr13	42185262	3782	-0.05 (-0.10, -0.01)	0.011	RANKL
rs1328650	C	chr13	35610330	3809	-0.06 (-0.11, -0.01)	0.011	RANKL
rs12055945	C	chr7	22778849	3961	-0.06 (-0.11, -0.01)	0.012	IL6
rs232574	T	chr2	38240731	3984	-0.06 (-0.10, -0.01)	0.012	CYP1B1
rs1325788	T	chr13	20937671	3987	-0.07 (-0.12, -0.01)	0.012	RANKL
rs6219	A	chr12	101314322	3990	-0.09 (-0.16, -0.02)	0.012	IGF1
rs2269368	C	chrX	152843013	4040	-0.09 (-0.16, -0.02)	0.012	IRAK1
rs980281	T	chr6	152039956	4048	-0.05 (-0.09, -0.01)	0.012	ESR1
rs9965948	T	chr18	58352844	4049	-0.05 (-0.10, -0.01)	0.012	RANK
rs9397066	A	chr6	151961629	4093	-0.06 (-0.11, -0.01)	0.012	ESR1
rs1555587	T	chr13	42189413	4128	-0.06 (-0.11, -0.01)	0.012	RANKL
rs9285265	G	chr13	22990744	4142	-0.05 (-0.10, -0.01)	0.012	RANKL
rs2963154	C	chr5	142722730	4145	-0.07 (-0.13, -0.02)	0.012	NR3C1
rs121046	G	chr13	31467815	4175	-0.05 (-0.10, -0.01)	0.012	RANKL
rs9576756	T	chr13	38677744	4187	-0.06 (-0.11, -0.01)	0.012	RANKL
rs12864419	C	chr13	28053904	4227	-0.05 (-0.10, -0.01)	0.013	RANKL
rs7997858	G	chr13	28070709	4238	-0.06 (-0.10, -0.01)	0.013	RANKL
rs11617228	C	chr13	22753056	4267	-0.06 (-0.11, -0.01)	0.013	RANKL
rs4355801	A	chr8	119993054	4278	-0.05 (-0.09, -0.01)	0.013	OPG
rs7337921	A	chr13	23381053	4293	-0.05 (-0.10, -0.01)	0.013	RANKL
rs2504065	G	chr6	152136860	4310	-0.05 (-0.09, -0.01)	0.013	ESR1
rs43054	G	chr7	94917358	4321	-0.06 (-0.10, -0.01)	0.013	PON1
rs3942629	T	chr3	123206728	4342	-0.06 (-0.11, -0.01)	0.013	CASR
rs1777670	A	chr13	35052966	4343	-0.07 (-0.12, -0.01)	0.013	RANKL
rs2107622	T	chr5	142531590	4400	-0.08 (-0.15, -0.02)	0.013	NR3C1
rs7992970	A	chr13	41843463	4460	-0.06 (-0.11, -0.01)	0.013	RANKL
rs1889926	T	chr1	65470767	4493	-0.06 (-0.10, -0.01)	0.013	LEPR
rs8070464	G	chr17	4459241	4508	-0.07 (-0.13, -0.02)	0.014	ALOX15
rs3785568	G	chr17	59377523	4540	-0.07 (-0.12, -0.01)	0.014	GH1
rs2235638	G	chr16	1513891	4630	-0.14 (-0.24, -0.03)	0.014	CLCN7
rs9315776	C	chr13	39901022	4644	-0.05 (-0.10, -0.01)	0.014	RANKL
rs10183112	A	chr2	38299283	4676	-0.10 (-0.17, -0.02)	0.014	CYP1B1
rs7337322	A	chr13	37475056	4700	-0.08 (-0.14, -0.02)	0.014	RANKL
rs586205	T	chr13	21263974	4745	-0.08 (-0.15, -0.02)	0.014	RANKL
rs4516035	C	chr12	46586093	4845	-0.05 (-0.09, -0.01)	0.015	VDR
rs10219883	C	chr13	31606478	4924	-0.06 (-0.11, -0.01)	0.015	RANKL
rs12165104	G	chr18	58201621	4995	-0.06 (-0.10, -0.01)	0.015	RANK

