

Supplementary Materials

Table S1. Single nucleotide polymorphisms (SNPs) selected in the study, chromosomal location, minor allele frequency and association with BMD and activity outcomes.

SNP	Chr	GRCh37Position	GeneSymbol	GeneLocation	MAF	Outcome BMD	Outcome Activity
rs363609	2	74902872	SEMA4F	INTRON	0.13		
rs989506	7	93147883	CALCR	INTRON	0.18		
rs10955898	8	119793583	LOC441377 TNFRSF11B	INTERGENIC	0.11		x
rs4130891	8	119921354	LOC441377 TNFRSF11B	INTERGENIC	0.18		
rs4355801	8	119923873	LOC441377 TNFRSF11B	INTERGENIC	0.46	x	x
rs3134058	8	119954108	TNFRSF11B	INTRON	0.42		x
rs10505346	8	119963843	TNFRSF11B	INTRON	0.22		x
rs6469804	8	120044829	TNFRSF11B COLEC10	INTERGENIC	0.42	x	x
rs6993813	8	120052238	TNFRSF11B COLEC10	INTERGENIC	0.45		x
rs11265876	9	92039416	LOC100133304 SEMA4D	INTERGENIC	0.36		
rs9410482	9	92054549	LOC100133304 SEMA4D	INTERGENIC	0.23		
rs11265905	9	92076595	SEMA4D LOC100128670	INTERGENIC	0.17		
rs2498315	9	92138399	SEMA4D GADD45G	INTERGENIC	0.32		
rs2988066	9	92144998	SEMA4D GADD45G	INTERGENIC	0.45		
rs3002331	9	92148993	SEMA4D GADD45G	INTERGENIC	0.40		
rs3002329	9	92151600	SEMA4D GADD45G	INTERGENIC	0.41		
rs2480490	9	92158225	SEMA4D GADD45G	INTERGENIC	0.40		
rs7093925	10	54129654	DKK1 MBL2	INTERGENIC	0.49		
rs1194669	10	54148289	DKK1 MBL2	INTERGENIC	0.52		
rs17521782	13	42898193	AKAP11 TNFSF11	INTERGENIC	0.20		
rs9525608	13	42898967	AKAP11 TNFSF11	INTERGENIC	0.13	x	
rs9566959	13	42899170	AKAP11 TNFSF11	INTERGENIC	0.30		
rs9533067	13	42900812	AKAP11 TNFSF11	INTERGENIC	0.14	x	
rs9566963	13	42902137	AKAP11 TNFSF11	INTERGENIC	0.43		
rs9533069	13	42904965	AKAP11 TNFSF11	INTERGENIC	0.30	x	
rs9533070	13	42904995	AKAP11 TNFSF11	INTERGENIC	0.19		
rs58327984	13	42905802	AKAP11 TNFSF11	INTERGENIC	0.44		
rs9562396	13	42905858	AKAP11 TNFSF11	INTERGENIC	0.29	x	
rs17521870	13	42907942	AKAP11 TNFSF11	INTERGENIC	0.14		
rs9566964	13	42908350	AKAP11 TNFSF11	INTERGENIC	0.33		

