Methods:

Candidate Gene Analysis: SNP-by-Sex Interaction

We also tested eighty-two previously reported BMD-associated SNPs identified through a meta-analysis of 83,894 subjects (1)for SNP-by-sex interactions.   This hypothesis-driven analysis also afforded us the opportunity to focus on the most promising SNPs from the BMD GEFOS II meta-analysis while reducing the penalty due to multiple testing (1). In addition, this sex by SNP interaction analysis offered an opportunity to determine whether the reason for 26 of those SNPs not replicating in the GEFOS II BMD meta-analysis could have been attributed to sex-specificity.

Functional Interaction Network:

Studies have suggested that genes under the same linkage analysis peak, and genes with similar expression profiles are related within hierarchical genetic networks or pathways (2). To further understand the potential functions of the genes annotated to the most significant SNPs in our analyses, we focused on their functional interactions with sex hormones (specifically β-estradiol and testosterone), and Wnt signaling pathway members, because these pathways are critical in skeletal development, which is when skeletal features begin to differ between the sexes. We constructed functional interaction networks using Ingenuity Pathways Analysis (IPA) (Ingenuity, Redwood City, CA). The Ingenuity database is a knowledge repository of networks and biological relationships that have been systematically encoded into ontology based on more than 200,000 original peer-reviewed articles on mammalian biology. Details are available in the IPA Web site (www.ingenuity.com). Direct molecular interactions and regulatory events among

genes/proteins have been manually extracted and curated from full text peer-reviewed articles of experimental findings in human, mice and rats to create the IPA database.

The details of the algorithm used to construct networks has been described elsewhere (3). In brief, after annotating the SNPs from each of our top SNP-sex interaction GWAS associations to a gene, we overlaid results onto a global molecular network from the Ingenuity database to form a sub-network. With the assumption of biological commonalities among top associated genes for a specific disease, sub-networks are then combined into small-networks that maximize their specific connectivity, which is a reflection of their interconnectedness with each other relative to all molecules they are connected to in the Ingenuity database. Additional molecules from the Ingenuity database are used to connect small-networks by merging them into a larger one. The finalized functional interaction networks are limited up to 35 molecules (genes/proteins) each to keep them to a usable size. A graphical network of the functional relationships between gene/gene products was extracted. Genes/gene products are represented as nodes, and the biological relationship between two nodes is represented as an edge (line). Nodes are displayed using various shapes that represent the functional class of the gene products. Edges are displayed with various labels that describe the nature of the relationship between the nodes. Statistical significance was calculated as a p-value of the probability of the genes forming a specific network in comparison to all possible networks, with the right-tailed Fisher's Exact Test based on the hypergeometric distribution.

Results:

Candidate Gene Analysis of SNP-by-Sex for Previously Reported SNPs

Supplementary Table 3 displays results for previously reported BMD-associated SNPs that demonstrated a significant interaction signal. One SNP, rs344081 (in *FLJ16641*), showed a

significant sex interaction for FNBMD, however it should be noted that none of these SNPs from discovery were successfully replicated. The results for the complete list of BMD-related loci are presented in Supplementary Table S3.

Functional Interaction Networks with Sex Hormones & Wnts

We constructed functional interaction networks using 10 of the final 12 gene-sex interaction loci (see main paper table 1) with functional information along with sex hormone relevant proteins and genes. Due to lack of biological or functional annotation, *RELL1* and *C4orf32* were excluded from analyses. A functional interaction network that linked to β-estradiol was constructed (**Supplementary Figure S3**), and we found that 8 out of 10 gene-sex interaction genes were physically (*GALR1* and *SERPINA1*) interacting with or indirectly linked to (*DOCK5, GRM7, MAT2B, TYRP1, UBE4B* and *UGCG* genes) β-estradiol ($p=10^{-25}$). The indirect links between *DOCK5, GRM7, MAT2B, TYRP1, UBE4B* and *UGCG* genes and β-estradiol are through their direct interaction with PPP2CA, TGFB1, SP1, TP53 and TNF molecules (gene, mRNA or protein). For example, UBE4B has been found to negatively regulate the level of p53 and to inhibit p53-dependent transactivation and apoptosis (4). Based on chromatin immunoprecipitation assays, studies found p53 to be recruited to the Estrogen Receptor (ER)-α promoter along with other transcription factors, such as CARM1, CBP, c-Jun, and Sp1 and that this complex was formed in a p53-dependent manner, which suggests that p53 regulates ER expression through transcriptional control of the ER promoter (5). β-estradiol increases expression of human SERPINA1 mRNA (6). Estradiol and progesterone also have been shown to decrease expression of rat Galr1 mRNA (5).

We also constructed functional interaction networks with the same 10 gene-sex interaction loci (excl. *RELL1* and *C4orf32* as above) along with Wnt signaling pathway. As is shown in the functional interaction network (**Supplementary Figure S4**), *UGCG, TYRP1* and *SERPINA1* were found to be functionally interacting with Wnt signaling pathways ($p=10^{-11}$) and *UGCG* and *SERPINA1* to be regulated by protein-protein complex that consists of human β-catenin (7).

References:

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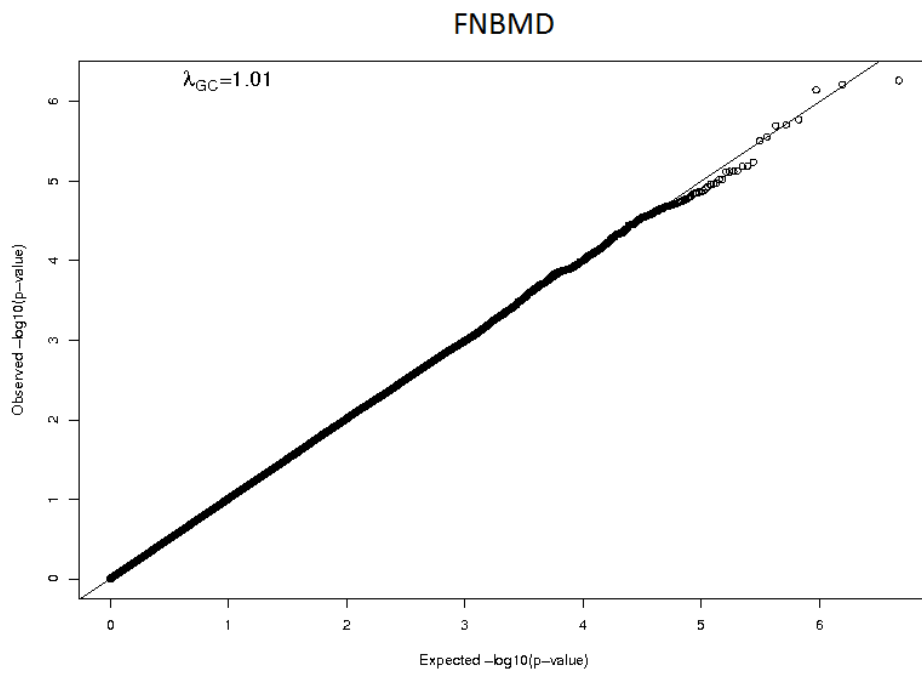
Supplementary Figure S1. Genome-wide association plots

