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Supplemental Data

Genome-wide Association Study Identifies

27 Loci Influencing Concentrations

of Circulating Cytokines and Growth Factors

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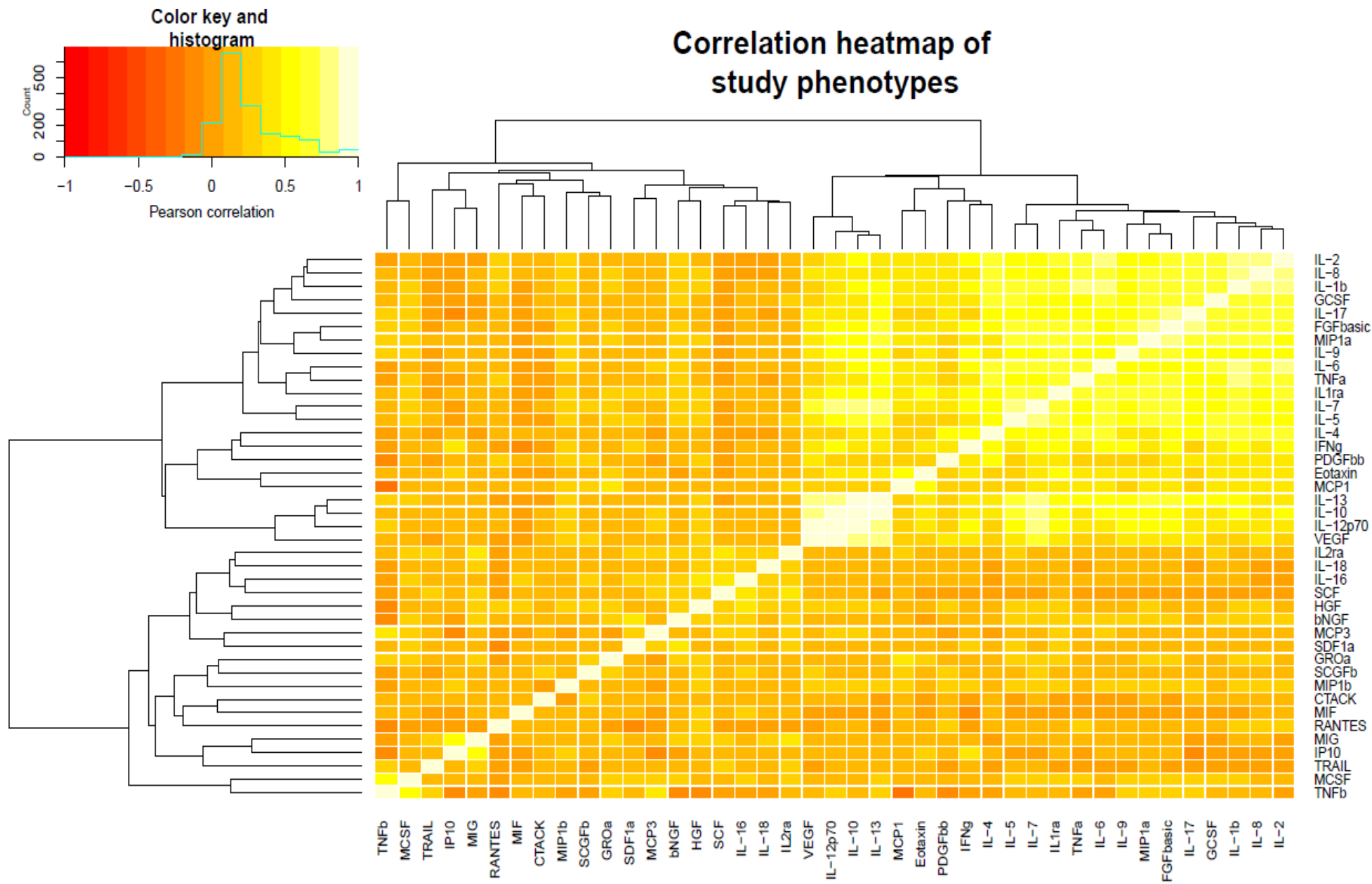


Figure S1 Correlation heat map across study phenotypes. Interleukin-13, interleukin-10, interleukin-12p70 and VEGF form a tightly correlated module.

bNGF

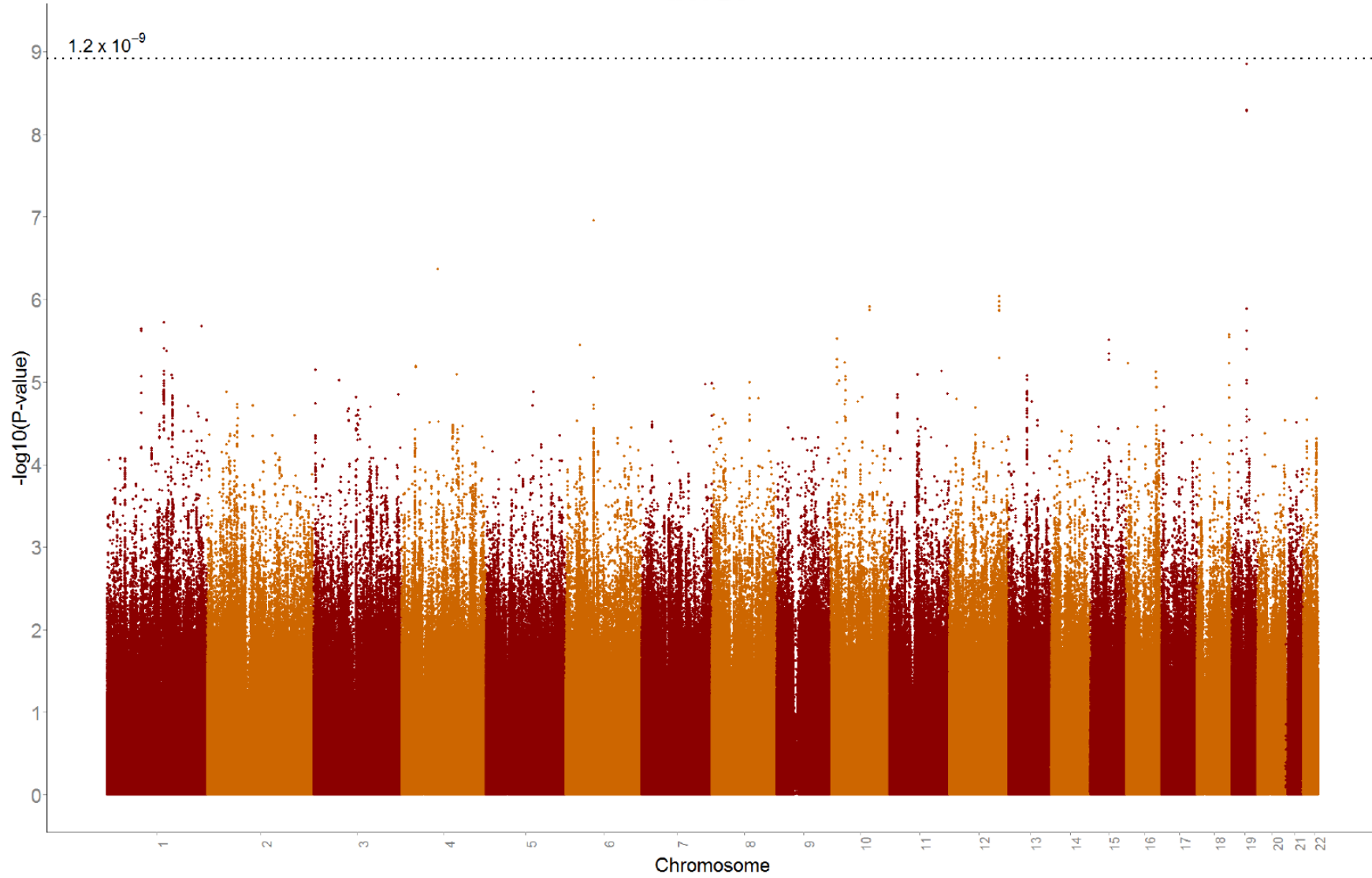


Figure S2 Manhattan plot for beta nerve growth factor (bNGF)

CTACK

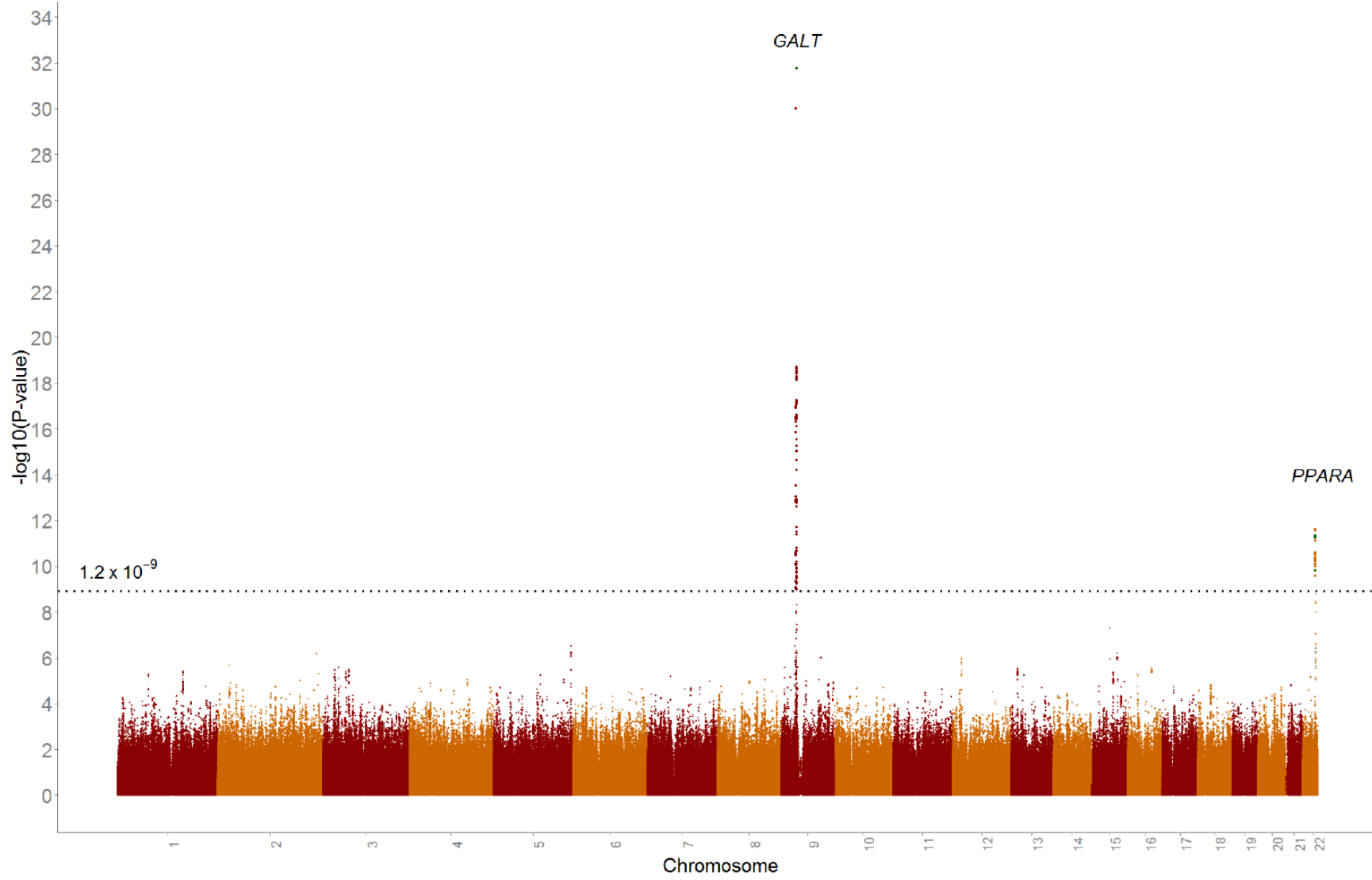


Figure S3 Manhattan plot for Cutaneous T-cell attracting (CCL27; CTACK)