rs151474	13	42908680	AKAP11 TNFSF11	INTERGENIC	0.29	x	
rs9525610	13	42909413	AKAP11 TNFSF11	INTERGENIC	0.14	x	
rs1555631	13	42910063	AKAP11 TNFSF11	INTERGENIC	0.29	x	
rs61959448	13	42910319	AKAP11 TNFSF11	INTERGENIC	0.20		
rs238334	13	42910921	AKAP11 TNFSF11	INTERGENIC	0.29	x	
rs9594729	13	42911922	AKAP11 TNFSF11	INTERGENIC	0.15		
rs9594731	13	42911955	AKAP11 TNFSF11	INTERGENIC	0.14		
rs9533078	13	42914081	AKAP11 TNFSF11	INTERGENIC	0.20		
rs238251	13	42914729	AKAP11 TNFSF11	INTERGENIC	0.49		
rs74053868	13	42915990	AKAP11 TNFSF11	INTERGENIC	0.11		x
rs238253	13	42916029	AKAP11 TNFSF11	INTERGENIC	0.14	x	
rs9533083	13	42917069	AKAP11 TNFSF11	INTERGENIC	0.38		
rs17063206	13	42917459	AKAP11 TNFSF11	INTERGENIC	0.14		x
rs77900571	13	42917860	AKAP11 TNFSF11	INTERGENIC	0.32		
rs9525613	13	42918648	AKAP11 TNFSF11	INTERGENIC	0.29		
rs77565961	13	42919194	AKAP11 TNFSF11	INTERGENIC	0.13		x
rs9525614	13	42920520	AKAP11 TNFSF11	INTERGENIC	0.19	x	
rs4614629	13	42920990	AKAP11 TNFSF11	INTERGENIC	0.19	x	
rs17063218	13	42922259	AKAP11 TNFSF11	INTERGENIC	0.23		
rs17522044	13	42923203	AKAP11 TNFSF11	INTERGENIC	0.19	x	
rs238255	13	42923361	AKAP11 TNFSF11	INTERGENIC	0.42		
rs7322303	13	42924647	AKAP11 TNFSF11	INTERGENIC	0.19	x	
rs238257	13	42924883	AKAP11 TNFSF11	INTERGENIC	0.38	x	
rs9594733	13	42925732	AKAP11 TNFSF11	INTERGENIC	0.14		
rs7999972	13	42930322	AKAP11 TNFSF11	INTERGENIC	0.28	x	
rs7995775	13	42933413	AKAP11 TNFSF11	INTERGENIC	0.28	x	
rs238273	13	42934017	AKAP11 TNFSF11	INTERGENIC	0.33		
rs238274	13	42934627	AKAP11 TNFSF11	INTERGENIC	0.32		
rs238275	13	42934811	AKAP11 TNFSF11	INTERGENIC	0.32		
rs11617713	13	42937043	AKAP11 TNFSF11	INTERGENIC	0.28	x	
rs9525616	13	42938839	AKAP11 TNFSF11	INTERGENIC	0.46		
rs9594735	13	42939932	AKAP11 TNFSF11	INTERGENIC	0.45		
rs9594736	13	42940207	AKAP11 TNFSF11	INTERGENIC	0.43		
rs386283	13	42942263	AKAP11 TNFSF11	INTERGENIC	0.12		
rs7992970	13	42945463	AKAP11 TNFSF11	INTERGENIC	0.27		
rs71429414	13	42945821	AKAP11 TNFSF11	INTERGENIC	0.23		
rs9525617	13	42947427	AKAP11 TNFSF11	INTERGENIC	0.19		
rs34211487	13	42947585	AKAP11 TNFSF11	INTERGENIC	0.22		
rs1886214	13	42948531	AKAP11 TNFSF11	INTERGENIC	0.23		
rs2209241	13	42948660	AKAP11 TNFSF11	INTERGENIC	0.16		x
rs1886215	13	42949359	AKAP11 TNFSF11	INTERGENIC	0.46		
rs17063269	13	42950035	AKAP11 TNFSF11	INTERGENIC	0.18		
rs9533087	13	42950320	AKAP11 TNFSF11	INTERGENIC	0.19		
rs12871509	13	42952075	AKAP11 TNFSF11	INTERGENIC	0.26		
rs9594738	13	42952145	AKAP11 TNFSF11	INTERGENIC	0.43	x	

