Table SI. List of gout candidate genes.

A1CF	*GCKR*	*NIPAL1*	*SLC16A5*	*SLC2A1*
ABCC4	*GEF*	*NLRP3*	*SLC16A6*	*SLC2A10*
ABCG2	*HADH*	*NOD2*	*SLC16A7*	*SLC2A11*
ACADS	*HIST1H2BF*	*NRG4*	*SLC16A8*	*SLC2A12*
ACVR1B	*HIST1H4E*	*OSTC*	*SLC16A9*	*SLC2A13*
ACVR2A	*HLF*	*P2RX7*	*SLC17A1*	*SLC2A14*
ACVRL1	*HNF1B*	*P2X7R*	*SLC17A2*	*SLC2A2*
ADRB3	*HNF4G*	*PDK2*	*SLC17A3*	*SLC2A3*
AGL	*HPRT1*	*PDZK1*	*SLC17A4*	*SLC2A3P1*
ALDH16A1	*IGF1R*	*PFKM*	*SLC17A5*	*SLC2A3P2*
ALDH2	*IGF1R*	*PKLR*	*SLC17A6*	*SLC2A3P4*
ALDOB	*IL12B*	*PLA2G12A*	*SLC17A7*	*SLC2A4*
ALPK1	*IL18R1*	*PPARGC1A*	*SLC17A8*	*SLC2A5*
AMPD1	*IL1A*	*PPARGC1B*	*SLC17A9*	*SLC2A6*
AOX1	*IL1B*	*PRKAG2*	*SLC22A1*	*SLC2A7*
ASAH2	*IL23R*	*PRKG2*	*SLC22A10*	*SLC2A8*
ATXN2	*IL33*	*PRPS1*	*SLC22A11*	*SLC2A9*
B3GNT4	*IL8*	*PRPSAP1*	*SLC22A12*	*SLC2AXP1*
BAZ1B	*INHBB*	*PTPN11*	*SLC22A13*	*SLC37A4*
BCAS3	*INHBC*	*PYGM*	*SLC22A14*	*STAT4*
C17orf82	*ITPR1*	*R3HDM2*	*SLC22A15*	*STC1*
CARD15	*JAK2*	*REN*	*SLC22A16*	*TGFB1*
CARD8	*KCNQ1*	*RFX3*	*SLC22A17*	*TGM4*
CD14	*LEF1*	*RREB1*	*SLC22A18*	*TLR2*
CLNK	*LRP2*	*SFMBT1*	*SLC22A2*	*TLR4*
CNIH2	*LRRC16A*	*SGK1*	*SLC22A20*	*TMEM171*
CNTN4	*LTBP3*	*SGMS2*	*SLC22A23*	*TNXIP*
COMT	*MAF*	*SLC16A1*	*SLC22A24*	*TRIM46*
CPT2	*MEFV*	*SLC16A10*	*SLC22A25*	*UBE2Q2*
CUX2	*MLXIPL*	*SLC16A11*	*SLC22A3*	*UGT1A*
CYP2U1	*MOCOS*	*SLC16A12*	*SLC22A31*	*UMOD*
DAPK1	*MTHFR*	*SLC16A13*	*SLC22A4*	*UOX*
DCP1A	*MUSTN1*	*SLC16A14*	*SLC22A5*	*VEGFA*
EGF	*MYD88*	*SLC16A14P1*	*SLC22A6*	*VEGFA*
ELOVL6	*MYL2*	*SLC16A2*	*SLC22A7*	*WDR1*
FAM35A	*NCF1*	*SLC16A3*	*SLC22A8*	*XDH*
G6PC	*NFAT5*	*SLC16A4*	*SLC22A9*	*ZNF518B*

Table SII. Results of conventional radiography, autoantibodies and HLA-B27 tests of patients with gout in three gout pedigrees.

Individual ID	HLA-B27	ANA+ENA	Joint X-ray
F1_I:1	-	-	+
F1_II:1	-	-	+
F2_I:1	-	-	+
F2_II:1	-	-	NA
F2_II:7	-	-	-
F2_III:1	-	-	NA
F2_III:9	-	-	-
F3_41	-	-	+
F3_45	-	-	-
F3_ II:2	-	-	+
F3_ III:2	-	-	NA
F3_ III:3	-	-	NA

Joint X-ray '+' means the patient has the typical manifestation of cortical erosion, soft tissue swelling, tophi or wormy appearance. NA, not applicable; HLA-B27, human leukocyte antigen B27; ANA, antinuclear antibody; ENA, extractable nuclear antigen.

Table SIII. Summary of whole-exome sequencing data.