(a) FNBMD
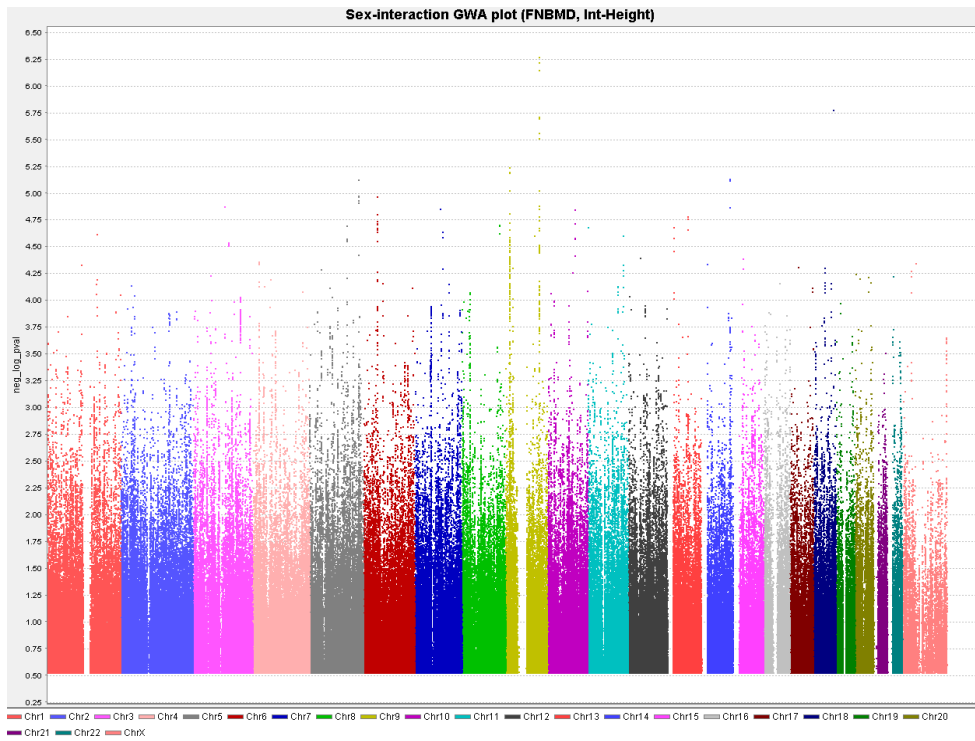
(b) LSBMD
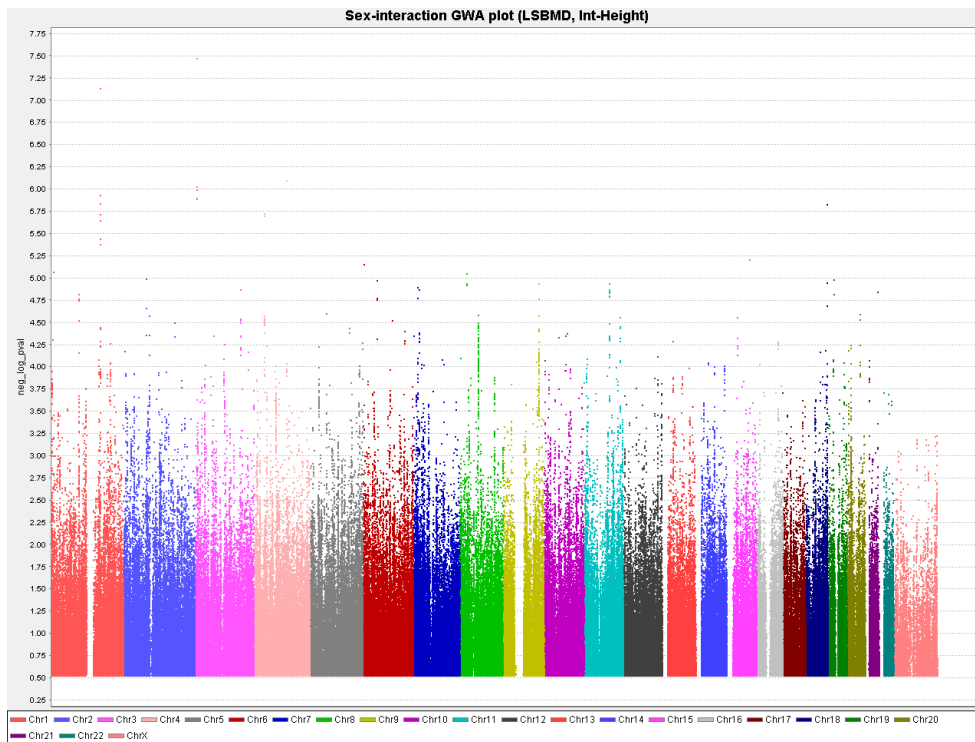