Eotaxin

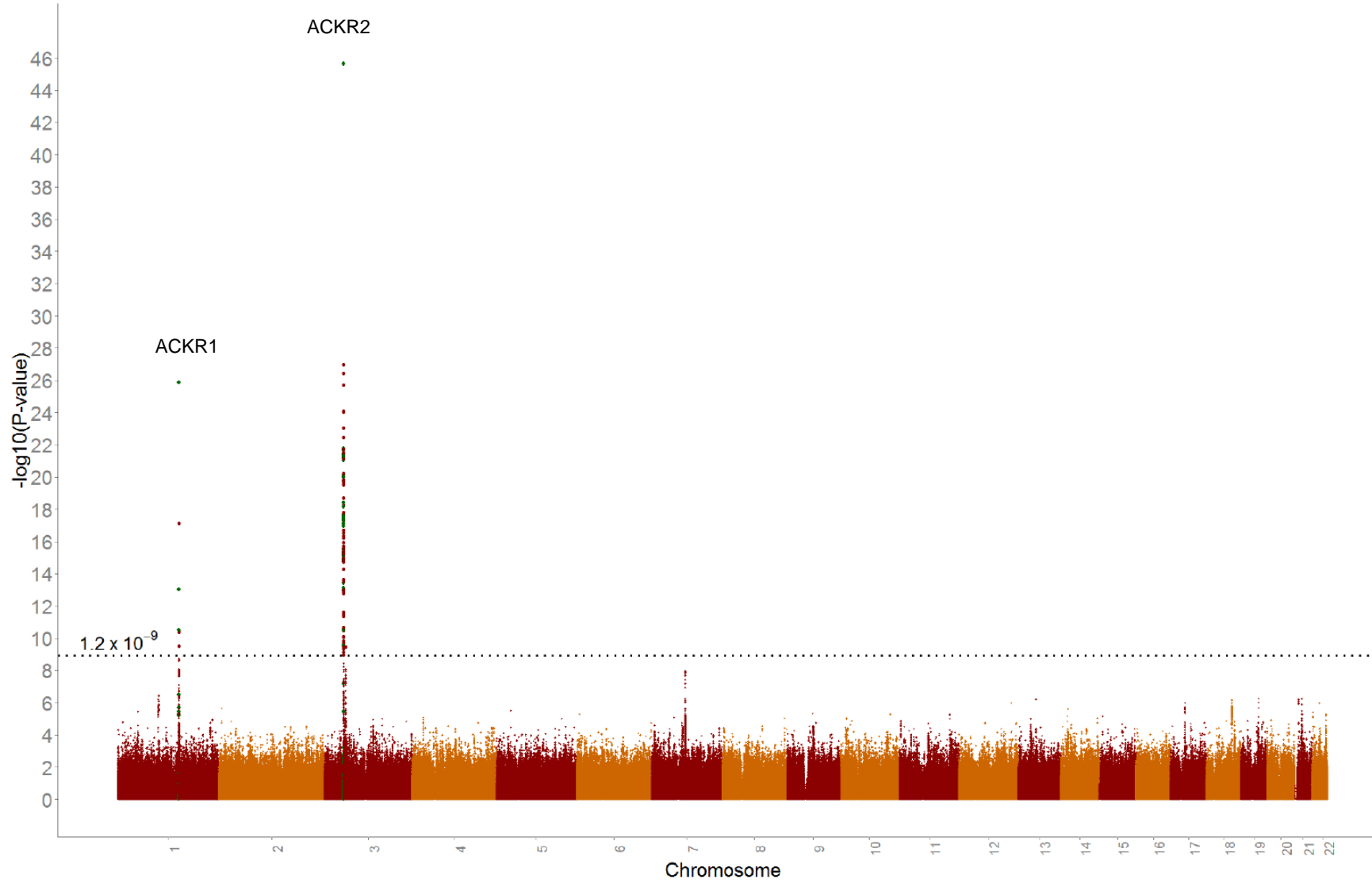


Figure S4 Manhattan plot for Eotaxin.

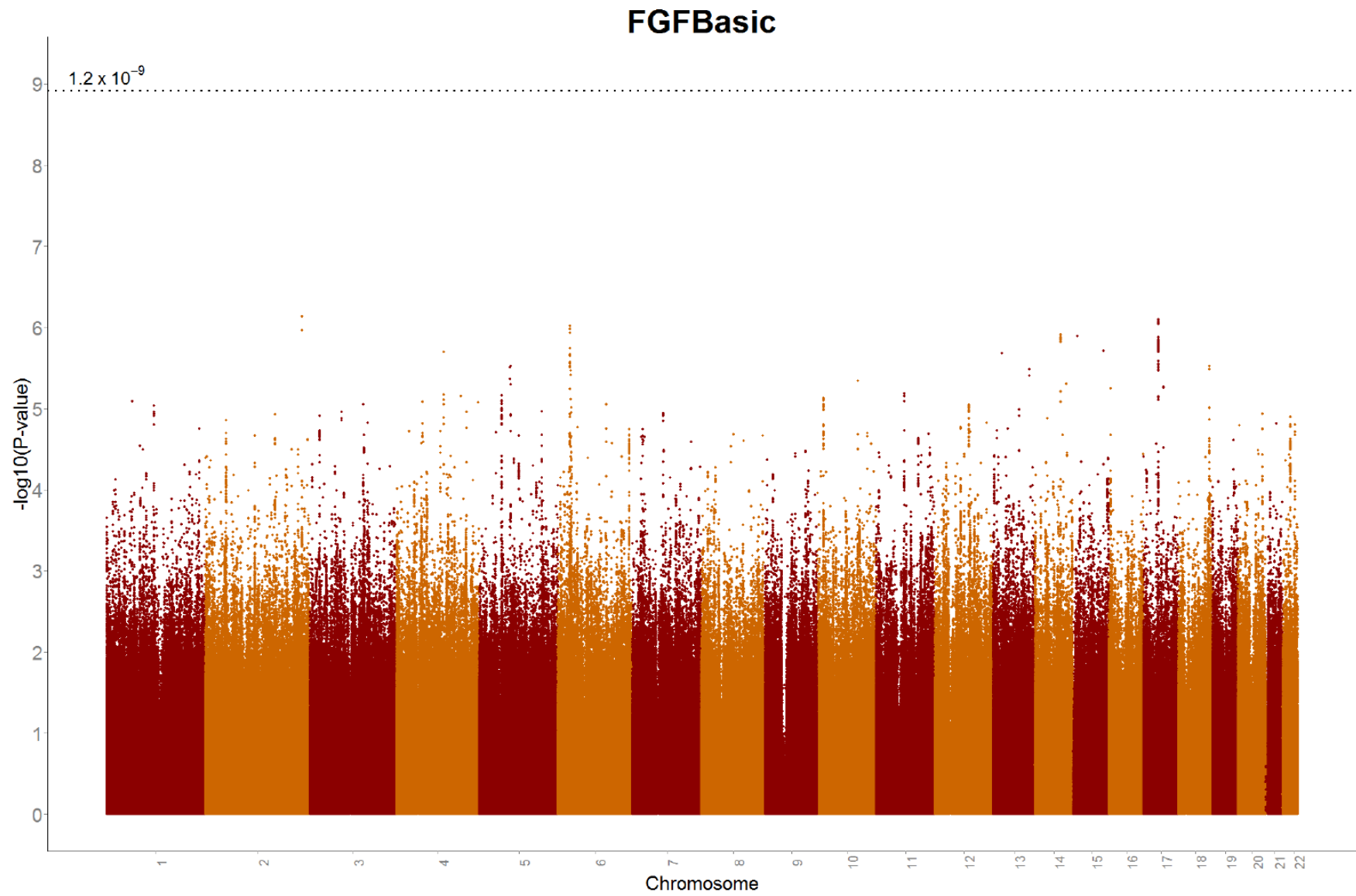
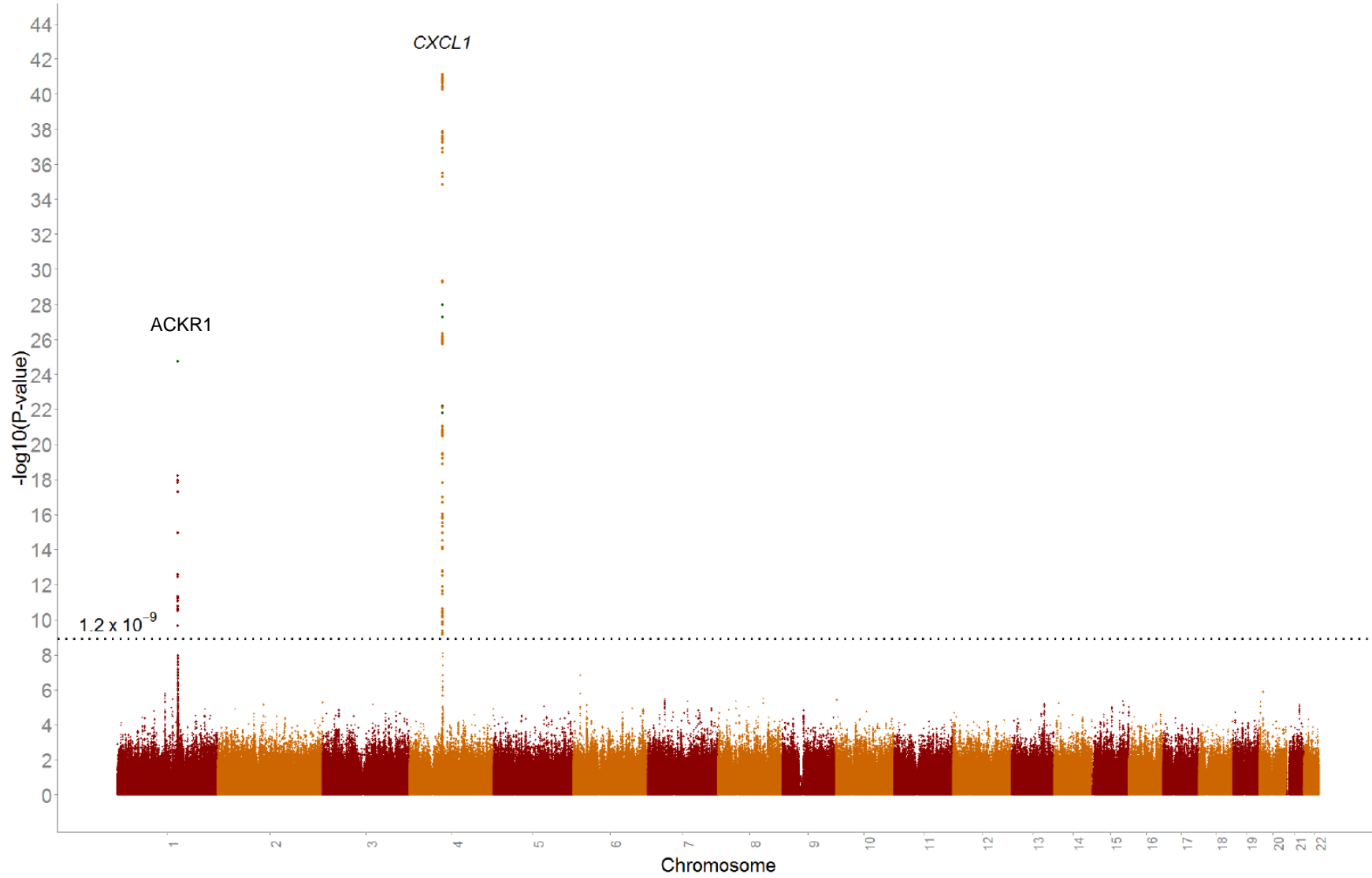