Sample	Clean data (Gb)	Initial bases on target (Mb)	Alignment rate (%)	Base covered on target (Gb)	Fraction of effective bases on target (%)	Mean sequencing depth	4x coverage (%)	10x coverage (%)	20x coverage (%)
F1:II:1	13.44	50.34	98.68	5.52	44.60	97.53	99.00	98.50	97.20
F2:II:1	13.91	50.34	98.81	6.20	44.70	123.26	99.00	98.60	97.70
F3:II:1	13.24	50.34	98.70	4.91	39.10	109.70	99.00	98.60	97.60
Mean	13.53	50.34	98.73	5.54	42.80	110.16	99.00	98.57	97.50
Standard deviation	0.35	0.00	0.07	0.65	3.20	12.87	0.00	0.06	0.26

Table SIV. Disease ontology enrichment analysis of genes in the coexpression network.

Description	GeneRatio	BgRatio	P-value	Adjust	q-value	Count
Hyperuricemia	9/40	20/8018	$1.18x10^{-16}$	8.02E-14	2.51E-14	9
Gout	9/40	29/8018	$6.80x10^{-15}$	2.32E-12	7.26E-13	9
Acquired metabolic disease	25/40	930/8018	$2.18x10^{-14}$	4.97E-12	1.56E-12	25
Disease of metabolism	26/40	1111/8018	$1.22x10^{-13}$	2.08E-11	6.52E-12	26
Obesity	15/40	313/8018	$8.89x10^{-12}$	1.21E-09	3.80E-10	15
Overnutrition	15/40	322/8018	$1.34x10^{-11}$	1.52E-09	4.76E-10	15
Nutrition disease	15/40	338/8018	$2.68x10^{-11}$	2.61E-09	8.17E-10	15
Artery disease	22/40	961/8018	$5.78x10^{-11}$	4.93E-09	1.54E-09	22
Hypertension	18/40	594/8018	$8.52x10^{-11}$	6.46E-09	2.02E-09	18
Cardiovascular system disease	24/40	1333/8018	$6.83x10^{-10}$	4.66E-08	1.46E-08	24

Table SV. Results of biological process analysis.