rs17457484	13	42952499	AKAP11 TNFSF11	INTERGENIC	0.27	
rs56008941	13	42952611	AKAP11 TNFSF11	INTERGENIC	0.27	
rs1475248	13	42953003	AKAP11 TNFSF11	INTERGENIC	0.26	
rs989354	13	42953336	AKAP11 TNFSF11	INTERGENIC	0.26	
rs1475249	13	42954505	AKAP11 TNFSF11	INTERGENIC	0.31	
rs12870516	13	42955965	AKAP11 TNFSF11	INTERGENIC	0.27	
rs11840862	13	42956463	AKAP11 TNFSF11	INTERGENIC	0.31	x
rs35246711	13	42956657	AKAP11 TNFSF11	INTERGENIC	0.32	
rs1408222	13	42956875	AKAP11 TNFSF11	INTERGENIC	0.26	
rs35406824	13	42957324	AKAP11 TNFSF11	INTERGENIC	0.27	
rs8001611	13	42965694	AKAP11 TNFSF11	INTERGENIC	0.43	x
rs9533094	13	42965837	AKAP11 TNFSF11	INTERGENIC	0.42	x
rs77855024	13	42971615	AKAP11 TNFSF11	INTERGENIC	0.12	
rs1324004	13	42974209	AKAP11 TNFSF11	INTERGENIC	0.26	
rs1324003	13	42976126	AKAP11 TNFSF11	INTERGENIC	0.31	
rs12853439	13	42978035	AKAP11 TNFSF11	INTERGENIC	0.26	
rs12865514	13	42979444	AKAP11 TNFSF11	INTERGENIC	0.28	
rs2324878	13	42980878	AKAP11 TNFSF11	INTERGENIC	0.28	
rs9566973	13	42986541	AKAP11 TNFSF11	INTERGENIC	0.25	
rs4942114	13	42986731	AKAP11 TNFSF11	INTERGENIC	0.26	
rs9533099	13	42987357	AKAP11 TNFSF11	INTERGENIC	0.26	
rs9594745	13	42987938	AKAP11 TNFSF11	INTERGENIC	0.26	
rs7327510	13	42988924	AKAP11 TNFSF11	INTERGENIC	0.46	
rs17638696	13	42989440	AKAP11 TNFSF11	INTERGENIC	0.18	
rs9562401	13	42990400	AKAP11 TNFSF11	INTERGENIC	0.25	
rs2324877	13	42991060	AKAP11 TNFSF11	INTERGENIC	0.25	
rs9590697	13	42994481	AKAP11 TNFSF11	INTERGENIC	0.27	
rs9533100	13	42996548	AKAP11 TNFSF11	INTERGENIC	0.45	
rs9525620	13	42996632	AKAP11 TNFSF11	INTERGENIC	0.25	
rs9533101	13	42996797	AKAP11 TNFSF11	INTERGENIC	0.25	
rs6561043	13	42997574	AKAP11 TNFSF11	INTERGENIC	0.28	
rs4942120	13	43005533	AKAP11 TNFSF11	INTERGENIC	0.30	x
rs1924416	13	43008994	AKAP11 TNFSF11	INTERGENIC	0.29	
rs9533103	13	43010483	AKAP11 TNFSF11	INTERGENIC	0.13	
rs4942121	13	43012590	AKAP11 TNFSF11	INTERGENIC	0.27	
rs9533104	13	43017895	AKAP11 TNFSF11	INTERGENIC	0.43	
rs9525625	13	43018030	AKAP11 TNFSF11	INTERGENIC	0.45	
rs4942122	13	43018898	AKAP11 TNFSF11	INTERGENIC	0.25	
rs2147160	13	43021639	AKAP11 TNFSF11	INTERGENIC	0.31	x
rs9315919	13	43029068	AKAP11 TNFSF11	INTERGENIC	0.28	
rs41482750	13	43030937	AKAP11 TNFSF11	INTERGENIC	0.33	x
rs12430303	13	43032027	AKAP11 TNFSF11	INTERGENIC	0.43	
rs9594759	13	43032593	AKAP11 TNFSF11	INTERGENIC	0.48	
rs1974021	13	43033102	AKAP11 TNFSF11	INTERGENIC	0.19	
rs9533109	13	43033187	AKAP11 TNFSF11	INTERGENIC	0.22	

rs17457881	13	43034284	AKAP11 TNFSF11	INTERGENIC	0.26	
rs1853573	13	43034968	AKAP11 TNFSF11	INTERGENIC	0.48	
rs9594766	13	43040043	AKAP11 TNFSF11	INTERGENIC	0.45	
rs1886211	13	43040438	AKAP11 TNFSF11	INTERGENIC	0.25	
rs7990020	13	43044946	AKAP11 TNFSF11	INTERGENIC	0.46	
rs2093816	13	43046036	AKAP11 TNFSF11	INTERGENIC	0.47	
rs927623	13	43046054	AKAP11 TNFSF11	INTERGENIC	0.25	
rs7322806	13	43046397	AKAP11 TNFSF11	INTERGENIC	0.25	
rs9533117	13	43046812	AKAP11 TNFSF11	INTERGENIC	0.30	
rs9594768	13	43049482	AKAP11 TNFSF11	INTERGENIC	0.49	
rs2062305	13	43052880	AKAP11 TNFSF11	INTERGENIC	0.45	
rs35486210	13	43054684	AKAP11 TNFSF11	INTERGENIC	0.27	
rs34132030	13	43056036	AKAP11 TNFSF11	INTERGENIC	0.30	
rs1351832	13	43057549	AKAP11 TNFSF11	INTERGENIC	0.31	x
rs9594770	13	43058031	AKAP11 TNFSF11	INTERGENIC	0.32	
rs17536071	13	43060407	AKAP11 TNFSF11	INTERGENIC	0.27	
rs2046387	13	43063646	AKAP11 TNFSF11	INTERGENIC	0.22	
rs12868231	13	43064910	AKAP11 TNFSF11	INTERGENIC	0.29	
rs9533128	13	43065404	AKAP11 TNFSF11	INTERGENIC	0.15	
rs9533129	13	43066117	AKAP11 TNFSF11	INTERGENIC	0.32	
rs4942132	13	43069998	AKAP11 TNFSF11	INTERGENIC	0.23	
rs4942133	13	43070050	AKAP11 TNFSF11	INTERGENIC	0.22	
rs35860234	13	43070206	AKAP11 TNFSF11	INTERGENIC	0.22	
rs9315922	13	43070780	AKAP11 TNFSF11	INTERGENIC	0.22	
rs9315923	13	43070894	AKAP11 TNFSF11	INTERGENIC	0.44	
rs66880203	13	43072531	AKAP11 TNFSF11	INTERGENIC	0.16	
rs10507510	13	43073157	AKAP11 TNFSF11	INTERGENIC	0.21	
rs12869389	13	43073459	AKAP11 TNFSF11	INTERGENIC	0.33	
rs17536113	13	43083876	AKAP11 TNFSF11	INTERGENIC	0.34	
rs9533133	13	43083934	AKAP11 TNFSF11	INTERGENIC	0.41	
rs346598	13	43084125	AKAP11 TNFSF11	INTERGENIC	0.20	
rs346599	13	43084305	AKAP11 TNFSF11	INTERGENIC	0.23	
rs56967493	13	43084877	AKAP11 TNFSF11	INTERGENIC	0.44	
rs35111182	13	43085198	AKAP11 TNFSF11	INTERGENIC	0.36	
rs7336228	13	43085216	AKAP11 TNFSF11	INTERGENIC	0.22	
rs4941430	13	43086351	AKAP11 TNFSF11	INTERGENIC	0.23	
rs4941431	13	43086478	AKAP11 TNFSF11	INTERGENIC	0.19	
rs376999	13	43086646	AKAP11 TNFSF11	INTERGENIC	0.22	
rs3862738	13	43086907	AKAP11 TNFSF11	INTERGENIC	0.32	x
rs9562406	13	43097559	AKAP11 TNFSF11	INTERGENIC	0.19	x
rs4942139	13	43098328	AKAP11 TNFSF11	INTERGENIC	0.21	
rs35230292	13	43098967	AKAP11 TNFSF11	INTERGENIC	0.22	
rs9533139	13	43099648	AKAP11 TNFSF11	INTERGENIC	0.41	
rs568215	15	48063076	SEMA6D	UTR	0.40	