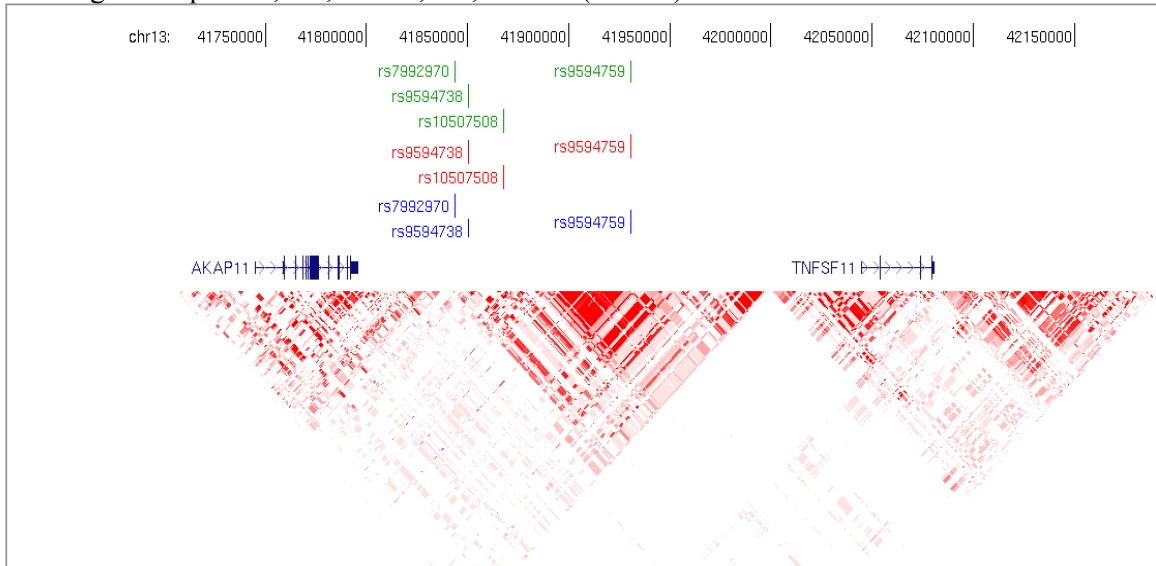
\* 200 kb in either direction of the gene was included in the analysis

### Appendix Figure 1

Schematic views of the BMD associated regions on 13q14, 8q24, 18q21, 6q25, 1p36, 6p21, 12q13 and 2p16.

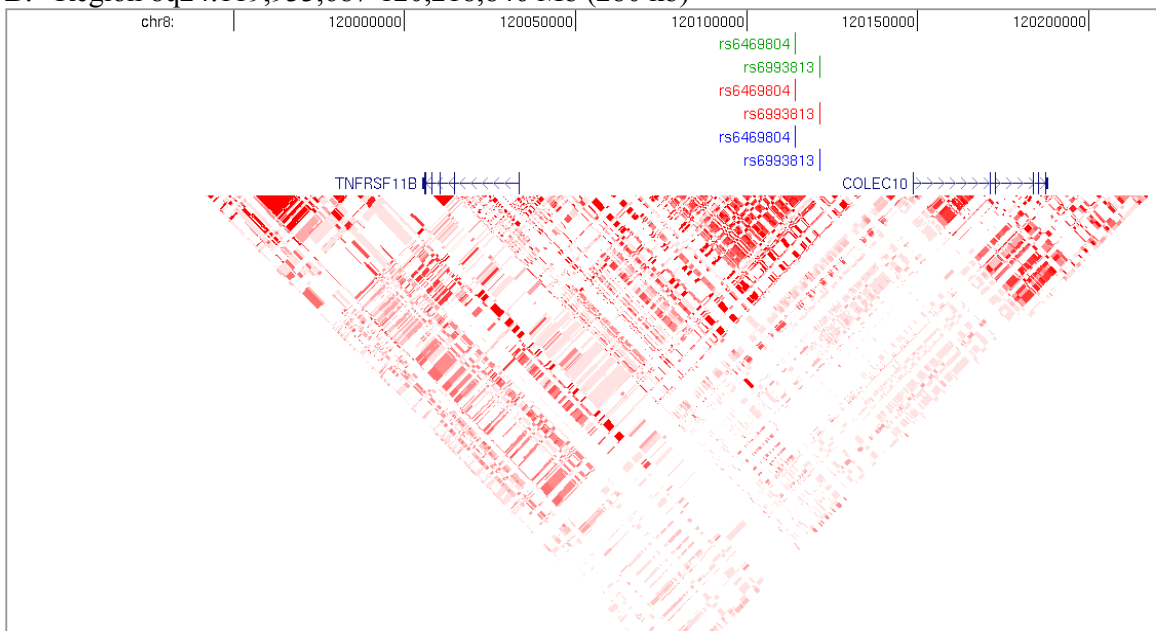
Base pair positions are NCBI Build 36 coordinates. SNP names marked in green are SNPs tested in the region displayed, SNPs in red are the ones that replicated significantly ( $P$ -combined  $\leq 0.05$ ) and SNPs in blue were genome-wide significant ( $P < 1.7 \times 10^{-7}$ ). Displayed schematically below the SNP names are known protein-coding genes from the NCBI mRNA reference sequences collection (RefSeq). LD plot figure, at the bottom, includes pair-wise  $r^2$  values for common SNPs in the region (with MAF > 5%) from the HapMap Phase II release 22 (unphased genotypes) for the CEU population. Tracks shown are from the UCSC browser (Genome Res. 12(6), 996-1006, 2002).