Figure S5 Manhattan plot for basic fibroblast growth factor

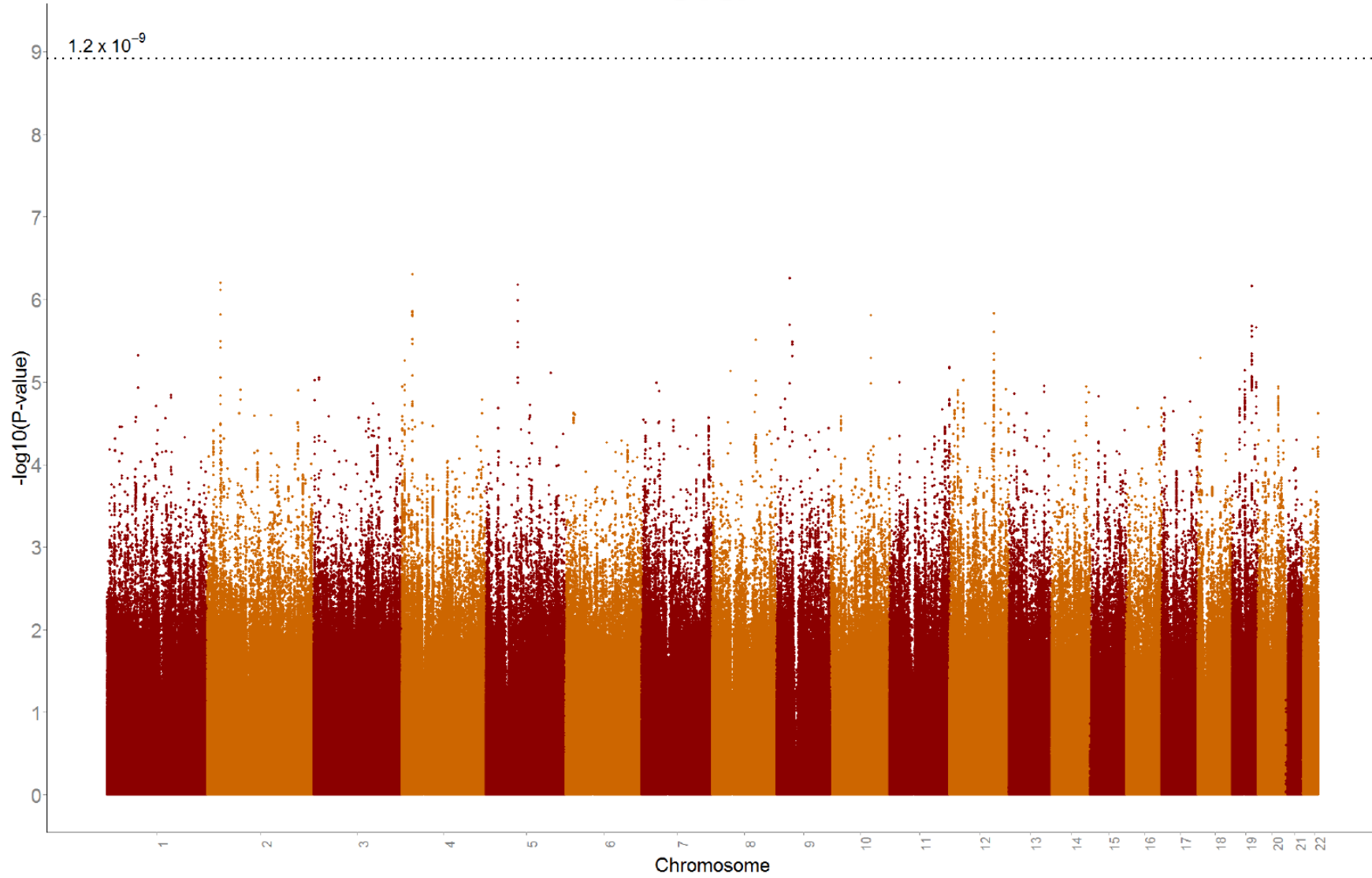
GROa



Manhattan plot for growth regulated oncogene- α (GROa; CXCL1)

Figure S6

GCSF



Manhattan plot for granulocyte colony-stimulating factor (GCSF).

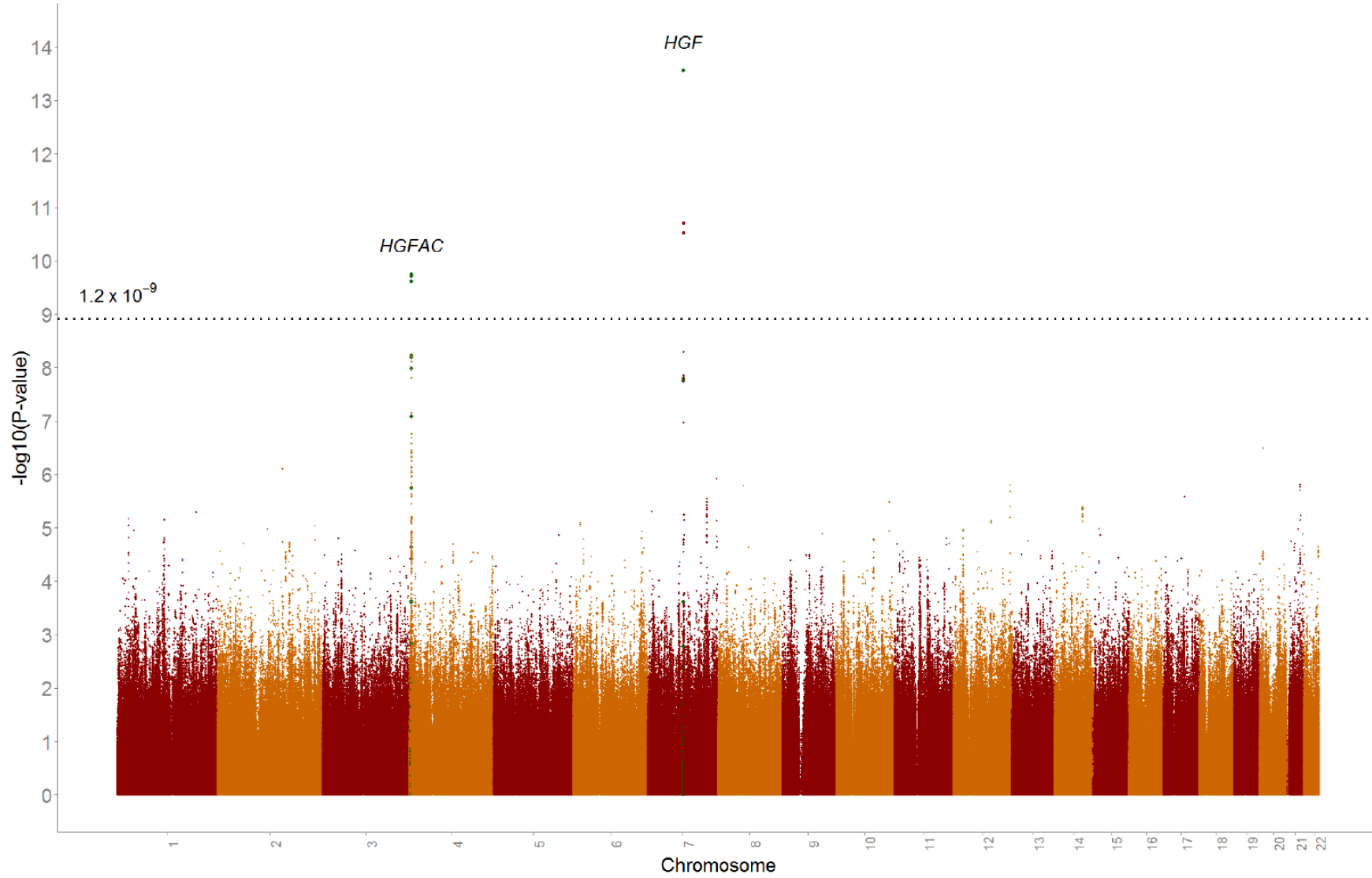
Figure S7

HGF

HGF

HGFAC

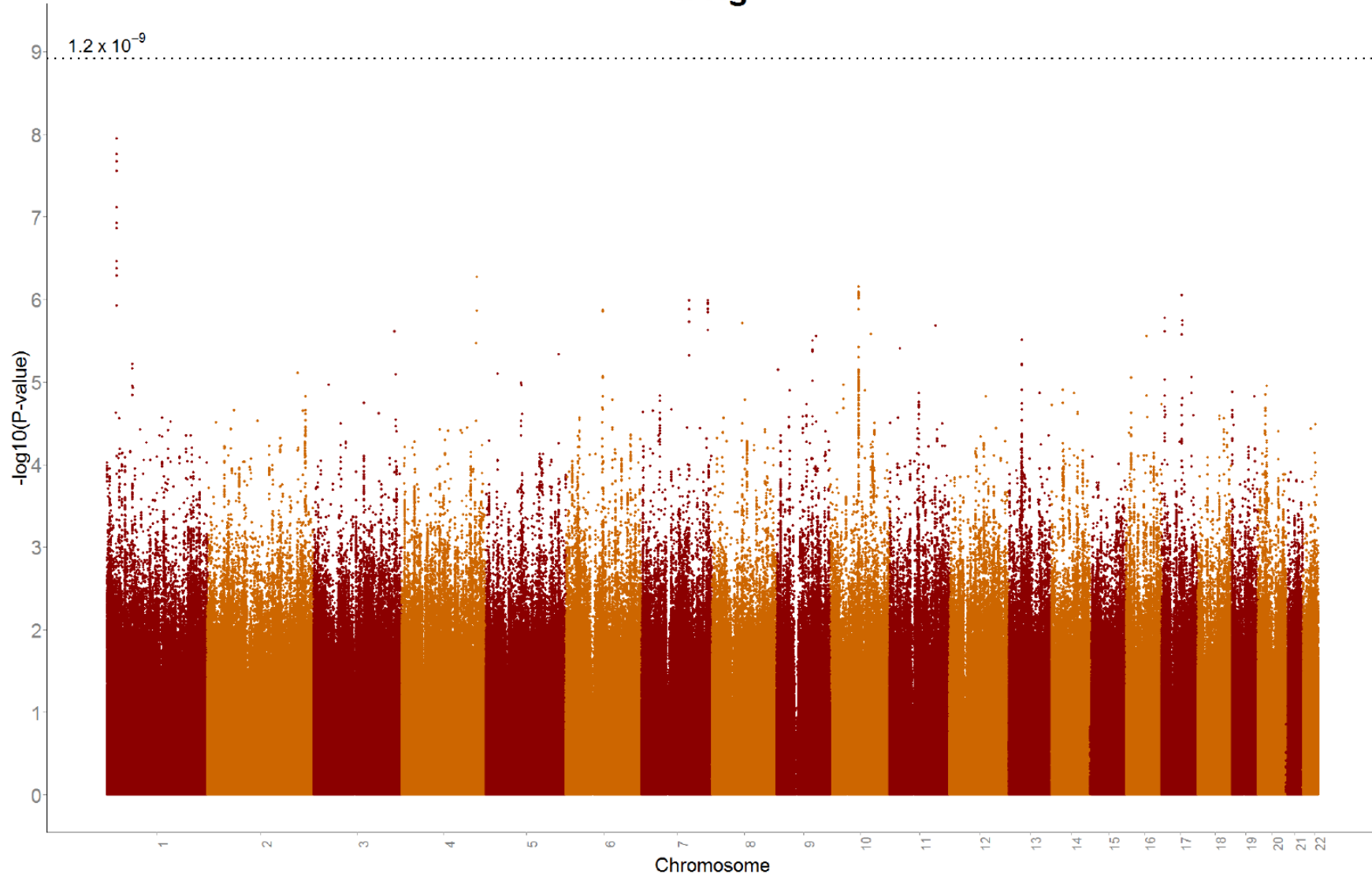
1.2×10^{-9}



Manhattan plot for hepatocyte growth factor (HGF)

Figure S8

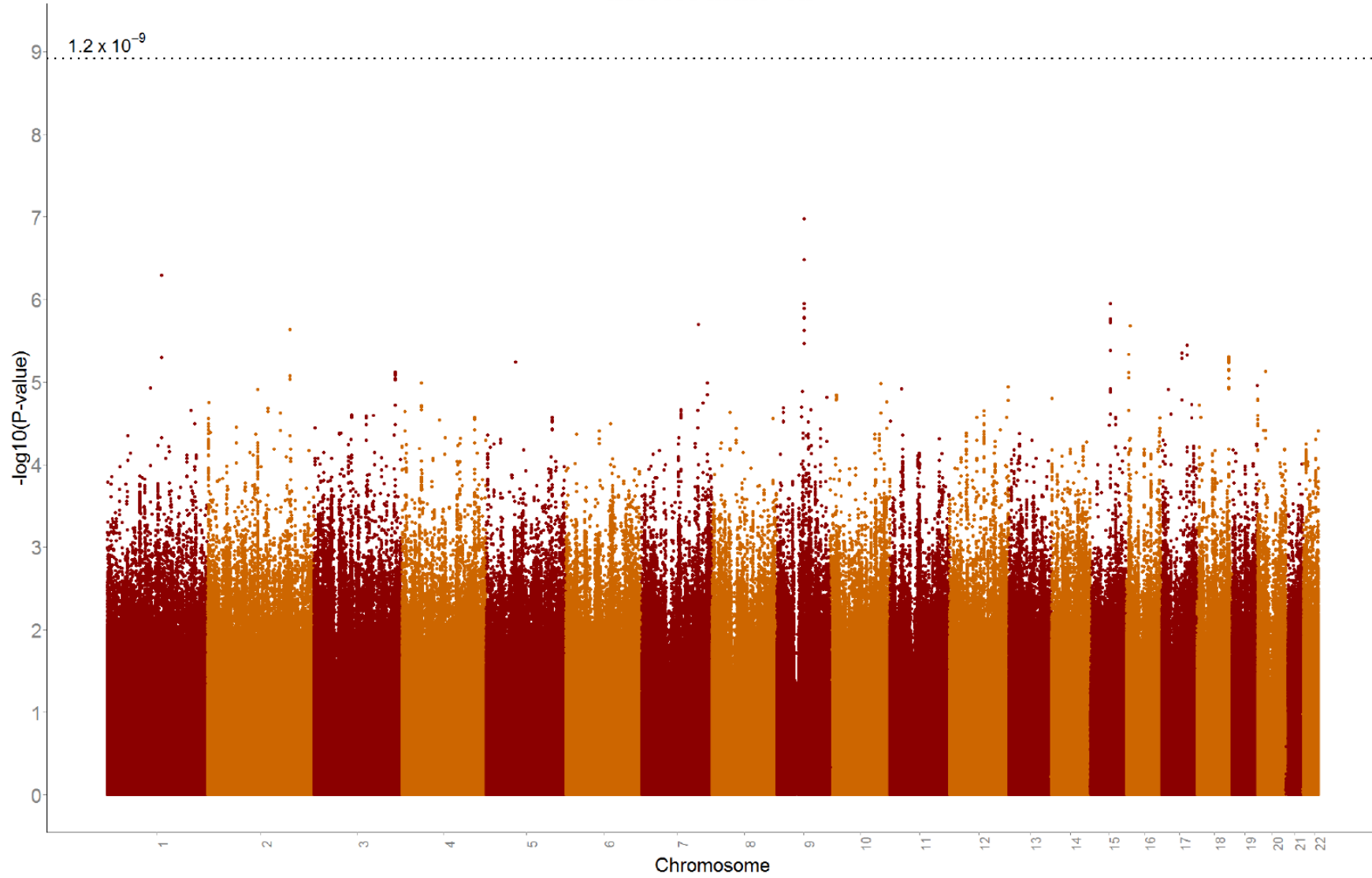
IFNg



Manhattan plot for interferon gamma (IFNg).