GO ID	GOTerm	Term P-value	Adjusted term P-value	Group P-value	Adjust group P-value	GO groups	% Associated genes	Number of genes
GO:0015747	Urate transport	$6.5x10^{-21}$	2.3E-19	2.1E-21	1.7E-20	Group0	90.00	9.00
GO:0043252	Sodium-independent organic anion transport	$2.2x10^{-19}$	4.0E-18	2.1E-21	1.7E-20	Group0	39.29	11.00
GO:0060986	Endocrine hormone secretion	$8.5x10^{-5}$	1.2E-4	1.3E-6	1.8E-6	Group1	8.00	4.00
GO:0050796	Regulation of insulin secretion	$3.1x10^{-6}$	6.9E-6	1.3E-6	1.8E-6	Group1	4.17	8.00
GO:0015697	Quaternary ammonium group transport	$4.3x10^{-15}$	3.9E-14	2.7E-12	1.0E-11	Group2	70.00	7.00
GO:0015838	Amino-acid betaine transport	$6.5x10^{-9}$	2.1E-8	2.7E-12	1.0E-11	Group2	66.67	4.00
GO:0072488	Ammonium transmembrane transport	$1.5x10^{-10}$	6.7E-10	2.7E-12	1.0E-11	Group2	33.33	6.00
GO:0015879	Carnitine transport	$2.1x10^{-9}$	7.8E-9	2.7E-12	1.0E-11	Group2	80.00	4.00
GO:0046942	Carboxylic acid transport	$2.8x10^{-11}$	1.7E-10	2.2E-11	5.8E-11	Group3	4.55	15.00
GO:0015718	Monocarboxylic acid transport	$2.2x10^{-10}$	9.0E-10	2.2E-11	5.8E-11	Group3	6.79	11.00
GO:0015908	Fatty acid transport	$1.1x10^{-3}$	1.2E-3	2.2E-11	5.8E-11	Group3	4.04	4.00
GO:1905039	Carboxylic acid transmembrane transport	$1.0x10^{-5}$	1.8E-5	2.2E-11	5.8E-11	Group3	5.66	6.00
GO:0006090	Pyruvate metabolic process	$3.7x10^{-5}$	6.2E-5	2.2E-11	5.8E-11	Group3	4.48	6.00
GO:0090100	Positive regulation of transmembrane receptor protein serine/threonine kinase signaling pathway	$8.9x10^{-6}$	1.6E-5	4.8E-5	5.5E-5	Group4	5.77	6.00
GO:0032924	Activin receptor signaling pathway	$3.1x10^{-5}$	5.4E-5	4.8E-5	5.5E-5	Group4	10.26	4.00
GO:0060389	Pathway-restricted SMAD protein phosphorylation	$6.1x10^{-7}$	1.5E-6	4.8E-5	5.5E-5	Group4	9.09	6.00
GO:0060393	Regulation of pathway-restricted SMAD protein phosphorylation	$4.6x10^{-7}$	1.2E-6	4.8E-5	5.5E-5	Group4	9.52	6.00
GO:0010862	Positive regulation of pathway-restricted SMAD protein phosphorylation	$7.8x10^{-8}$	2.3E-7	4.8E-5	5.5E-5	Group4	12.77	6.00
GO:0008645	Hexose transport	$3.2x10^{-11}$	1.6E-10	3.2E-11	6.5E-11	Group5	6.78	12.00
GO:1905950	Monosaccharide transmembrane transport	$1.8x10^{-16}$	2.2E-15	3.2E-11	6.5E-11	Group5	42.86	9.00
GO:0015758	Glucose transport	$2.8x10^{-11}$	2.0E-10	3.2E-11	6.5E-11	Group5	6.86	12.00
GO:0035428	Hexose transmembrane transport	$1.8x10^{-16}$	2.2E-15	3.2E-11	6.5E-11	Group5	42.86	9.00
GO:0046323	Glucose import	$4.7x10^{-5}$	7.4E-5	3.2E-11	6.5E-11	Group5	5.88	5.00
GO:1904659	Glucose transmembrane transport	$1.8x10^{-16}$	2.2E-15	3.2E-11	6.5E-11	Group5	42.86	9.00
GO:0042345	Regulation of NF-κB import into nucleus	$7.2x10^{-5}$	1.0E-4	5.4E-5	5.4E-5	Group6	8.33	4.00
GO:0042990	Regulation of transcription factor import into nucleus	$1.2x10^{-3}$	1.2E-3	5.4E-5	5.4E-5	Group6	4.00	4.00
GO:0031663	Lipopolysaccharide-mediated signaling pathway	$1.6x10^{-4}$	2.0E-4	5.4E-5	5.4E-5	Group6	6.78	4.00
GO:0031058	Positive regulation of histone modification	$9.7x10^{-4}$	1.0E-3	5.4E-5	5.4E-5	Group6	4.26	4.00
GO:1904591	Positive regulation of protein import	$1.3x10^{-4}$	1.7E-4	5.4E-5	5.4E-5	Group6	4.72	5.00
GO:0042307	Positive regulation of protein import into nucleus	$1.2x10^{-4}$	1.6E-4	5.4E-5	5.4E-5	Group6	4.81	5.00
GO:0042348	Nuclear factor-κβ import into nucleus	$7.2x10^{-5}$	1.0E-4	5.4E-5	5.4E-5	Group6	8.33	4.00
GO:0031663	Lipopolysaccharide-mediated signaling pathway	$1.6x10^{-4}$	2.0E-4	6.0E-9	9.6E-9	Group7	6.78	4.00
GO:0009124	Nucleoside monophosphate biosynthetic process	$8.0x10^{-6}$	1.6E-5	6.0E-9	9.6E-9	Group7	5.88	6.00
GO:0009142	Nucleoside triphosphate biosynthetic process	$6.9x10^{-4}$	7.5E-4	6.0E-9	9.6E-9	Group7	4.65	4.00
GO:0031058	Positive regulation of histone modification	$9.7x10^{-4}$	1.0E-3	6.0E-9	9.6E-9	Group7	4.26	4.00
GO:1905039	Carboxylic acid transmembrane transport	$1.0x10^{-5}$	1.8E-5	6.0E-9	9.6E-9	Group7	5.66	6.00

Table SV. Continued.

GO ID	GOTerm	Term P-value	Adjusted term P-value	Group P-value	Adjust group P-value	GO groups	% Associated genes	Number of genes
GO:0006090	Pyruvate metabolic process	$3.7x10^{-5}$	6.2E-5	6.0E-9	9.6E-9	Group7	4.48	6.00
GO:0009127	Purine nucleoside monophosphate biosynthetic process	$2.0x10^{-6}$	5.0E-6	6.0E-9	9.6E-9	Group7	7.41	6.00
GO:0009145	Purine nucleoside triphosphate biosynthetic process	$2.8x10^{-4}$	3.3E-4	6.0E-9	9.6E-9	Group7	5.88	4.00
GO:0009156	Ribonucleoside monophosphate biosynthetic process	$4.9x10^{-6}$	1.0E-5	6.0E-9	9.6E-9	Group7	6.38	6.00
GO:0009201	Ribonucleoside triphosphate biosynthetic process	$4.1x10^{-4}$	4.6E-4	6.0E-9	9.6E-9	Group7	5.33	4.00
GO:0009168	Purine ribonucleoside monophosphate biosynthetic process	$2.0x10^{-6}$	5.0E-6	6.0E-9	9.6E-9	Group7	7.41	6.00
GO:0009206	Purine ribonucleoside triphosphate biosynthetic process	$2.6x10^{-4}$	3.2E-4	6.0E-9	9.6E-9	Group7	5.97	4.00
GO:0006754	ATP biosynthetic process	$1.0x10^{-4}$	1.3E-4	6.0E-9	9.6E-9	Group7	7.69	4.00

GO, gene ontology.