rs1513670	17	41807331	LOC100128016 SOST	INTERGENIC	0.40	x
rs1805034	18	60027241	TNFRSF11A	CODING	0.44	x
rs4426449	18	60042817	TNFRSF11A	INTRON	0.34	
rs2957145	18	60076799	TNFRSF11A ZCCHC2	INTERGENIC	0.37	
rs599323	18	60165701	TNFRSF11A ZCCHC2	INTERGENIC	0.21	x

Abbreviations: SNPs: single nucleotide polymorphisms; Chr: chromosome; MAF: minor allele frequencies; BMD: bone mineral density; x: association with outcome with $p < 0.05$.

Table S2. Multivariable model of relationship between activity at 2-year follow-up assessed by HUPI and rs3134058 in *TNFRSF11B*.

	B-Coeff.	Std. Err.	P> z	[95% Conf. Interval]	
Age of disease onset, years					
< 45	Ref.				
45 - 65	1.199	0.755	0.001	0.463	1.935
> 65	1.033	0.398	0.009	0.253	1.813
Diagnosis					
RA	Ref.				
UA	-0.446	0.330	0.177	-1.093	0.201
ACPA					
Negative	Ref.				
Positive	-0.167	0.291	0.567	-0.737	0.404
TNFRSF11B (rs3134058)					
GG	Ref.				
GA	0.497	0.274	0.070	-0.040	1.034
AA	1.551	0.658	0.018	0.260	2.841

Abbreviations: HUPI: hospital universitario de la Princesa index; Coeff: coefficient; Ref: reference; CI: confidence interval; RA: rheumatoid arthritis; UA: undifferentiated arthritis; ACPA: anti-citrullinated protein antibodies.

Table S3. Multivariable model of relationship between activity at 2-year follow-up assessed by HUPI and Combined Genotypic Model of SNPs related to *TNFRSF11B* gene.

	B-Coeff.	Std. Err.	P> z	[95% Conf. Interval]	
Age of disease onset,					
years					
< 45	Ref.				
45 - 65	0.181	0.573	0.752	-0.942	1.305
> 65	-0.021	0.595	0.972	-1.187	1.145
Diagnosis					
RA	Ref.				
UA	-1.635	0.602	0.007	-2.815	-0.456
ACPA					
Negative	Ref.				
Positive	-0.569	0.443	0.199	-1.437	0.299
CGM					
0	Ref.				
1	0.570	0.446	0.201	-0.304	1.444
2	1.901	0.742	0.010	0.447	3.355

Abbreviations: HUPI: hospital universitario de la Princesa index; SNPs: single nucleotide polymorphisms; Coeff: coefficient; Ref: reference; CI: confidence interval; RA: rheumatoid arthritis; UA: undifferentiated arthritis; ACPA: anti-citrullinated protein antibodies, CGM: Combined Genotypic Model (CGM=0 for patients who are carriers of CC-rs10505346, GG-rs3134058 and GG-rs4355801; CGM=2 for patients who are carriers of AA-rs10505346, AA-rs3134058 and AA-rs4355801 and CGM=1 for patients heterozygotes of each SNP).