Figure S9

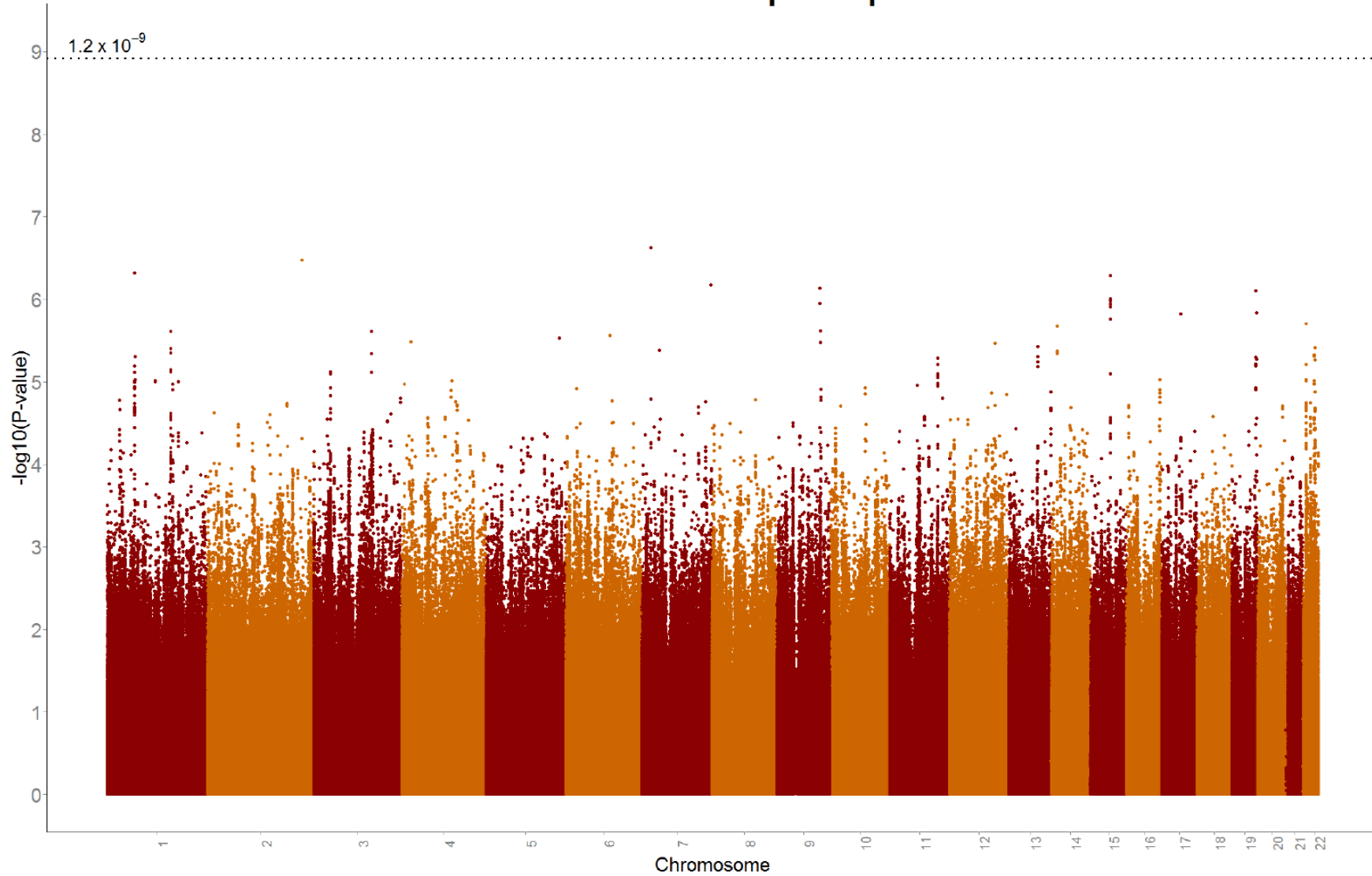
Interleukin-1b



Manhattan plot for interleukin-1-beta.

Figure S10

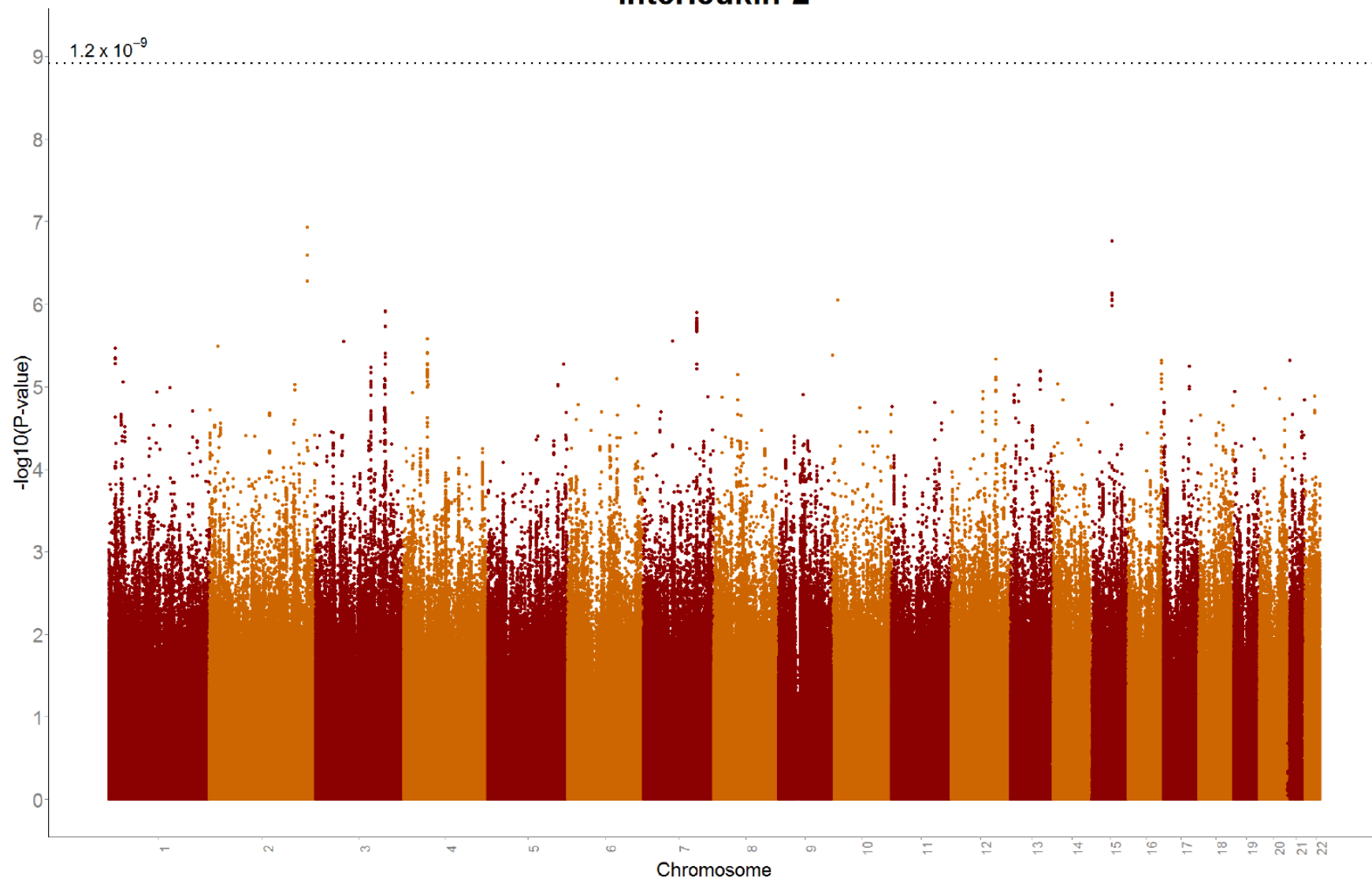
Interleukin-1 receptor alpha



Manhattan plot for interleukin-1 receptor alpha

Figure S11

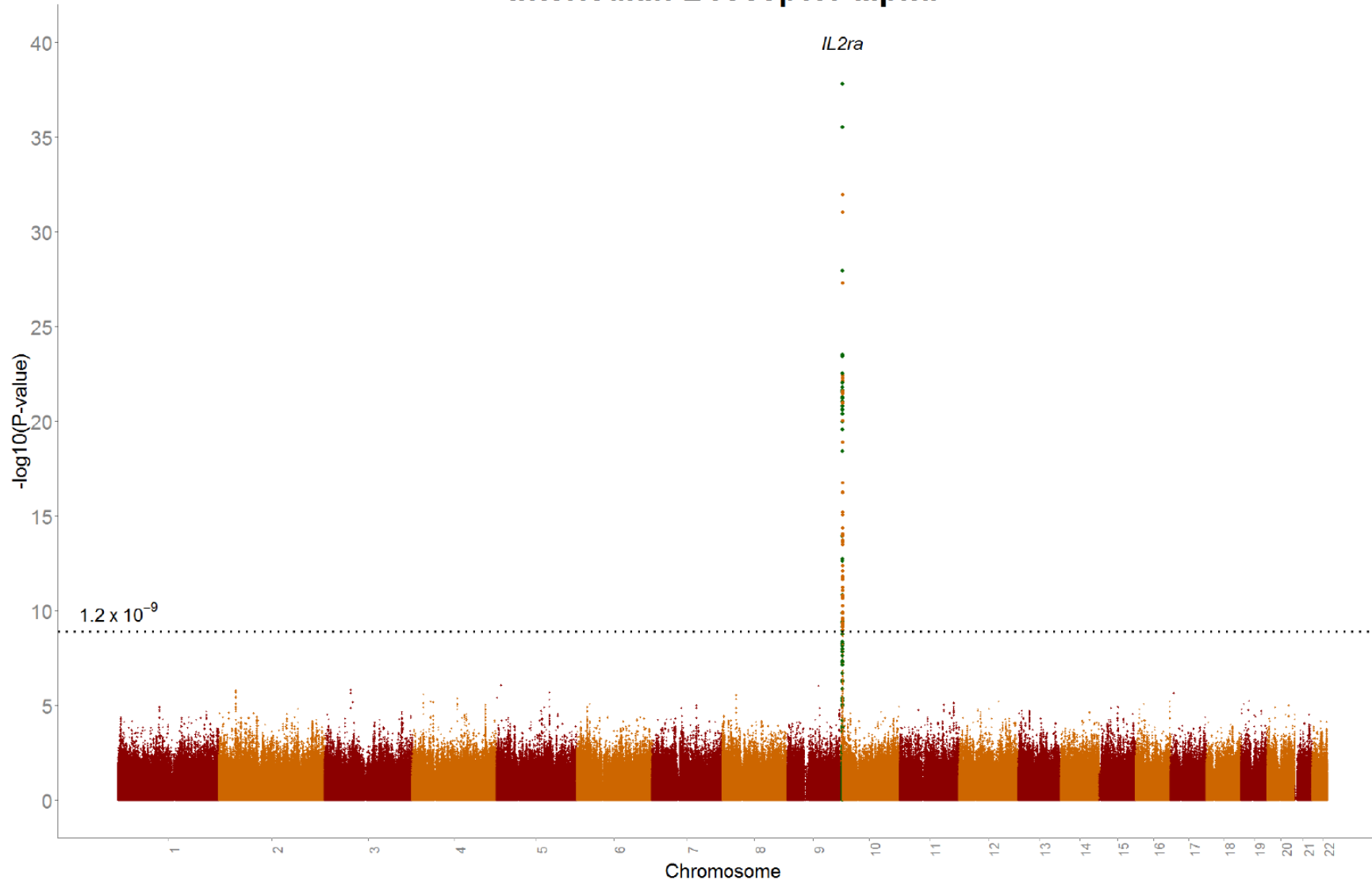
Interleukin-2



Manhattan plot for interleukin-2.