Supplementary Figure S2. Quantile-quantile plots
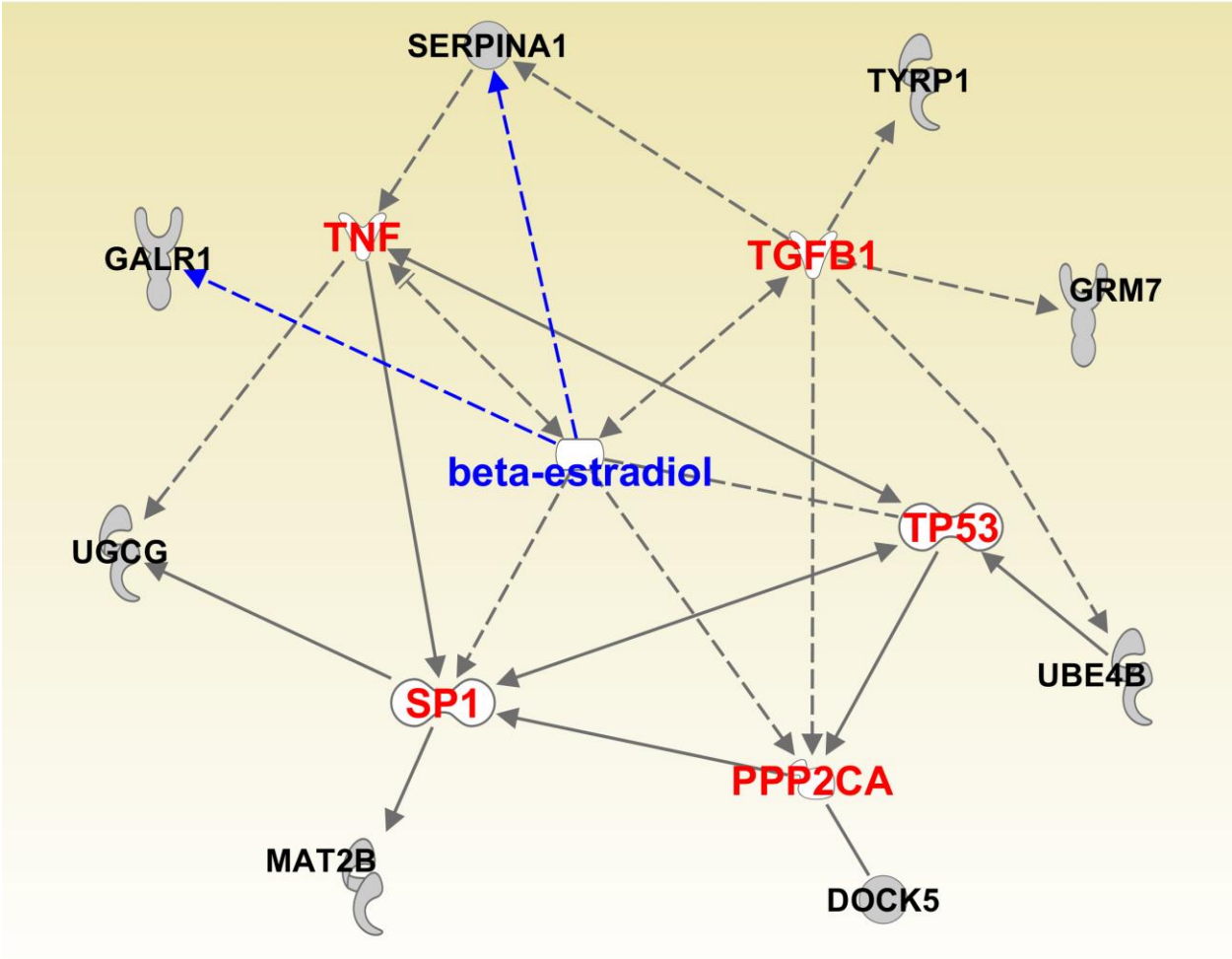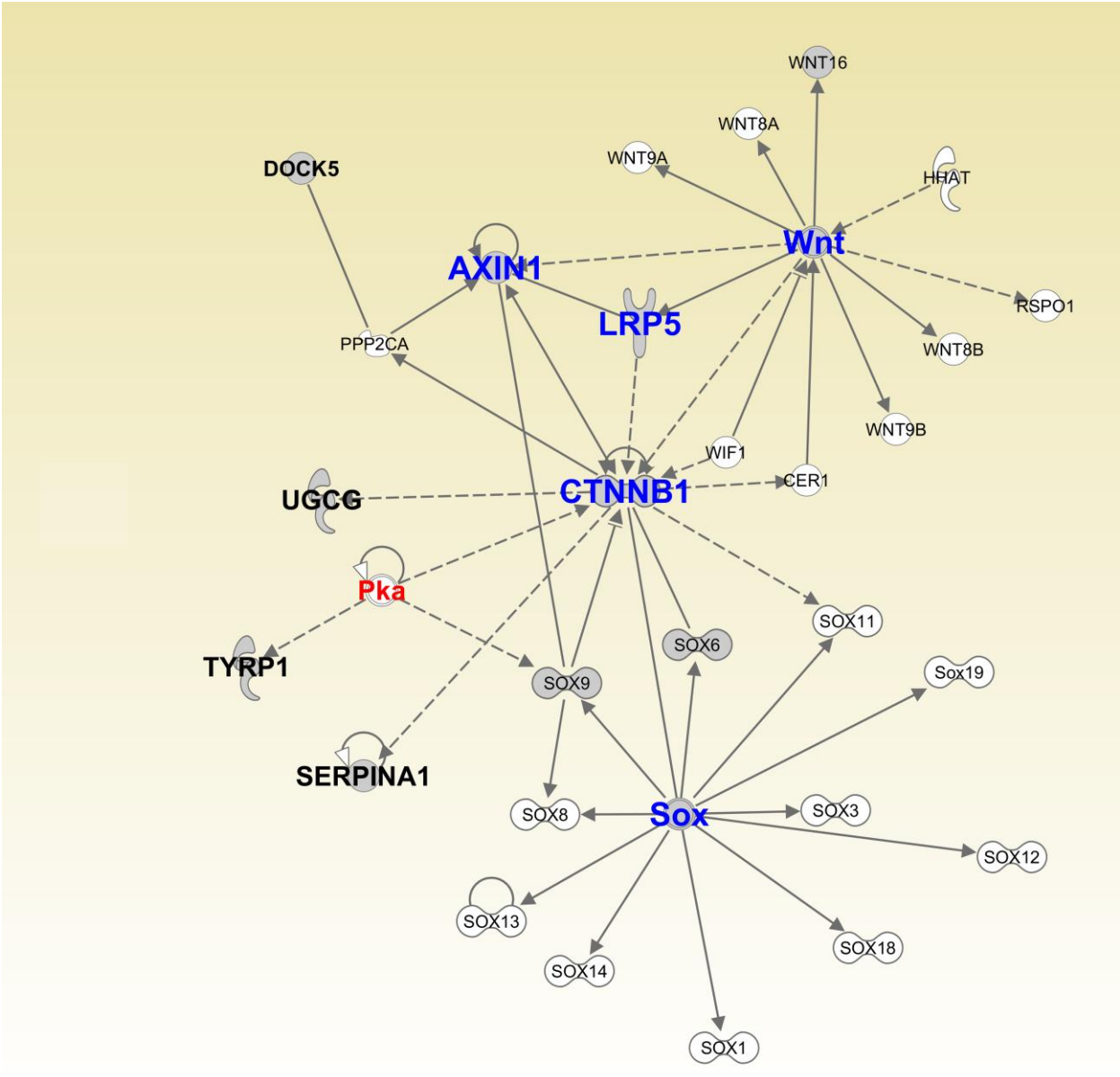
(a)

