SUPPLEMENTARY MATERIAL

Supplementary Table 1. Association of *IL6R* locus SNPs with joint damage in the discovery stage under alternative genetic models.

SNP	Basepair	Genetic Model	*P*-value
rs4845618	154400015	Genotypic	0.012
		Dominant	0.0025*
		Recessive	0.16
rs4453032	154414086	Genotypic	0.37
		Dominant	0.38
		Recessive	0.80
rs4845374	154426947	Genotypic	0.0020*
		Dominant	0.0027*
		Recessive	0.59
rs6698040	154432948	Genotypic	0.21
		Dominant	0.74
		Recessive	0.08
rs4379670	154439865	Genotypic	0.60
		Dominant	0.99
		Recessive	0.21

*****Significance *P-values* showing modest improvement over original genetic association under the additive model.

Supplementary Table 2. Association of *IL6R* locus SNPs with joint damage in the discovery stage according to ACPA or RF status.

SNP	Basepair	Autoantibody Group	*P*-value
rs4845618	154400015	ACPA+	0.0096
		ACPA-	0.26
		RF+	0.024
		RF-	0.08
rs4453032	154414086	ACPA+	0.31
		ACPA-	0.62
		RF+	0.42
		RF-	0.97
rs4845374	154426947	ACPA+	0.094
		ACPA-	0.055
		RF+	0.16
		RF-	0.026
rs6698040	154432948	ACPA+	0.16
		ACPA-	0.47
		RF+	0.16
		RF-	0.44
rs4379670	154439865	ACPA+	0.18
		ACPA-	0.98
		RF+	0.21
		RF-	0.84

None of the 5 IL6R tagSNPs showed an improvement of the association with joint damage after stratifying for ACPA or RF status.

Supplementary Table 3. Enhancer histone marks associated with SNP *IL6R* rs4845618 SNP identified in 111 reference epigenomes from the Epigenome Roadmap Project.

Cell ID	Cell description	State (25-state HMM)
COL.SMUS	Colon Smooth Muscle	2_TssF
R.MUC29	Rectal Mucosa.Donor 29	6_TssD2
PFM.2	Penis Foreskin Melanocyte Primary Cells.Donor skin02	2_TssF
CD4.NP	CD4 Naive Primary Cells	11_EnhWk1
CD4.MP	CD4 Memory Primary Cells	11_EnhWk1
CCIP.LSTP	CD4+ CD25- IL17+ PMA-Ionomcyin stimulated Th17 Primary Cells	11_EnhWk1
SK.MUS	Skeletal Muscle	13_EnhA
ST.MUC	Stomach Mucosa	13_EnhA
LIV.A	Adult Liver	13_EnhA
PFK.3	Penis Foreskin Keratinocyte Primary Cells.Donor skin03	11_EnhWk1
BR.H35	Breast vHMEC.Donor RM035	11_EnhWk1
PFM.3	Penis Foreskin Melanocyte Primary Cells.Donor skin03	11_EnhWk1
DUO.SMUS	Duodenum Smooth Muscle	13_EnhA
ESO	Esophagus	13_EnhA
GAS	Gastric	13_EnhA
LV	Left Ventricle	13_EnhA
PFK.2	Penis Foreskin Keratinocyte Primary Cells.Donor skin02	11_EnhWk1
SK.MUS63	Skeletal Muscle.Donor 63	13_EnhA
ADI.NUC	Adipose Nuclei	13_EnhA
COL.MUC32	Colonic Mucosa.Donor 32	11_EnhWk1
R.MUC31	Rectal Mucosa.Donor 31	13_EnhA
SK.MUS62	Skeletal Muscle.Donor 62	13_EnhA
ADI.MSC	Adipose Derived Mesenchymal Stem Cell Cultured Cells	11_EnhWk1
BR.MYO	Breast Myoepithelial Cells	11_EnhWk1
BN.GM2	Brain Germinal Matrix.Donor HuFGM02	11_EnhWk1
HRT.FE	Fetal Heart	11_EnhWk1
DUO.MUC61	Duodenum Mucosa.Donor 61	13_EnhA
PFM.1	Penis Foreskin Melanocyte Primary Cells.Donor skin01	13_EnhA
BN.ITL	Brain Inferior Temporal Lobe	11_EnhWk1
CCCRA.NP	CD4+ CD25- CD45RA+ Naive Primary Cells	13_EnhA
PANC	Pancreas	13_EnhA
H1.DMSC	H1 Derived Mesenchymal Stem Cells	13_EnhA
IMR90	IMR90 Cell Line	9_TxEnhG1
CD34.MBP1562	Mobilized CD34 Primary Cells.Donor RO 01562	11_EnhWk1
BN.MFL	Brain Mid Frontal Lobe	13_EnhA
PFF.1	Penis Foreskin Fibroblast Primary Cells.Donor skin01	11_EnhWk1