Figure S12

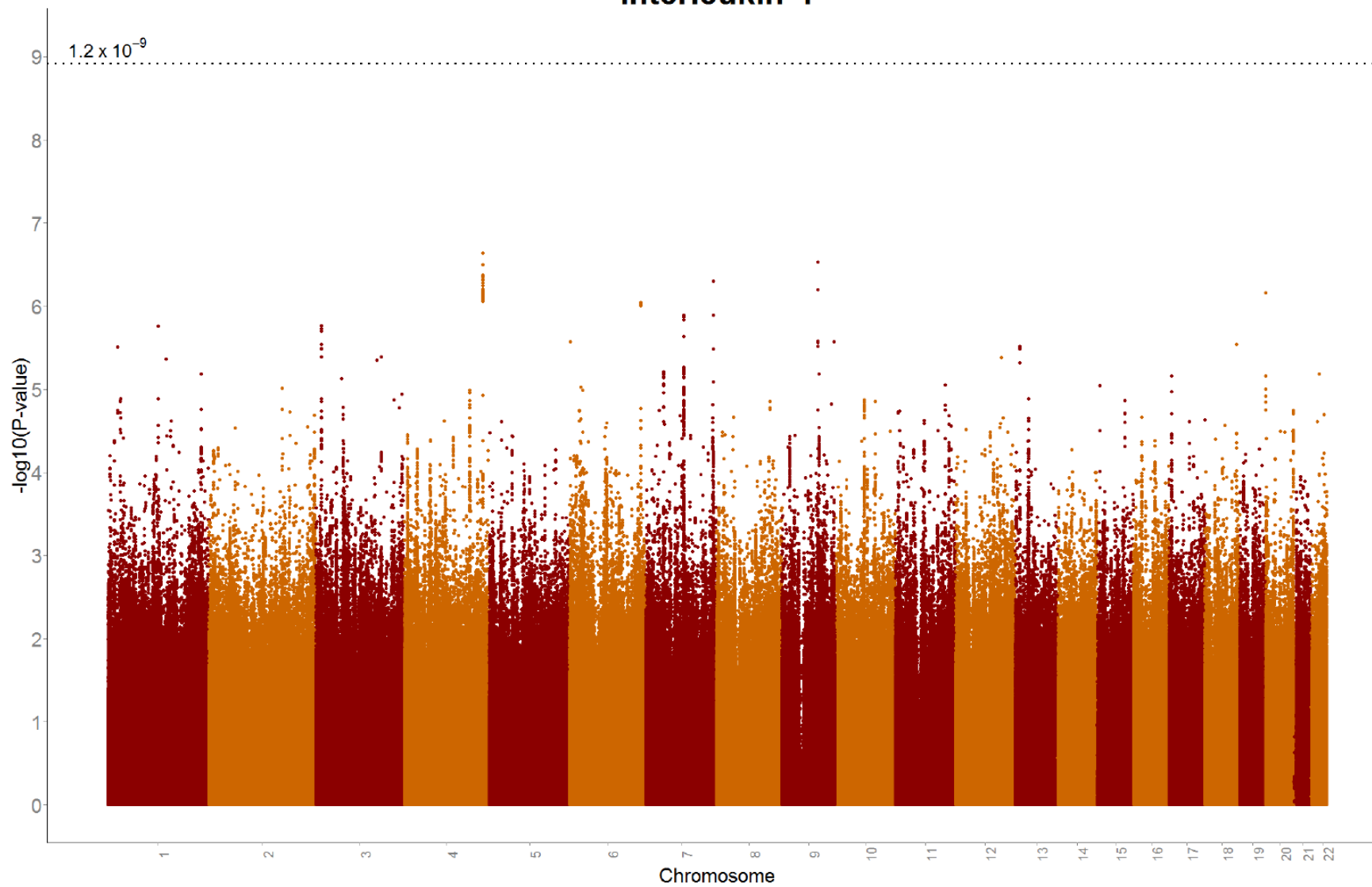
Interleukin-2 receptor alpha



Manhattan plot for interleukin-2 receptor alpha.

Figure S13

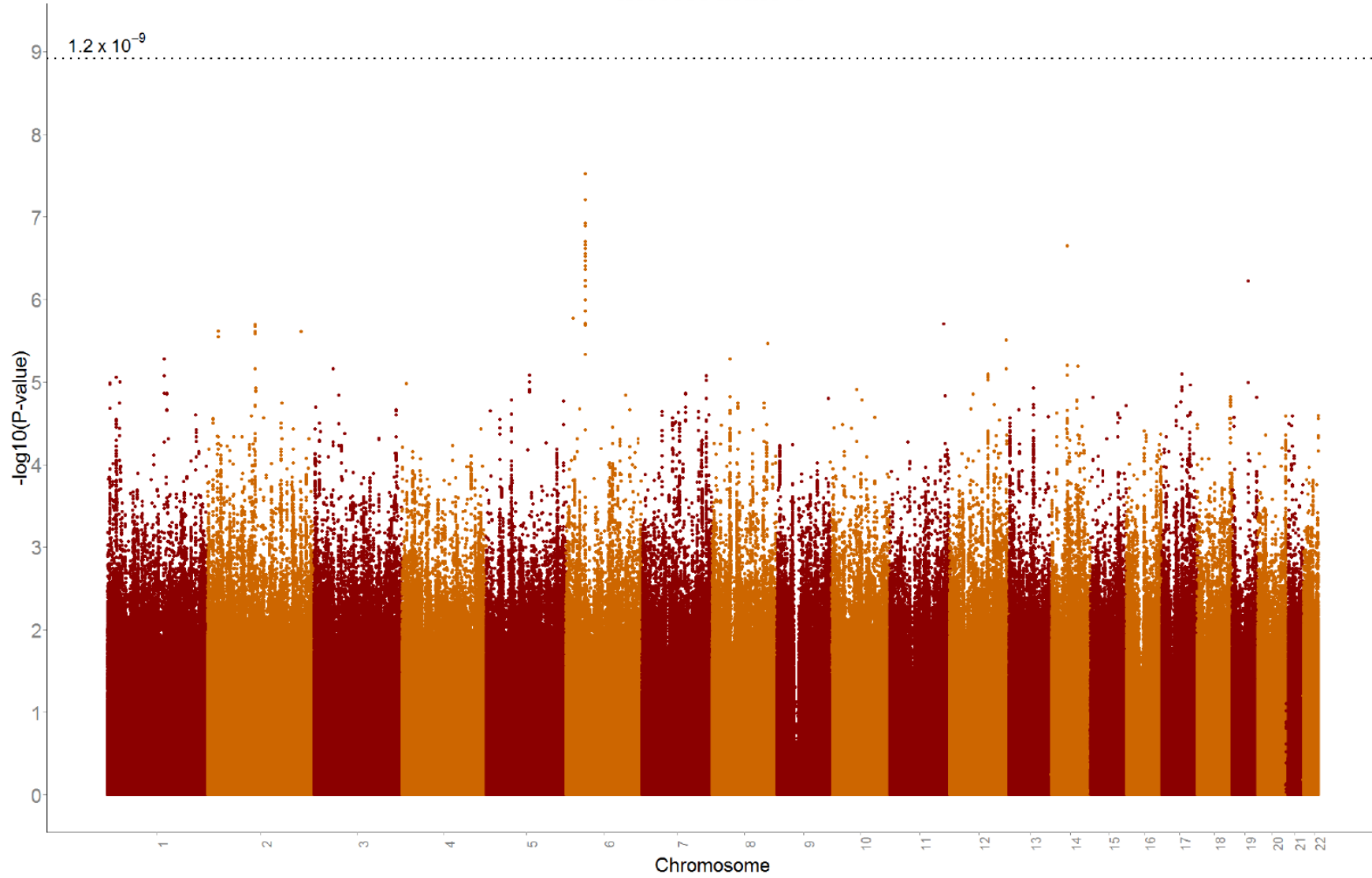
Interleukin-4



Manhattan plot for interleukin-4.

Figure S14

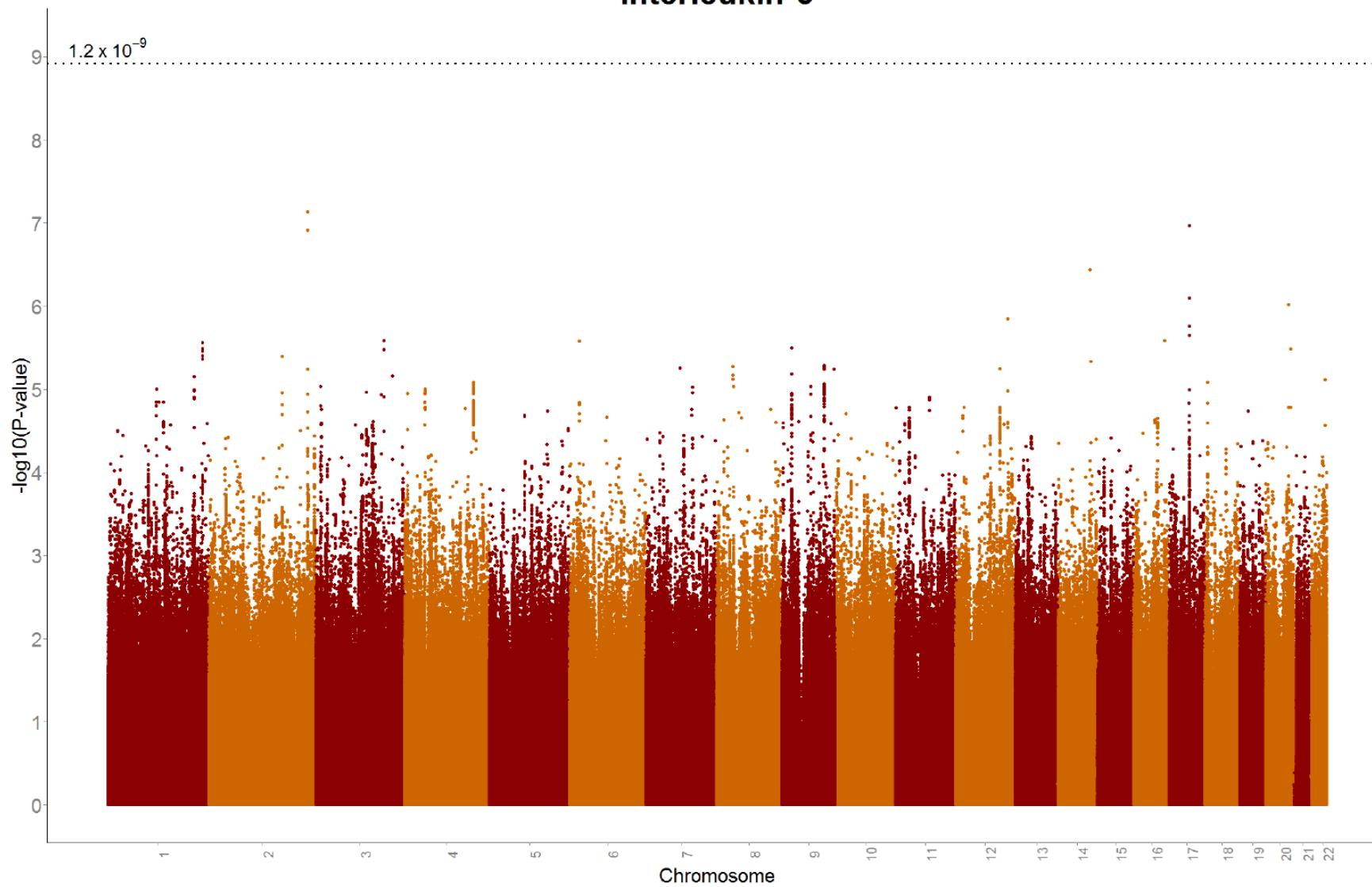
Interleukin-5



Manhattan plot for interleukin-5.