FNBMD

$\lambda_{GC}=1.01$

(b)

LSBMD

$\lambda_{GC}=1.003$
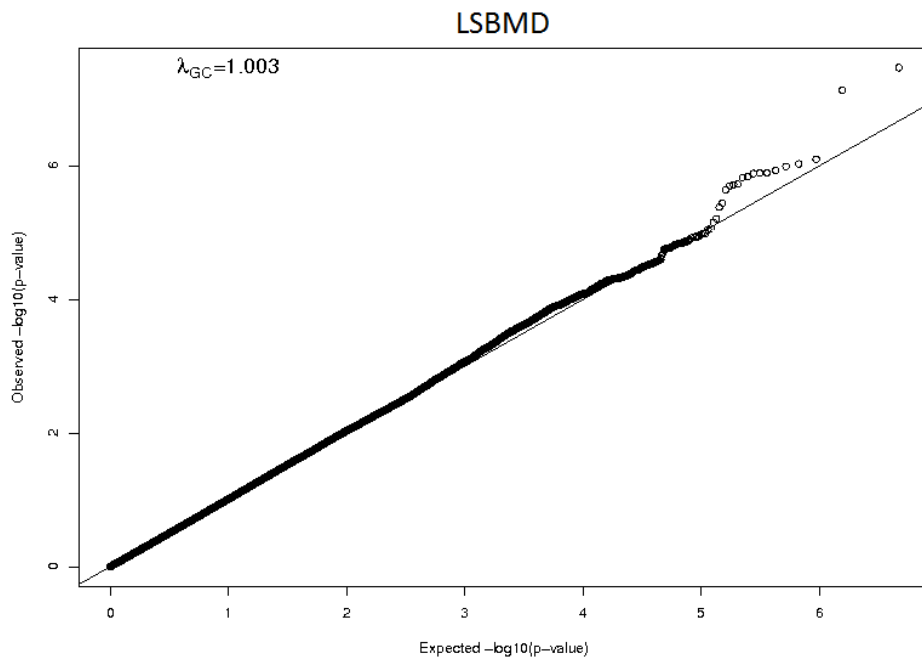
Supplementary Figure S3. Functional interaction network focusing on β-estradiol

Supplementary Figure S4. Functional interaction network focusing on Wnt signaling

Supplementary Table S1. Description of Participating Cohorts

Study	Gender	N	Age (yrs) mean (SD)	Height (cm) mean (SD)	Weight (kg) mean (SD)	FNBMD (g/cm2) mean (SD)	LSBMD (g/cm2) mean (SD)
Discovery Cohorts							
AMISH	Males	443	51.3 (15.5)	171.00 (6.40)	77.90 (12.20)	0.85 (0.13)	0.97 (0.13)
	Females	475	52.2 (14.6)	160.00 (5.90)	72.20 (14.50)	0.82 (0.14)	0.94 (0.15)
	Combined	918	51.7 (15.1)	165.00 (8.60)	74.90 (13.70)	0.84 (0.14)	0.96 (0.14)
CHS	Males	340	77.0 (4.8)	172.70 (6.50)	78.40 (12.20)	0.76 (0.14)	1.12 (0.24)
	Females	568	76.3 (4.2)	158.90 (6.40)	65.80 (13.70)	0.63 (0.11)	0.91 (0.24)
	Combined	908	76.6 (4.4)	164.10 (9.30)	70.50 (14.50)	0.68 (0.14)	0.99 (0.25)
DECODE	Males	1136	66.1 (14.2)	176.50 (6.70)	83.40 (14.40)	0.80 (0.10)	1.00 (0.20)
	Females	6469	59.7 (13.8)	164.40 (6.20)	71.10 (13.40)	0.70 (0.10)	0.90 (0.20)
	Combined	7605	60.7 (13.9)	166.21 (6.28)	72.94 (13.55)	0.71 (0.10)	0.91 (0.20)
ERF	Males	908	48.8 (14.5)	174.44 (7.23)	83.00 (14.23)	0.97 (0.15)	1.17 (0.17)
	Females	1191	47.7 (14.4)	161.75 (6.60)	69.18 (13.76)	0.91 (0.13)	1.12 (0.16)
	Combined	2099	48.2 (14.5)	167.23 (9.32)	75.21 (15.59)	0.93 (0.14)	1.15 (0.17)
FRAMINGHAM	Males	2561	54.9 (15.3)	175.45 (7.10)	86.54 (14.58)	0.98 (0.15)	1.31 (0.20)
	Females	3240	55.8 (15.7)	161.40 (6.83)	69.57 (15.09)	0.88 (0.16)	1.17 (0.20)
	Combined	5801	55.4 (15.5)	167.61 (9.85)	77.06 (17.09)	0.93 (0.16)	1.23 (0.21)
HEALTHABC	Males	833	73.9 (2.9)	173.55 (6.40)	81.51 (12.45)	0.76 (0.12)	1.07 (0.19)
	Females	734	73.6 (2.8)	159.44 (5.88)	66.31 (12.15)	0.65 (0.11)	0.91 (0.17)
	Combined	1567	73.8 (2.8)	166.94 (9.36)	74.39 (14.46)	0.71 (0.13)	1.00 (0.20)
RS I	Males	2110	68.1 (8.2)	174.85 (6.76)	78.58 (10.74)	0.92 (0.14)	1.17 (0.20)
	Females	2794	70.3 (9.6)	161.33 (6.65)	69.59 (11.29)	0.83 (0.14)	1.04 (0.18)
	Combined	4904	69.4 (9.0)	167.14 (6.70)	73.46 (11.06)	0.87 (0.14)	1.10 (0.19)
RS II	Males	781	63.7 (6.8)	176.05 (6.47)	83.50 (11.40)	0.97 (0.13)	1.21 (0.19)
	Females	898	63.8 (7.4)	162.87 (6.19)	72.80 (12.50)	0.89 (0.14)	1.11 (0.19)
	Combined	1679	63.8 (7.1)	169.00 (6.32)	77.78 (12.00)	0.93 (0.14)	1.16 (0.19)
Replication Cohorts							
RS III	Males	528	56.1 (5.5)	178.80 (6.70)	89.70 (14.10)	1.00 (0.10)	1.20 (0.20)
	Females	683	56.1 (5.5)	165.00 (6.20)	75.20 (14.30)	0.90 (0.10)	1.20 (0.20)
	Combined	1211	56.1 (5.5)	171.02 (6.42)	81.52 (14.21)	0.94 (0.10)	1.20 (0.20)
SAFOS	Males	370	42.4 (15.5)	170.68 (6.47)	85.71 (17.83)	0.90 (0.15)	1.05 (0.13)
	Females	611	44.2 (15.3)	156.75 (6.38)	76.65 (18.03)	0.84 (0.14)	1.01 (0.14)
	Combined	981	43.5 (15.4)	162.00 (9.31)	80.07 (18.48)	0.87 (0.14)	1.02 (0.14)
TWINS UK 1	Females	2174	61.4 (12.2)	162.12 (6.20)	67.27 (12.23)	0.81 (0.13)	1.00 (0.15)
TWINS UK 23	Males	473	58.9 (12.6)	175.26 (6.39)	81.85 (11.69)	0.87 (0.14)	1.03 (0.15)
	Females	3029	61.4 (12.2)	162.12 (6.20)	67.27 (12.23)	0.80 (0.14)	0.99 (0.15)
	Combined	3502	61.4 (12.2)	162.39 (6.47)	67.57 (12.39)	0.81 (0.14)	0.99 (0.15)
HKOS	Females	800	48.9 (15.5)	155.11 (6.71)	54.74 (10.27)	0.70 (0.17)	0.89 (0.21)
GOOD	Males	938	18.9 (0.56)	181.40 (6.75)	73.84 (11.89)	1.17 (0.16)	1.21 (0.15)
AROS	Males	171	54.3 (15.7)	176.20 (7.40)	78.10 (12.40)	0.70 (0.10)	0.90 (0.20)
	Females	605	61.8 (12.9)	161.70 (6.70)	63.80 (11.00)	0.70 (0.10)	0.80 (0.20)
	Combined	776	60.1 (13.9)	165.00 (9.00)	66.77 (12.71)	0.67 (0.14)	0.84 (0.18)