#### A. Region 13q14: 41,705,000-42,190,738 Mb (485 kb)



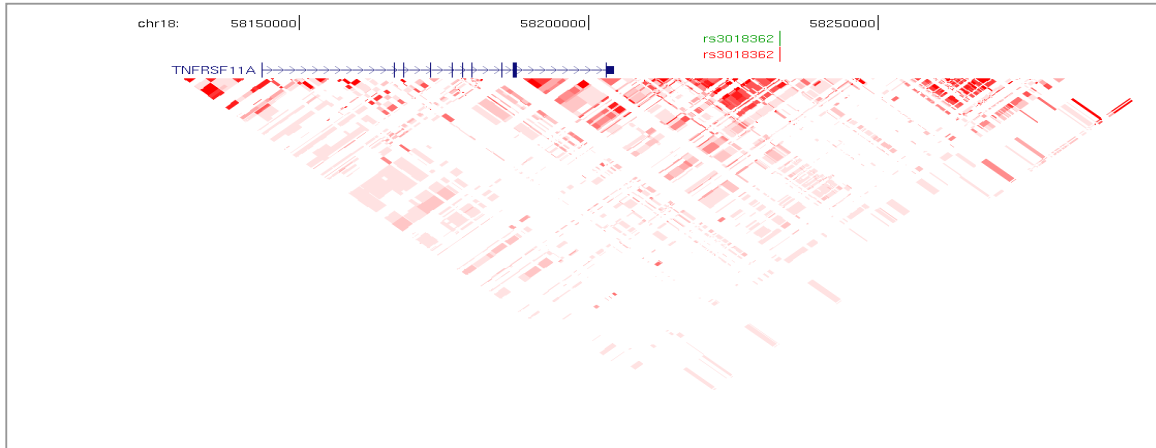
AKAP11 (A-kinase anchor protein 11), TNFSF11 (tumor necrosis factor ligand superfamily member 11)