Figure S15

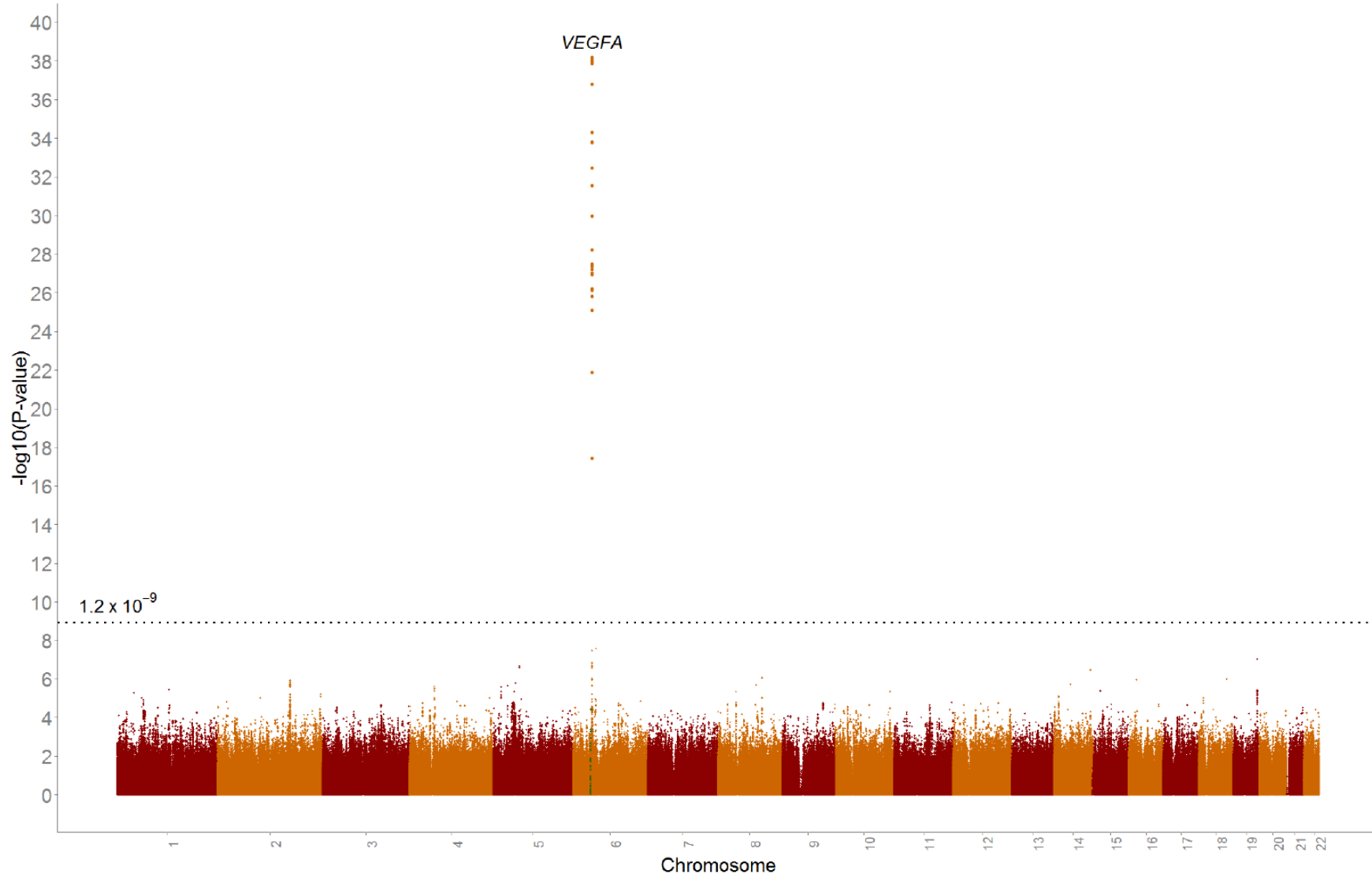
Interleukin-6



Manhattan plot for interleukin-6.

Figure S16

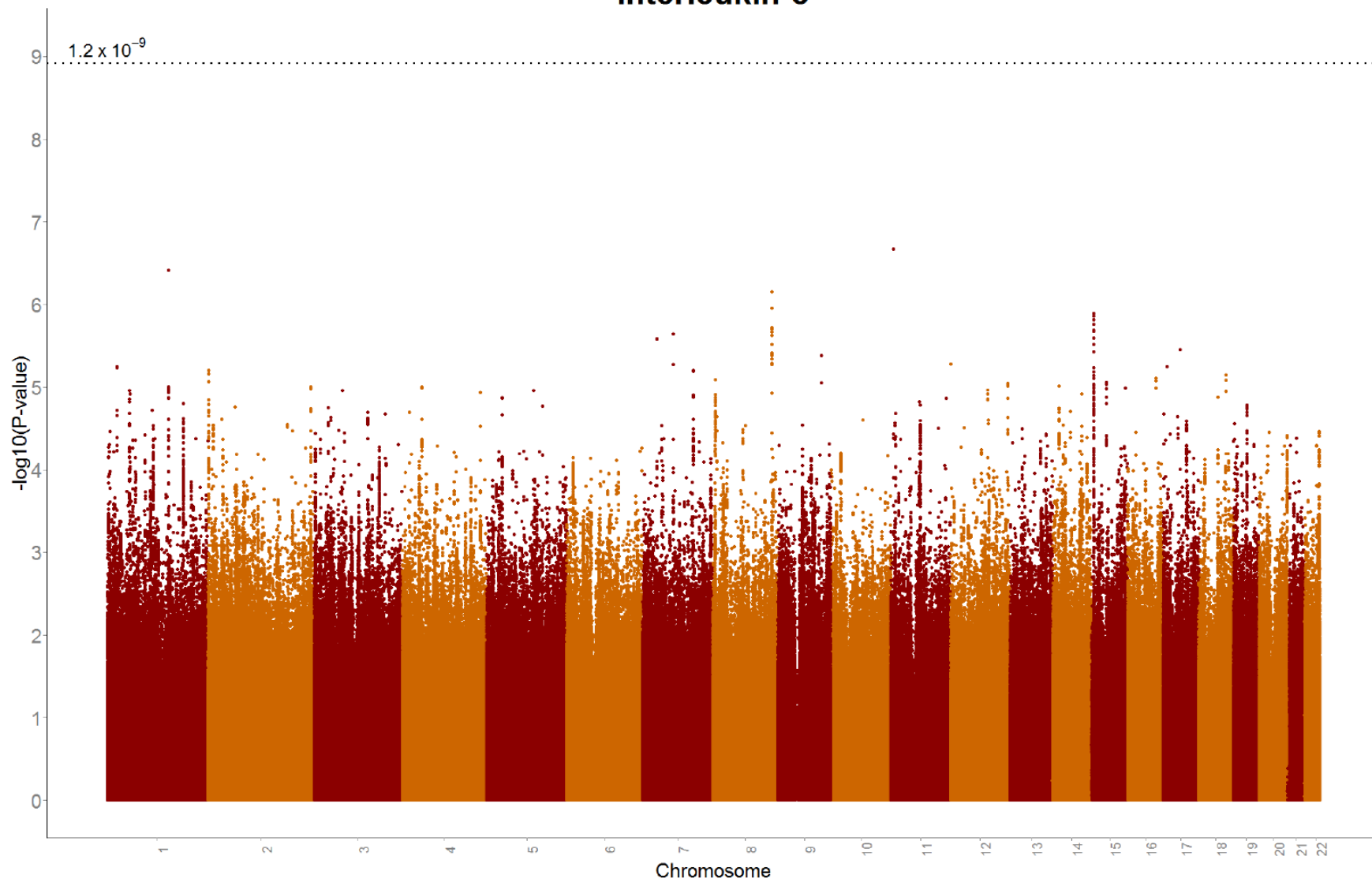
Interleukin-7



Manhattan plot for interleukin-7.

Figure S17

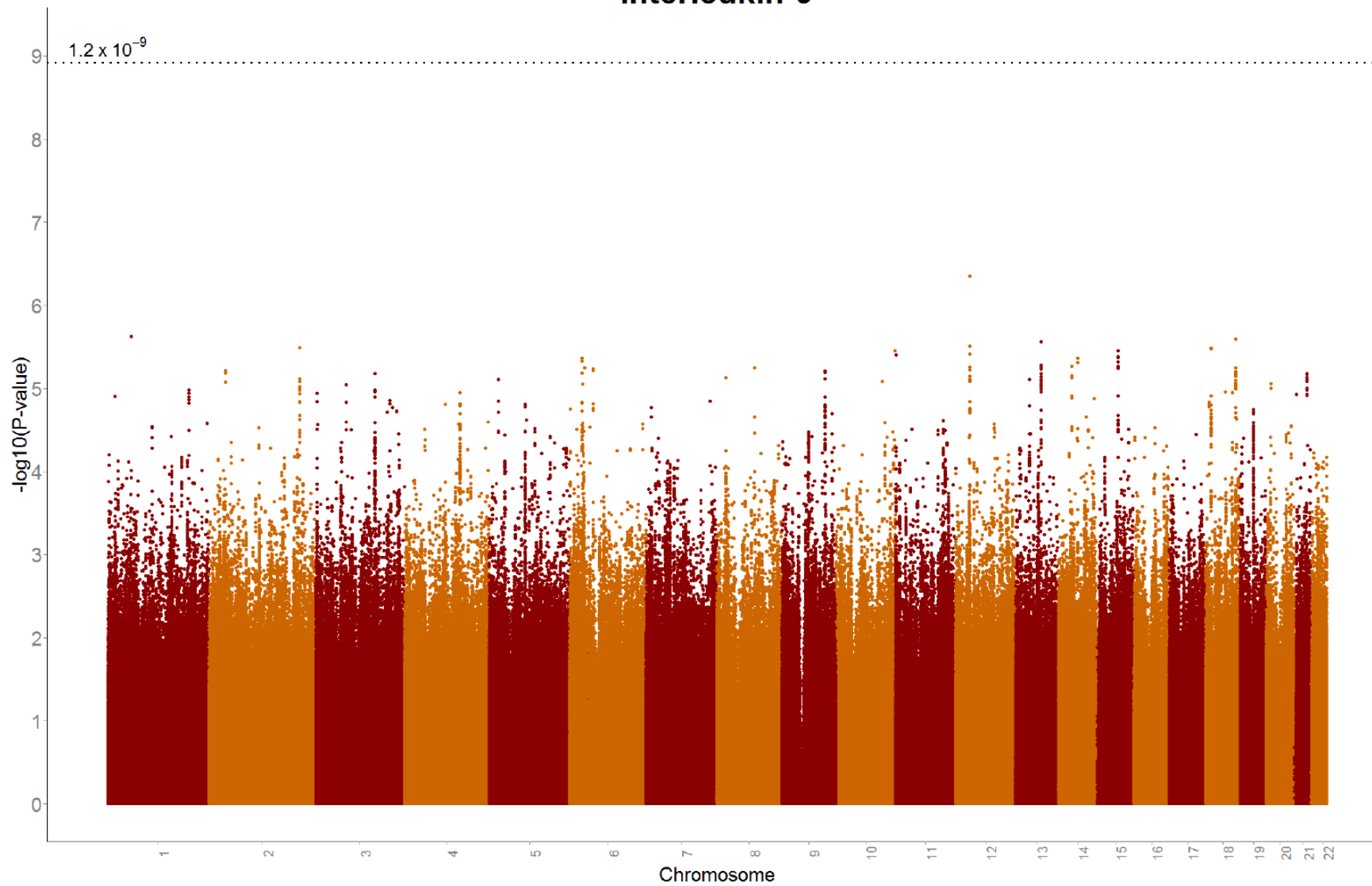
Interleukin-8



Manhattan plot for interleukin-8.