BARCOS	Females	1443	65.5 (9.1)	157.00 (6.00)	64.95 (10.48)	0.69 (0.11)	0.86 (0.15)
CABRIO-C	Males	529	63.9 (8.5)	168.20 (6.10)	81.50 (11.00)	0.80 (0.10)	1.00 (0.20)
	Females	902	62.0 (9.8)	155.90 (6.00)	68.70 (12.00)	0.70 (0.10)	0.90 (0.10)
	Combined	1431	62.7 (9.4)	161.00 (8.00)	73.58 (13.16)	0.76 (0.13)	0.96 (0.15)
CAIFOS	Females	1082	80.2 (2.7)	158.00 (6.00)	67.64 (12.10)	0.68 (0.10)	0.95 (0.18)
CAMOS	Males	715	65.4 (16.6)	174.10 (7.10)	81.70 (13.40)	0.80 (0.10)	1.00 (0.20)
	Females	1593	67.3 (14.9)	160.60 (6.40)	69.40 (13.70)	0.70 (0.10)	1.00 (0.20)
	Combined	2308	57.9 (14.0)	165.00 (9.00)	73.03 (14.40)	0.76 (0.13)	0.98 (0.17)
DOPS	Females	1710	50.6 (2.8)	165.00 (6.00)	67.72 (11.84)	0.80 (0.11)	1.03 (0.14)
EDOS	Males	354	62.4 (13.6)	170.60 (8.80)	77.30 (17.20)	0.70 (0.10)	0.90 (0.20)
	Females	1615	66.2 (12.4)	158.00 (7.10)	65.10 (13.70)	0.60 (0.10)	0.80 (0.20)
	Combined	1969	65.5 (12.8)	160.00 (9.00)	67.30 (15.15)	0.64 (0.13)	0.81 (0.18)
FLOS	Males	159	53.9 (14.7)	175.60 (7.00)	80.80 (13.60)	0.80 (0.20)	1.00 (0.10)
	Females	834	60.9 (12.0)	160.00 (6.70)	61.80 (9.30)	0.70 (0.20)	0.90 (0.20)
	Combined	993	59.8 (12.7)	163.00 (9.00)	64.83 (12.30)	0.72 (0.17)	0.89 (0.18)
GEOS	Females	2377	53.8 (9.6)	159.00 (6.00)	64.99 (11.86)	0.88 (0.14)	1.11 (0.17)
GEVUR	Males	75	59.2 (12.9)	170.80 (7.50)	76.20 (14.00)	0.90 (0.20)	0.90 (0.20)
	Females	397	62.2 (8.2)	159.30 (6.30)	70.60 (13.20)	0.80 (0.20)	0.90 (0.20)
	Combined	472	61.8 (9.0)	161.00 (7.00)	71.25 (13.37)	0.78 (0.17)	0.89 (0.18)
GROS	Males	41	70.2 (12.8)	164.80 (10.40)	71.50 (12.30)	0.80 (0.20)	0.90 (0.20)
	Females	252	69.1 (11.7)	161.80 (7.30)	71.70 (10.90)	0.80 (0.10)	0.80 (0.20)
	Combined	293	69.3 (11.8)	162.00 (8.00)	71.68 (11.12)	0.80 (0.15)	0.82 (0.17)
MrOS Sweden	Males	2893	75.4 (3.2)	175.00 (7.00)	80.70 (12.07)	0.85 (0.15)	1.15 (0.22)
OAS	Males	589	68.1 (4.2)	174.00 (7.00)	83.70 (12.53)	0.76 (0.11)	1.05 (0.17)
SLO-PREVAL	Males	121	67.9 (6.5)	171.70 (6.30)	81.60 (12.60)	0.80 (0.20)	1.00 (0.20)
	Females	590	62.1 (10.6)	160.40 (6.30)	69.10 (12.20)	0.70 (0.10)	0.90 (0.20)
	Combined	711	63.1 (10.3)	162.00 (8.00)	71.24 (13.12)	0.71 (0.13)	0.90 (0.17)