CD15.P	CD15 Primary Cells	9_TxEnhG1
SPL	Spleen	11_EnhWk1
BN.HM150	Brain Hippocampus Middle.Donor 150	11_EnhWk1
LNG.FE	Fetal Lung	11_EnhWk1
BN.CC	Brain Cingulate Gyrus	11_EnhWk1
BN.SN	Brain Substantia Nigra	13_EnhA
PANC.I	Pancreatic Islets	14_Enh
BN.AC	Brain Anterior Caudate	13_EnhA
CCIP.LSMPTP	CD4+ CD25- IL17- PMA-Ionomycin stimulated MACS purified Th Primary Cells	9_TxEnhG1
CCC.TREGP	CD4+ CD25+ CD127- Treg Primary Cells	9_TxEnhG1
ST.SMUS28	Stomach Smooth Muscle.Donor 28	13_EnhA
R.SMUS	Rectal Smooth Muscle	13_EnhA
BN.AG	Brain Angular Gyrus	13_EnhA
CD34.C	CD34 Cultured Cells	11_EnhWk1
CHON.BMMSC	Chondrocytes from Bone Marrow Derived Mesenchymal Stem Cell Cultured Cells	11_EnhWk1
CC.TPC	CD4+ CD25- Th Primary Cells	13_EnhA
MUS.SC	Muscle Satellite Cultured Cells	11_EnhWk1
MSC.ADIPC	Mesenchymal Stem Cell Derived Adipocyte Cultured Cells	11_EnhWk1
PFF.2	Penis Foreskin Fibroblast Primary Cells.Donor skin02	14_Enh

In 55 out of 111 epigenomes from different human cell subtypes there is evidence of regulatory activity for the genomic region harboring SNP rs4845618. The data retrieval was performed using HaploReg v3 (http://www.broadinstitute.org/mammals/haploreg/haploreg_v3.php) a software tool developed to explore genomic annotations on the noncoding genome and therefore identify new mechanistic hypotheses of non-coding variants on clinical phenotypes. TssP: TSS_poised; TssF: TSS_flanking_more_upstream; TssA: TSS_active; TssWk:TSS_weak; TssD1: TSS_flanking_downstream; TssD2: TSS_flanking_more_downstream; Tx: Transcription; TxWk: Transcription_weak; TxEnhG1: Transcription Enhancer-like; TxEnhG2: Transcription Enhancer-like; EnhWk1: Enhancer_weak; EnhWk2: Enhancer_weak; EnhA: Enhancer_active; Enh: Enhancer_active_with_weakK4me1_strong_K27ac; EnhP: Enhancer_poised; ReprPCWk: Repressed_polycomb_weak; ReprPC: Repressed_polycomb; K9K27me3: H3K9me3_K27me3; ZNF: Zinc_finger_genes_H3K36me3_K9me3; HetRpts: Heterochromatin_at_repeats; Het: Heterochromatin.