#### B. Region 8q24: 119,933,687-120,218,846 Mb (280 kb)



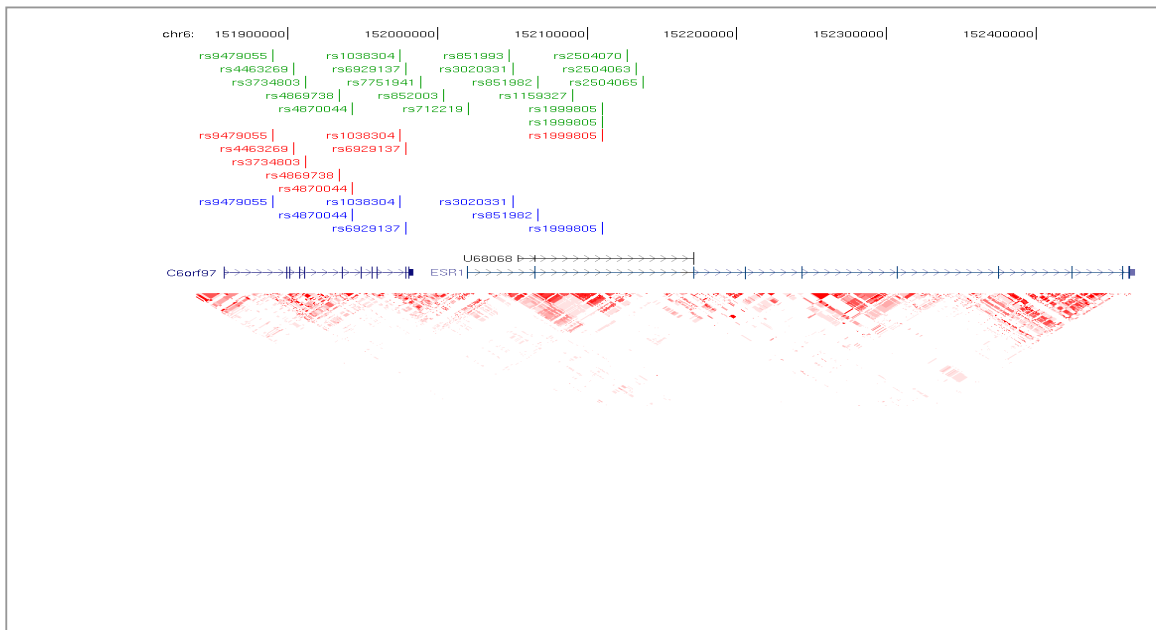
TNFRSF11B (tumor necrosis factor receptor superfamily, member 11) = RANKL (receptor activator of nuclear factor kB ligand), COLEC10 (collectin sub-family member 10)

**C. Region 18q21: 58,130,000-58,299,627 Mb (169 kb)**



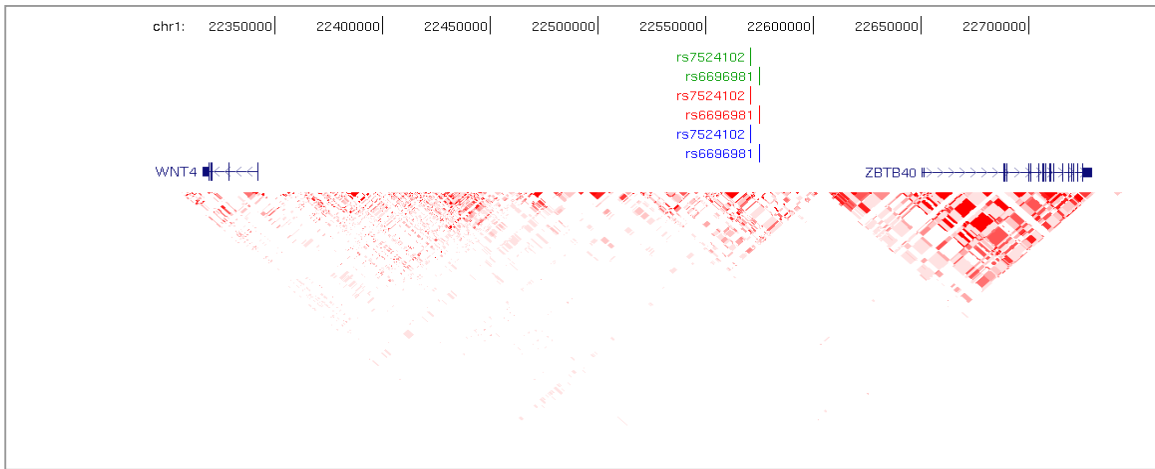
TNFRSF11A (Tumor necrosis factor receptor superfamily, member 11A) = RANK (receptor activator of nuclear factor  $\kappa$ B)