Supplementary Table S2. Genotype, Imputation and Sample QC information for Participating Cohorts

Study	Genotyping		SNP Inclusion criteria				SNP Imputation				Samples		Sample QC / Other exclusions	Association
	Platform(s) / Chip(s)	Calling Algorithm	MAF	Call Rate	P-test HWE	Included SNPs	Method	MAF	Quality metric	Total # SNPs	Genotyped samples	Call rate* selection		Software
Discovery Cohorts														
AMISH	Affymetrix / 500K or 6.0	Birdseed	≥ 1%	95%	>10-6	338,598	MACH	≥ 1%	MACH R2	2543013	1213	>95.0%	1. Missing BMD data. 2 Missing Covariate	MMAP (J.O'Connell)
CHS	Illumina 370CNV	BeadStudio	> 1%	≥97%	> 10⁻⁵	306,655	BimBam	≥1%	Variance on the allele dosage >0.01	2,335,99	3291	>95%	1) presence at study baseline of coronary heart disease, congestive heart failure, peripheral vascular disease, valvular heart disease, stroke or transient ischemic attack; 2) missing DNA; 3) non-Caucasian ethnicity; 4) gender mismatch; 5) discordance with prior genotyping.	R
DECODE	Illumina HH300 and 370CNV	BeadStudio	> 1%	> 96%	> 10⁻⁶	281,410	IMPUTE	≥1%	MACH R2 ≥ 0.3	2,454,808	7605	≥91%	1) missing BMD measurement; 2) missing body weight and height.	SNPTEST
ERF	Illumina	Beadstudio	>0.5%	>98%	≥ 10⁻⁶		MACH				1602	>95%	1) gender mismatch; 2) ethnic outliers; 3) Missing phenotype data; 4) high IBS; 5) excess heterozygosity.	ProbABEL
	Affymetrix	BRLMM	>1%	>95%	≥ 10⁻⁶	upto 487,573	MACH		O/E Variance	2543887	2385	>95%	1) high IBS 2) high autosomal heterozygosity 3) ethnic outliers 4) missing trait 5) sex mismatch	
FRAMINGHAM	Affymetrix 500K Dual GeneChip + 50K gene-centered MOP set	BRLMM	≥ 1%	≥ 97%	≥ 10⁻⁶	378163	MACH	≥ 1%	(O/E)σ² ratio ≥ 0.3	2540224	9274	≥ 97.0%	1. autosomal heterozygosity <0.33 or > 0.37 2. ethnic outliers (using Eigenstraat) 3. missing BMD or weight measurements	Kinship R-Package
HEALTHABC	Illumina Human1M-Duo BeadC	Illumina BeadStudio	>1%	>97%	>10e-6	914,263	MACH v1.0.16		O/E Variance	2,543,887	1663	≥ 97.0%	1) Missing DNA 2) 1st or 2nd degree relatives 3) missing body weight and height 4) ethnic outliers	ProbABEL
RS I	Illumina / HumanHap 550K V.3 ADHumanHap 550 V.3 DUO;	Beadstudio Genecall	≥ 1%	≥ 97.5%	> 10⁻⁶	512,349	MACH	≥1%	MACH R2 ≥ 0.3	2,448,227	5,746	≥ 97.5%	1) missing DNA; 2) gender mismatch with typed X-linked markers; 3) excess autosomal heterozygosity > 0.336~FDR>0.1%; 4) duplicates and/or 1st or 2nd degree relatives using IBS probabilities >97% from PLINK; 5) ethnic outliers using IBS distances > 3SD from PLINK; 6) Missing body weight and height.	MACH2QTL via GRIMP
RS II	Illumina / HumanHap 550K V.3 ADHumanHap 550 V.3 DUO;	Beadstudio Genecall	≥ 1%	≥ 97.5%	> 10⁻⁶	466,389	MACH	≥1%	MACH R2 ≥ 0.3	2,448,227	2,157	≥ 97.5%	1) missing DNA; 2) gender mismatch with typed X-linked markers; 3) excess autosomal heterozygosity > 0.336~FDR>0.1%; 4) duplicates and/or 1st or 2nd degree relatives using IBS probabilities >97% from PLINK; 5) ethnic outliers using IBS distances > 3SD from PLINK; 6) Missing body weight and height.	MACH2QTL via GRIMP
Replication Cohorts														
In-silico replication														
RS III	Illumina / HumanHap610	Beadstudio Genecall	≥ 1%	≥ 97.5%	> 10⁻⁶	514,073	MACH	≥1%	MACH R2 ≥ 0.3	2,448,227	1212	≥ 97.5%	1) missing DNA; 2) gender mismatch with typed X-linked markers; 3) excess autosomal heterozygosity > 0.336~FDR>0.1%; 4) duplicates and/or 1st or 2nd degree relatives using IBS probabilities >97% from PLINK; 5) ethnic outliers using IBS distances > 3SD from PLINK; 6) Missing body weight and height.	MACH2QTL via GRIMP
SAFOS	Illumina HumanHap 550	Beadstudio	≥ 1%	≥ 95%	> 10-6	531,800	MACH	≥ 1%	MACH R2 ≥ 0.3	1,387,467 *note HapMap3 reference data	1860	≥ 95%	1) Missing BMD measurements. 2) Missing co 2) Missing covariate data	MMAP (J.O'Connell)
TWINS UK	Illumina HumanHap 300 & 550. Illumina HumanCNV370 Duo	Beadstudio Genecall	≥ 1%	≥ 95%	> 10⁻⁶	313,575	IMPUTE	≥1%	Prop_info >0.4	2,561,701	1511	≥ 95%	1) autosomal heterozygosity <0.33 or > 0.37; 2) ethnic outliers (using STRUCTURE); 3) missing BMD or weight measurements.	GenABEL
TWINS UK-23	Illumina 610k	Beadstudio Genecall	≥ 1%	≥ 95%	> 10⁻⁶	545,026	IMPUTE	≥1%	Prop_info >0.4	2,561,701	2801	≥ 95%		GenABEL
HKOS	Human610-Quad Chip	Illumina BeadStudio	≥0.01	≥95%	≥10e-6	489,068	IMPUTE	\≥0.01	proper_info>=0.3	2,426,092 for autoso	800	95%	(1) genotyping call rate less than 95% ; (2) autosomal heterozygosity less than 28% or more than 30% ; (3) being related or identical to other individuals in the sample and (4) discordance of observed gender and estimated gender.	SNPTEST v2.2.0
GOOD	Illumina610	BeadStudio	≥ 1%	>98%	>10-6	521,160	MACH 1.0		MACH R2	2,543,887	938	98%	1) heterozygosity > 33%; 2) ethnic outliers 3) related individuals and duplicates	GRIMP
De novo genotyped														
GENOMOS	KASPar assay	SNPviewer2	≥ 1%	>90%	> 10-6	12	NA	NA	NA	NA	27715	80%	Discordance of observed gender and estimated gender .	Plink v1.07