Figure S18

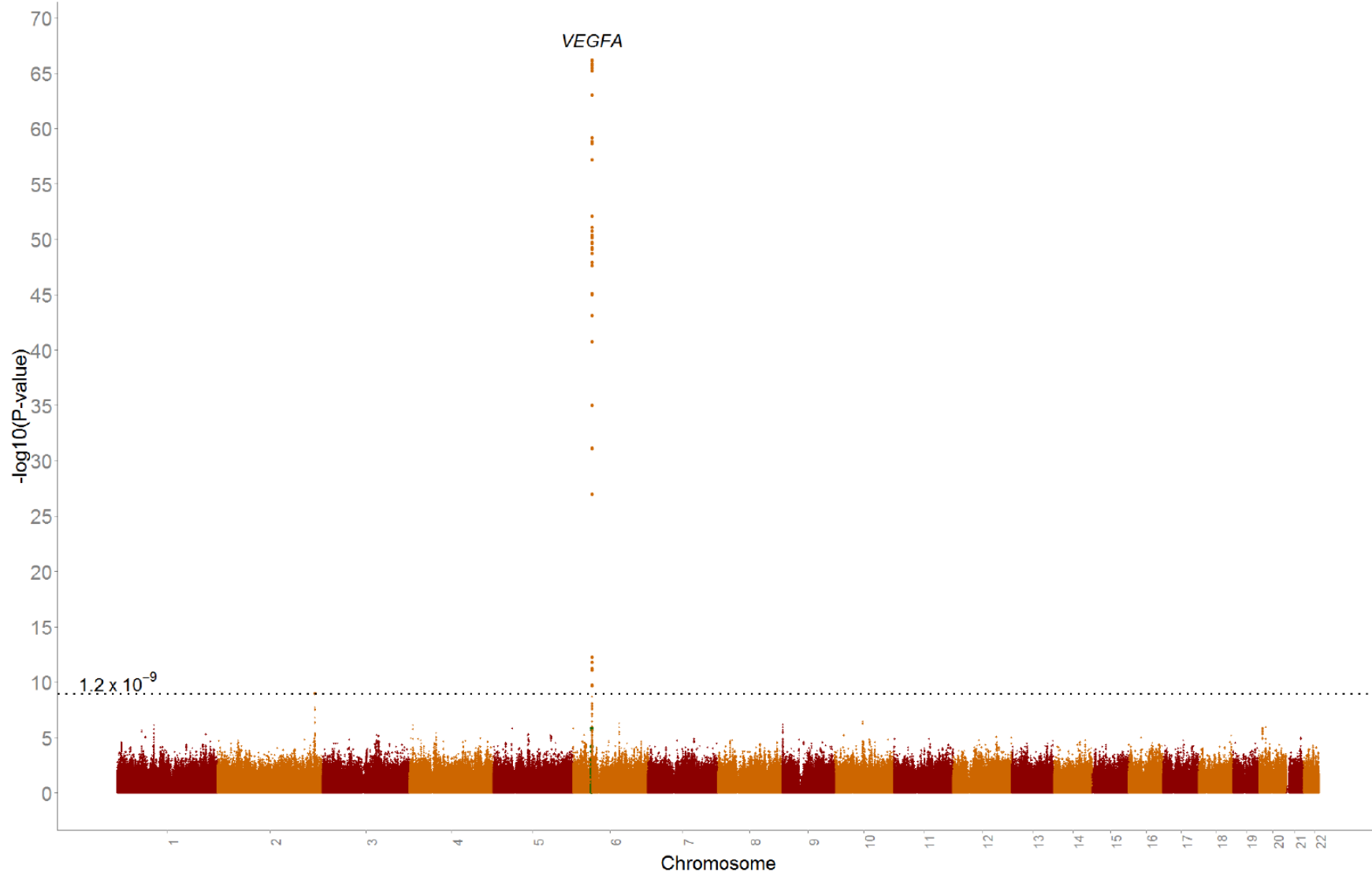
Interleukin-9



Manhattan plot for interleukin-9.

Figure S19

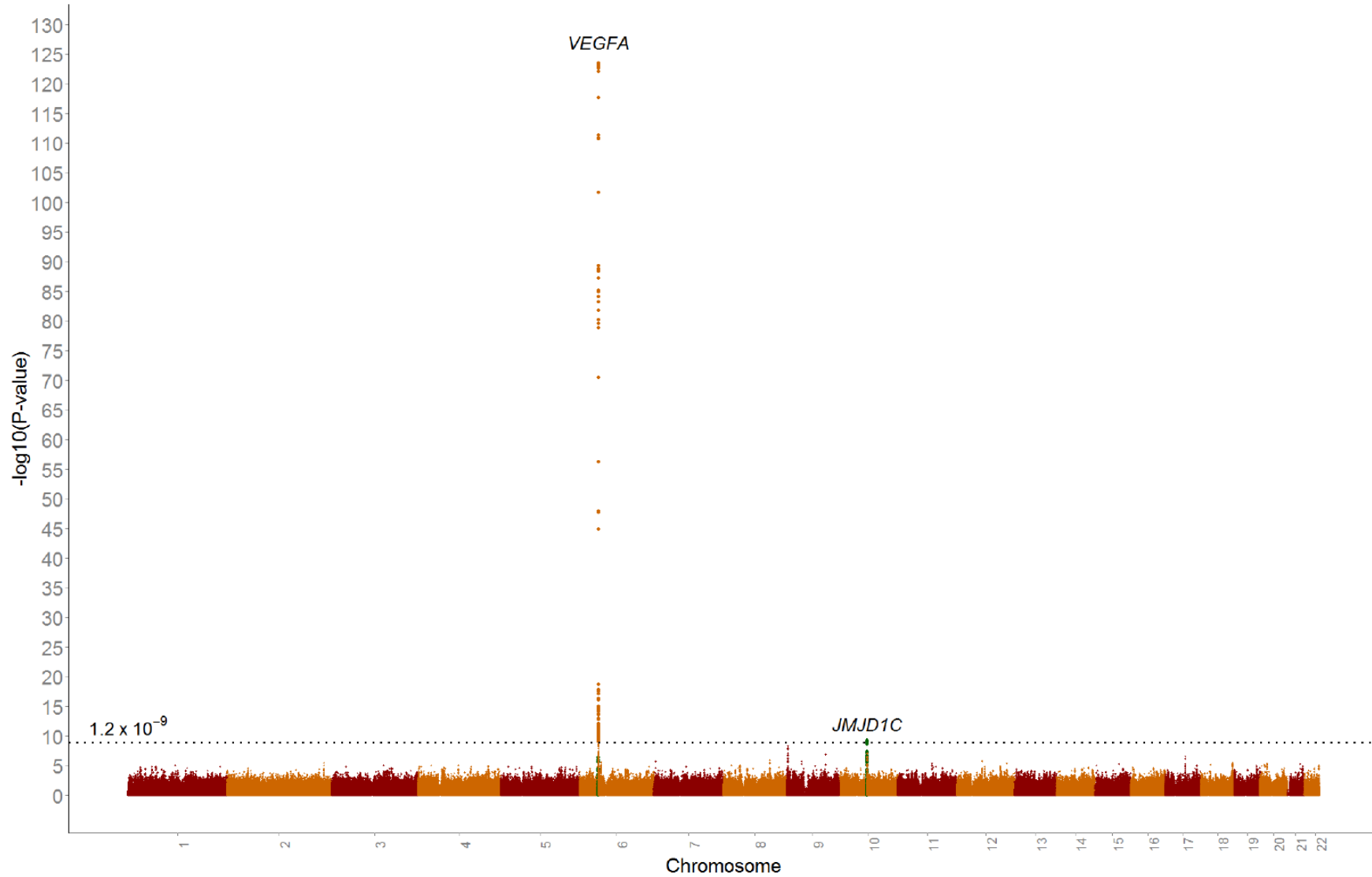
Interleukin-10



Manhattan plot for interleukin-10.

Figure S20

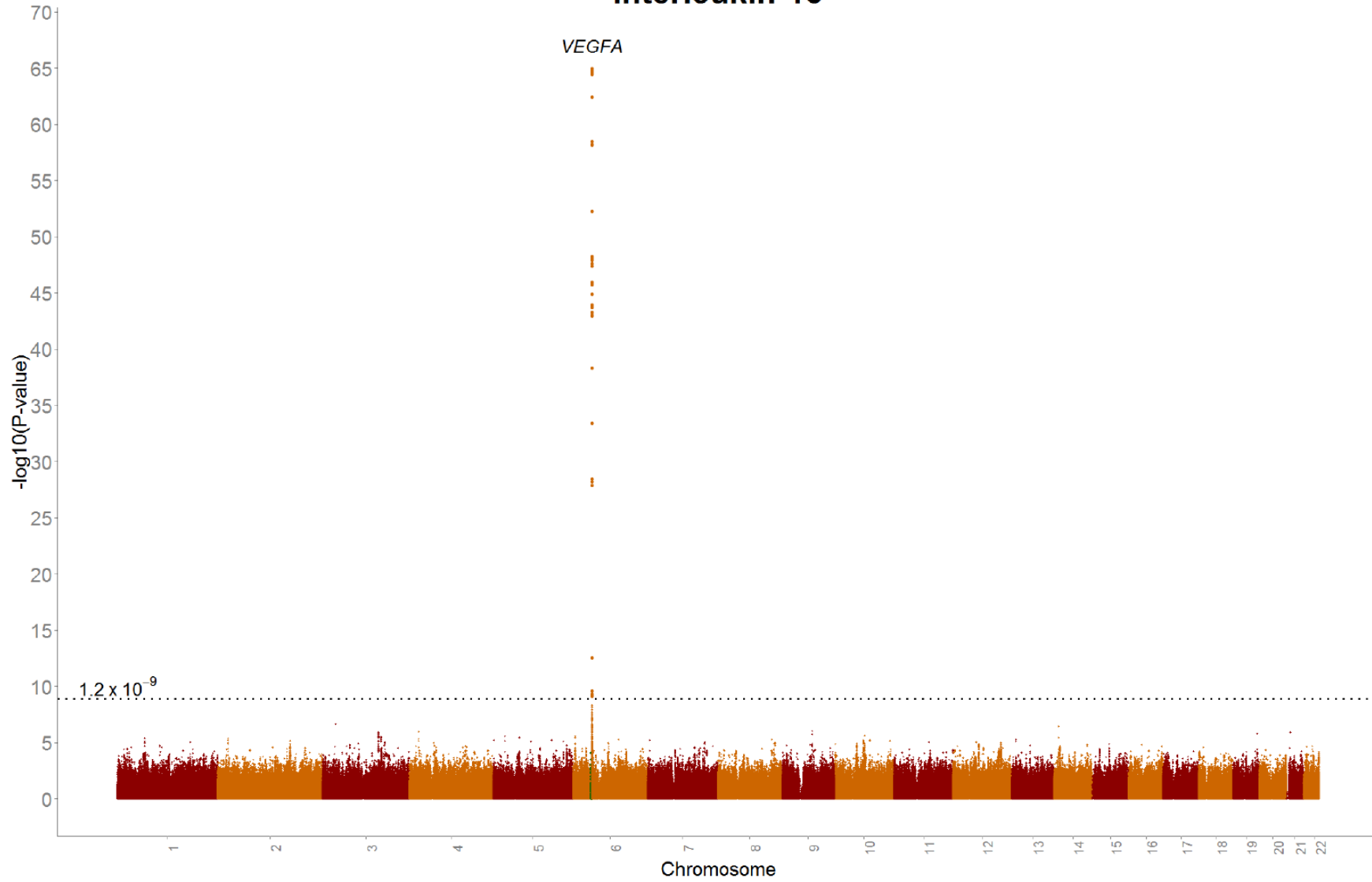
Interleukin-12p70



Manhattan plot for interleukin-12p70.

Figure S21

Interleukin-13



Manhattan plot for interleukin-13.