**D. Region 6q25: 151,840,000-152,470,000 Mb (630 kb)**



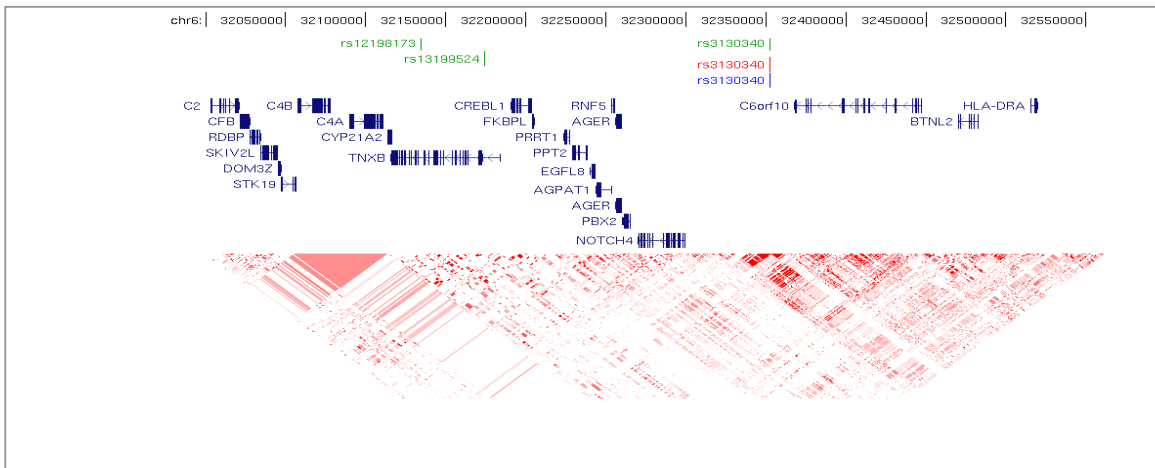
C6orf96 (chromosome 6 open reading frame 97), ESR1 (estrogen receptor 1)

**E. Region 1p36: 22,310,000-22,750,000 Mb (440 kb)**



WNT4 (wingless-type MMTV integration site family member 4), ZBTB40 (zinc finger and BTB domain containing 40)

**F. Region 6p21:32,000,000-32,580,000 Mb (580 kb)**

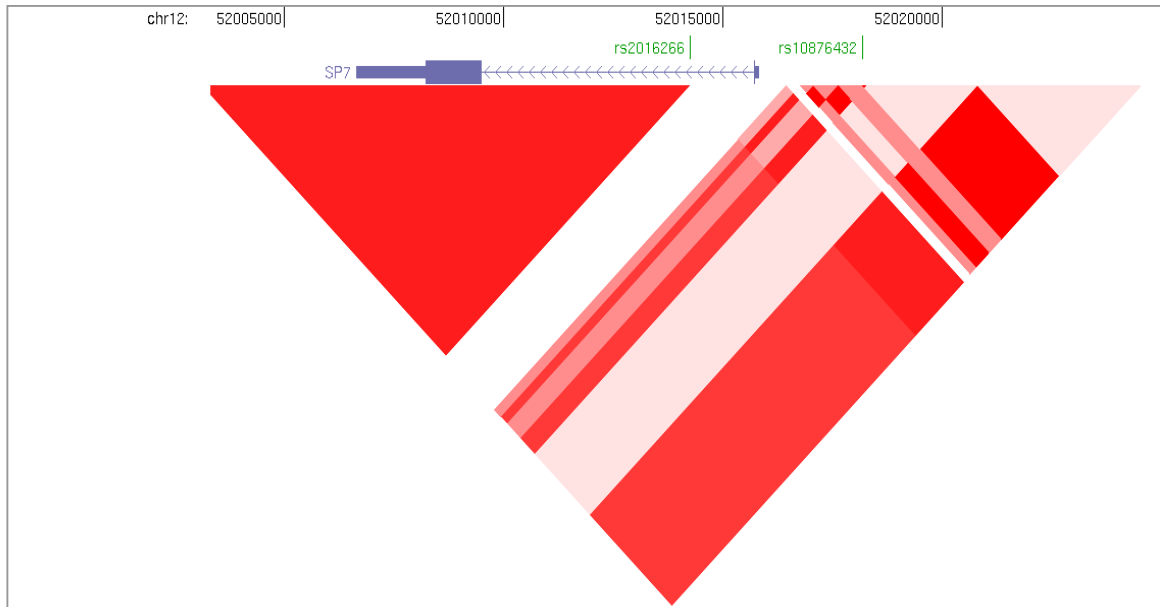


Notch4 (Notch homolog 4), C6orf10 (chromosome 6 open reading frame 10), TNXB (tenascin XB)





I. Region 12q13: 52,002,900-52,024,982 Mb (22 kb)



SP7 (transcription factor specificity protein 7) = osx (osterix)