Supplementary Table 3. Investigation of Sex-by-Gene Interaction for 56 BMD-related Loci

SNP	Locus	Closest Gene	EA/No n-EA	Allele Freq	FNBMD			LSBMD		
					Beta	SE	P-value	Beta	SE	P-value
rs12407028	1p31.3	GPR177	t/c	0.593	-0.0006	0.0024	8.00×10^{-1}	0.0008	0.0036	8.24×10^{-1}
rs6426749	1p36.12	ZBTB40	c/g	0.170	0.001	0.0032	7.53×10^{-1}	-0.0037	0.0047	4.32×10^{-1}
rs479336	1q24.3	DNM3	t/g	0.747	-0.001	0.0027	7.20×10^{-1}	0.0043	0.0041	2.95×10^{-1}
rs3790160	20p12.2	JAG1	t/c	0.508	0.0007	0.0024	7.67×10^{-1}	-0.0009	0.0036	8.07×10^{-1}
rs4233949	2p16.2	SPTBN1	c/g	0.377	0.0009	0.0025	7.23×10^{-1}	-0.0009	0.0037	8.07×10^{-1}
rs7584262	2p21	LOC91461	t/c	0.248	0.0059	0.0028	3.56×10^{-2}	0.0012	0.0041	7.75×10^{-1}
rs17040773	2q13	ANAPC1	a/c	0.759	0.0024	0.003	4.18×10^{-1}	0.0021	0.0044	6.30×10^{-1}
rs1878526	2q14.2	INSIG2	a/g	0.215	-0.0031	0.0029	3.00×10^{-1}	-0.0098	0.0043	2.31×10^{-2}
rs1346004	2q24.3	GALNT3	a/g	0.499	-0.0023	0.0025	3.46×10^{-1}	-0.0075	0.0035	3.48×10^{-2}
rs430727	3p22.1	CTNNB1	t/c	0.470	-0.0012	0.0024	6.05×10^{-1}	-0.0061	0.0036	8.35×10^{-2}
rs1026364	3q13.2	KIAA2018	t/g	0.378	-0.003	0.0025	2.28×10^{-1}	-0.0021	0.0036	5.60×10^{-1}
rs344081	3q25.31	LEKR1	t/c	0.868	0.0136	0.0036	1.31×10^{-4}	0.0105	0.0051	3.92×10^{-2}
rs3755955	4p16.3	IDUA	a/g	0.152	-0.0069	0.004	8.17×10^{-2}	-0.006	0.0059	3.14×10^{-1}
rs6532023	4q22.1	MEPE	t/g	0.339	-0.0025	0.0025	3.01×10^{-1}	-0.0021	0.0036	5.65×10^{-1}
rs1366594	5q14.3	MEF2C	a/c	0.543	0.0007	0.0023	7.56×10^{-1}	-0.0012	0.0034	7.20×10^{-1}
rs11755164	6p21.1	SUPT3H	t/c	0.410	0.002	0.0025	4.27×10^{-1}	-0.0006	0.0037	8.77×10^{-1}
rs9466056	6p22.3	CDKAL1	a/g	0.382	-0.0051	0.0024	3.36×10^{-2}	-0.01	0.0036	5.09×10^{-3}
rs13204965	6q22.32	RSPO3	a/c	0.762	-0.0061	0.0029	3.59×10^{-2}	-0.0023	0.0043	5.82×10^{-1}
rs4869742	6q25.1	C6orf97/ESR1	t/c	0.302	-0.001	0.0025	7.01×10^{-1}	-0.0014	0.0038	7.19×10^{-1}
rs6959212	7p14.1	STARD3NL	t/c	0.320	-0.0008	0.0025	7.55×10^{-1}	-0.0006	0.0037	8.69×10^{-1}
rs4727338	7q21.3	SLC25A13	c/g	0.656	0.0006	0.0024	7.90×10^{-1}	0.0065	0.0037	7.39×10^{-2}
rs3801387	7q31.31	WNT16	a/g	0.732	0.0031	0.0027	2.42×10^{-1}	0.0083	0.004	3.78×10^{-2}
rs7812088	7q36.1	ABCF2	a/g	0.128	0.0013	0.0036	7.25×10^{-1}	0.004	0.0054	4.57×10^{-1}
rs7017914	8p13.3	XKR9	a/g	0.481	-0.0054	0.0023	2.04×10^{-2}	-0.0089	0.0034	9.74×10^{-3}
rs2062377	8q24.12	TNFRSF11B	a/t	0.563	-0.0048	0.0024	4.47×10^{-2}	-0.0003	0.0035	9.31×10^{-1}
rs7851693	9q34.11	FUBP3	c/g	0.656	0.0002	0.0025	9.46×10^{-1}	-0.0025	0.0038	5.12×10^{-1}
rs3905706	10p11.23	MPP7	t/c	0.201	0.0001	0.003	9.62×10^{-1}	-0.0034	0.0043	4.36×10^{-1}
rs1373004	10q21.1	MBL2	t/g	0.125	0.0062	0.0039	1.07×10^{-1}	0.0139	0.0057	1.44×10^{-2}
rs7071206	10q22.3_1	KCNMA1	t/c	0.788	0.0025	0.0029	3.92×10^{-1}	0.0031	0.0043	4.65×10^{-1}
rs7084921	10q24.2	CPN1	t/c	0.398	-0.0039	0.0025	1.15×10^{-1}	0.0023	0.0035	5.06×10^{-1}
rs7932354	11p11.2	ARHGAP1	t/c	0.295	-0.0012	0.0027	6.50×10^{-1}	-0.0025	0.0039	5.22×10^{-1}
rs10835187	11p14.1_1	LIN7C	t/c	0.556	0.0072	0.0024	2.34×10^{-3}	0.007	0.0035	4.53×10^{-2}
rs163879	11p14.1_2	DCDC5	t/c	0.698	0.0009	0.0025	7.10×10^{-1}	0.0056	0.0038	1.39×10^{-1}
rs7108738	11p15.2	SOX6	t/g	0.820	0.0013	0.003	6.76×10^{-1}	0.0012	0.0045	7.96×10^{-1}
rs3736228	11q13.2	LRP5	t/c	0.160	-0.0045	0.0033	1.72×10^{-1}	-0.005	0.0048	3.00×10^{-1}
rs7953528	12p11.22	KLHDC5	a/t	0.175	0.0034	0.0031	2.78×10^{-1}	0.0087	0.0048	6.89×10^{-2}
rs2887571	12p13.33	ERC1	a/g	0.760	0.0024	0.0027	3.84×10^{-1}	0	0.004	9.96×10^{-1}
rs12821008	12q13.12	DHH	t/c	0.380	0.0019	0.0025	4.50×10^{-1}	-0.0035	0.0037	3.48×10^{-1}
rs2016266	12q13.13	SP7	a/g	0.682	-0.0002	0.0025	9.27×10^{-1}	0.0062	0.0038	1.01×10^{-1}
rs1053051	12q23.3	C12orf23	t/c	0.515	0.0013	0.0023	5.78×10^{-1}	-0.0029	0.0035	4.06×10^{-1}
rs9533090	13q14.11	AKAP11/RANKl	t/c	0.483	0.0026	0.0024	2.71×10^{-1}	-0.001	0.0036	7.86×10^{-1}
rs1286083	14q32.12	RPS6KA5	t/c	0.814	-0.0041	0.0031	1.82×10^{-1}	-0.006	0.0045	1.83×10^{-1}
rs11623869	14q32.32	MARK3	t/g	0.355	0.0019	0.0025	4.49×10^{-1}	0.0035	0.0037	3.42×10^{-1}
rs4985155	16p13.11	NTAN1	a/g	0.678	-0.0077	0.0025	1.96×10^{-3}	-0.0041	0.0038	2.80×10^{-1}
rs9921222	16p13.3_1	AXIN1	t/c	0.484	0.001	0.0025	6.80×10^{-1}	-0.0012	0.0036	7.42×10^{-1}

rs13336428	16p13.3_2	LOC390667	a/g	0.425	0.0006	0.0026	8.03×10^{-1}	0.0041	0.0038	2.80×10^{-1}
rs1566045	16q12.1	SALL1	t/c	0.796	-0.0031	0.0035	3.80×10^{-1}	0.0025	0.0052	6.32×10^{-1}
rs10048146	16q24.1	FOXL1	a/g	0.809	0.0017	0.0032	5.93×10^{-1}	0.0014	0.0048	7.66×10^{-1}
rs4790881	17p13.3	SMG6	a/c	0.709	0.0033	0.0026	2.05×10^{-1}	-0.0034	0.0039	3.77×10^{-1}
rs227584	17q21.31_1	C17orf53	a/c	0.711	-0.0014	0.0027	5.95×10^{-1}	-0.0041	0.0039	2.98×10^{-1}
rs1864325	17q21.31_2	MAPT	t/c	0.222	0.0003	0.0028	9.11×10^{-1}	0.0004	0.0042	9.24×10^{-1}
rs7217932	17q24.3	SOX9	a/g	0.471	0.0016	0.0024	4.96×10^{-1}	0.0003	0.0036	9.39×10^{-1}
rs4796995	18p11.21	C18orf19	a/g	0.637	0.0004	0.0024	8.68×10^{-1}	0.0045	0.0035	2.09×10^{-1}
rs884205	18q21.33	TNFRSF11A	a/c	0.273	0.0002	0.0028	9.36×10^{-1}	0.0014	0.004	7.36×10^{-1}
rs10416218	19q13.11	GPATCH1	t/c	0.745	0.0022	0.0027	4.27×10^{-1}	0.0044	0.004	2.76×10^{-1}
rs5934507*	Xp22.31	FAM9B	a/g	0.720	-0.008	0.0044	6.67×10^{-2}	-0.0159	0.0065	1.47×10^{-2}
Secondary signals										
rs17482952	1p31.3	WLS	a/g	0.925	-0.0011	0.0044	8.05×10^{-1}	0.0001	0.0068	9.92×10^{-1}
rs7521902	1p36.12	WNT4	a/c	0.216	-0.0015	0.003	6.16×10^{-1}	0.001	0.0044	8.17×10^{-1}
rs7751941	6q25.1	C6orf97	a/g	0.209	-0.001	0.0029	7.24×10^{-1}	-0.0097	0.0043	2.42×10^{-2}
rs10226308	7p14.1	TXNDC3	a/g	0.808	-0.0003	0.003	9.32×10^{-1}	0.007	0.0044	1.07×10^{-1}
rs13245690	7q31.31	C7orf58	a/g	0.599	0.001	0.0024	6.84×10^{-1}	-0.0049	0.0037	1.81×10^{-1}
rs736825	12q13.13	HOXC6	c/g	0.625	0.0025	0.0026	3.26×10^{-1}	0.0028	0.0038	4.49×10^{-1}
rs1564981	16q12.1	CYLD	a/g	0.471	0.0019	0.0024	4.33×10^{-1}	0.0028	0.0035	4.18×10^{-1}
rs4792909	17q21.31_1	SOST	t/g	0.369	-0.0028	0.0025	2.51×10^{-1}	-0.0032	0.0036	3.79×10^{-1}