Figure S22

Interleukin-16

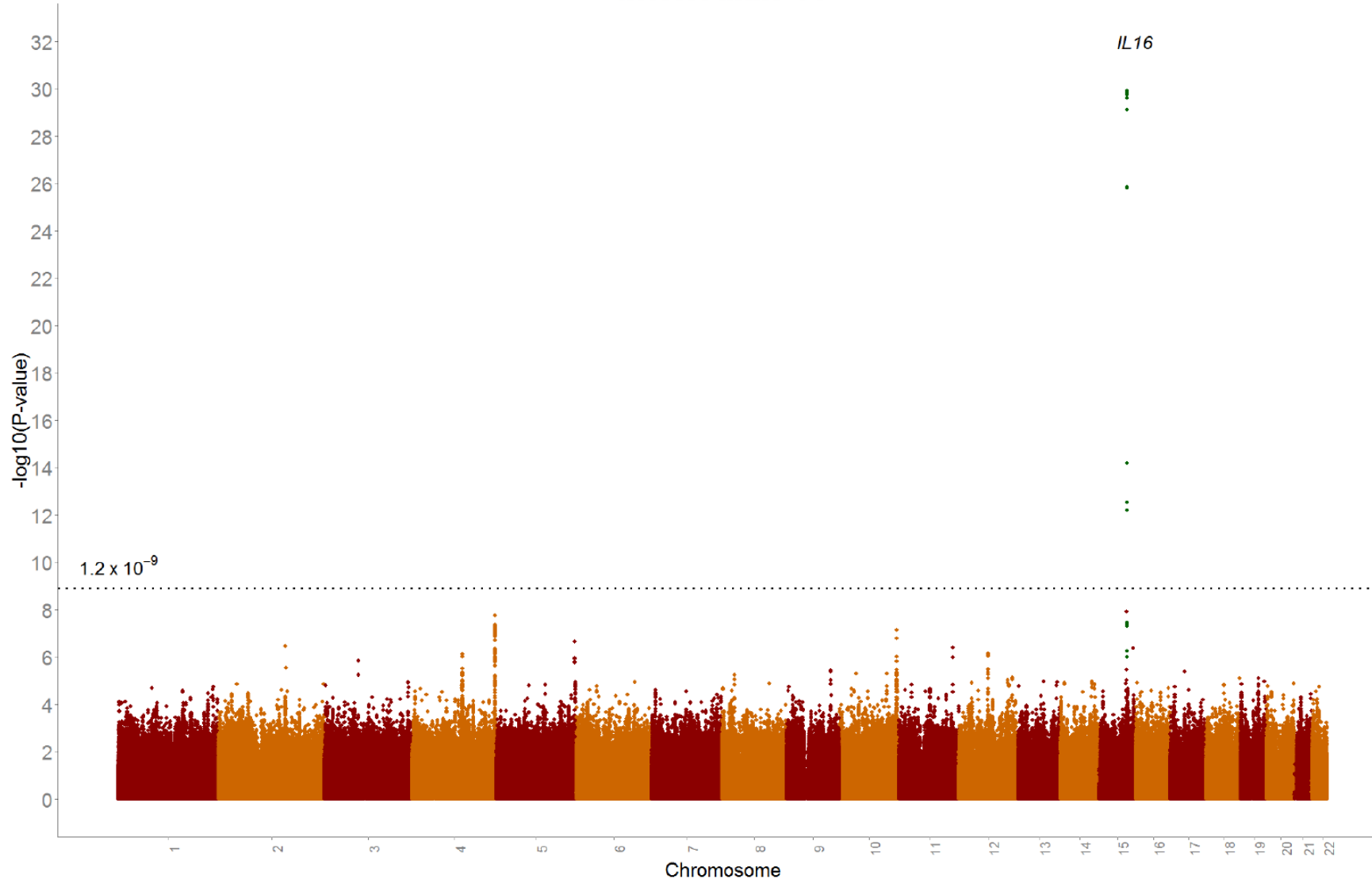
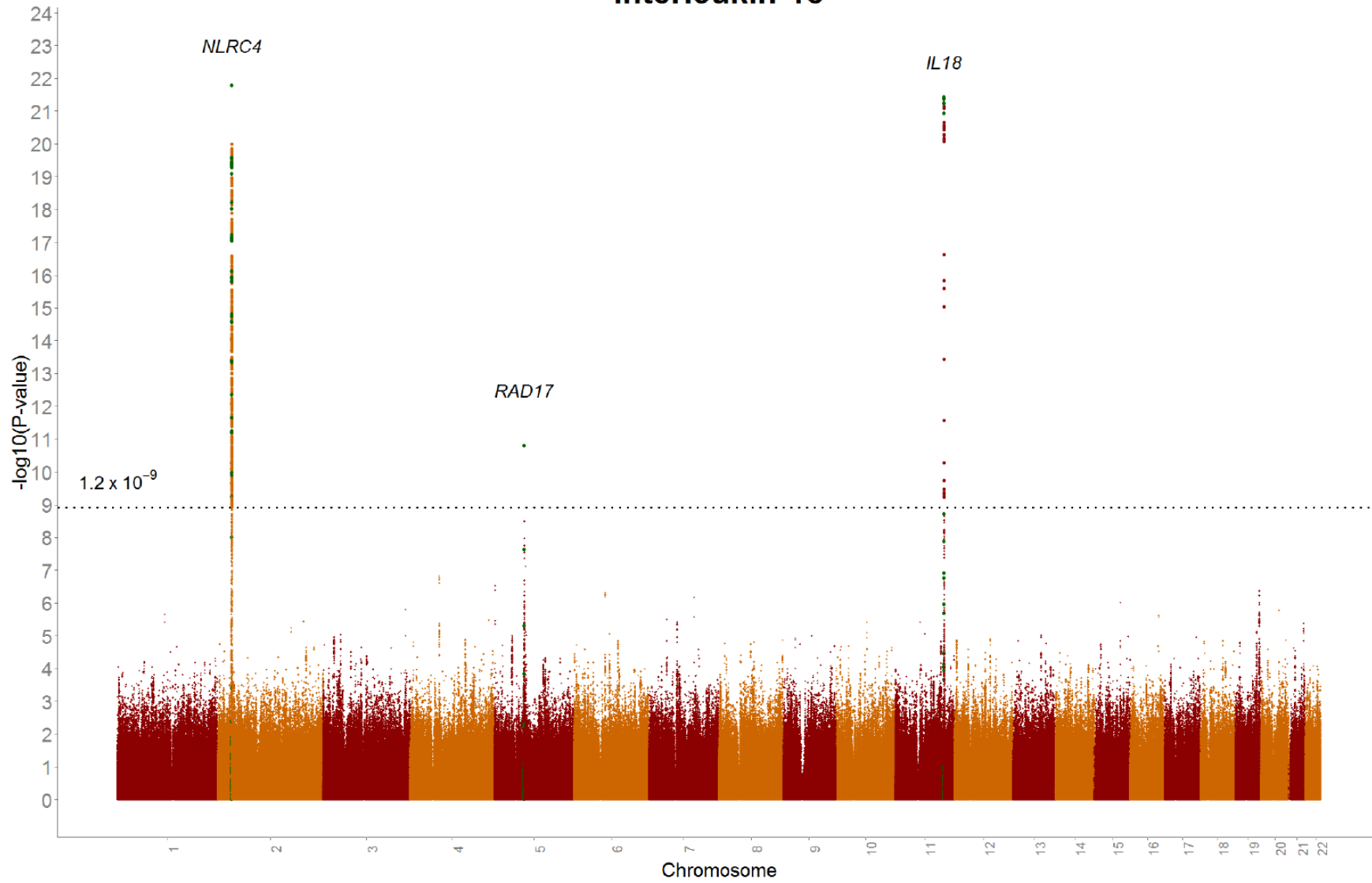


Figure S23

Manhattan plot for interleukin-16.

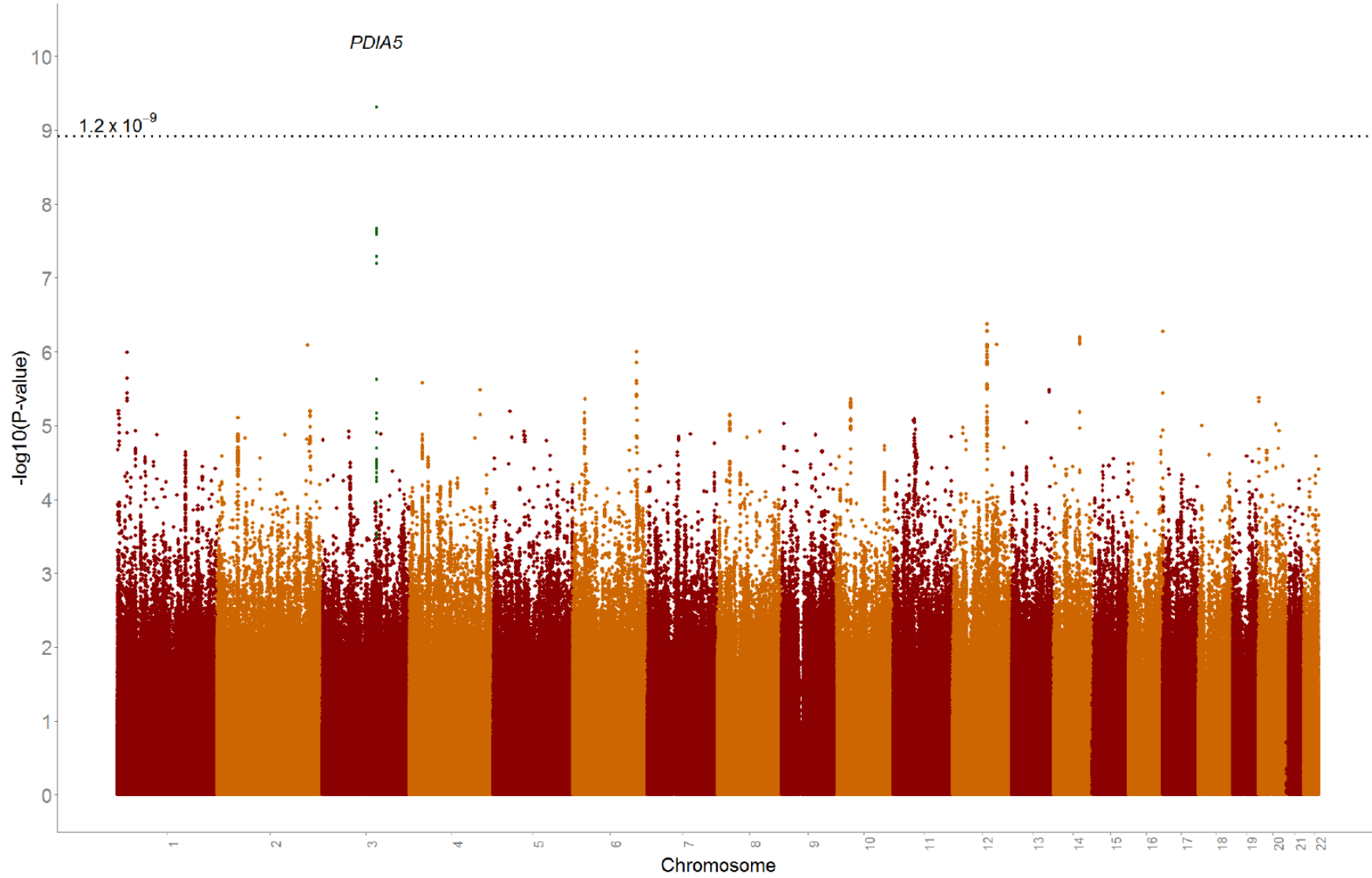
Interleukin-18



Manhattan plot for interleukin-18.

Figure S24

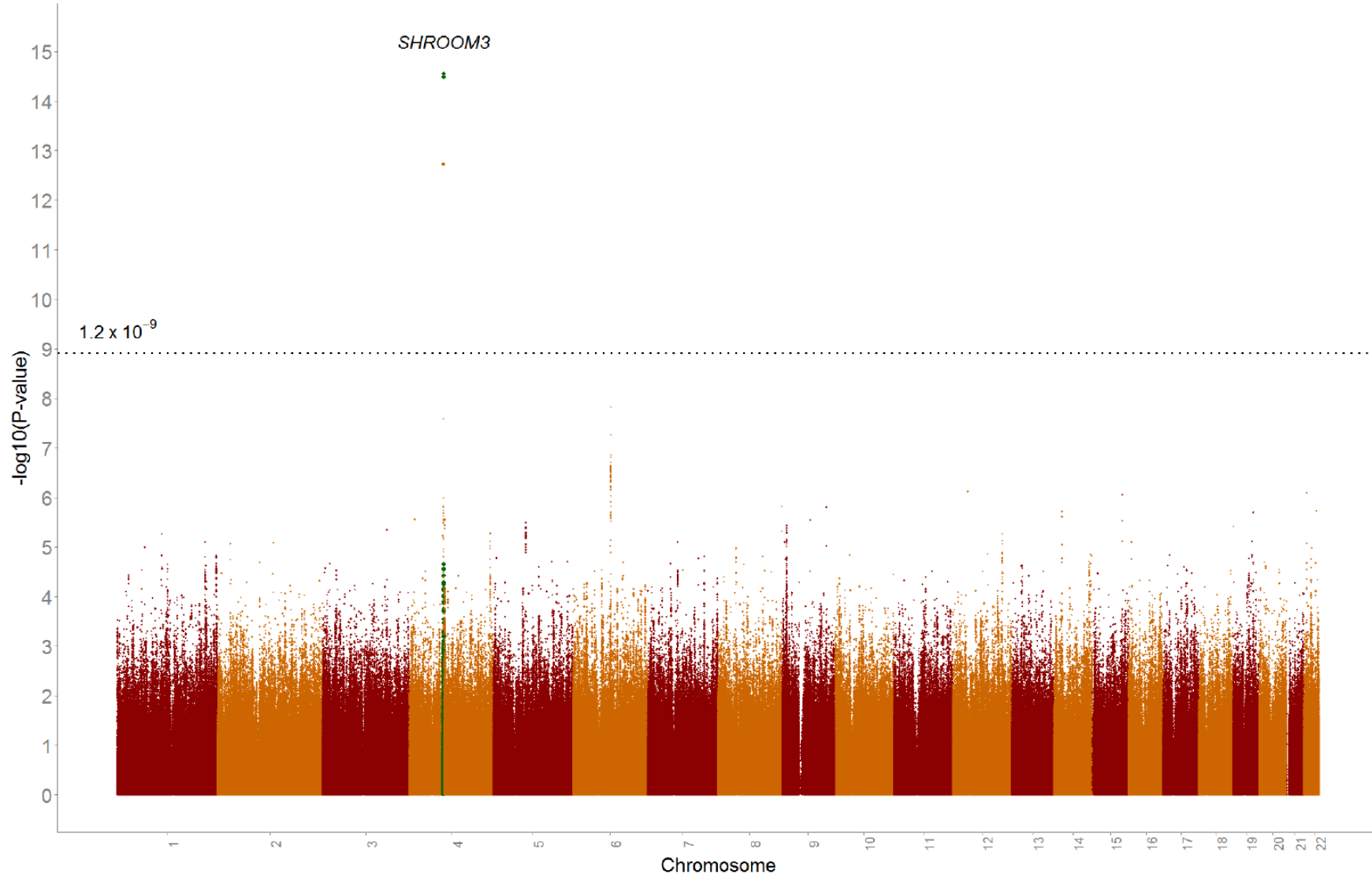
Interleukin-17



Manhattan plot for interleukin-17.

Figure S25

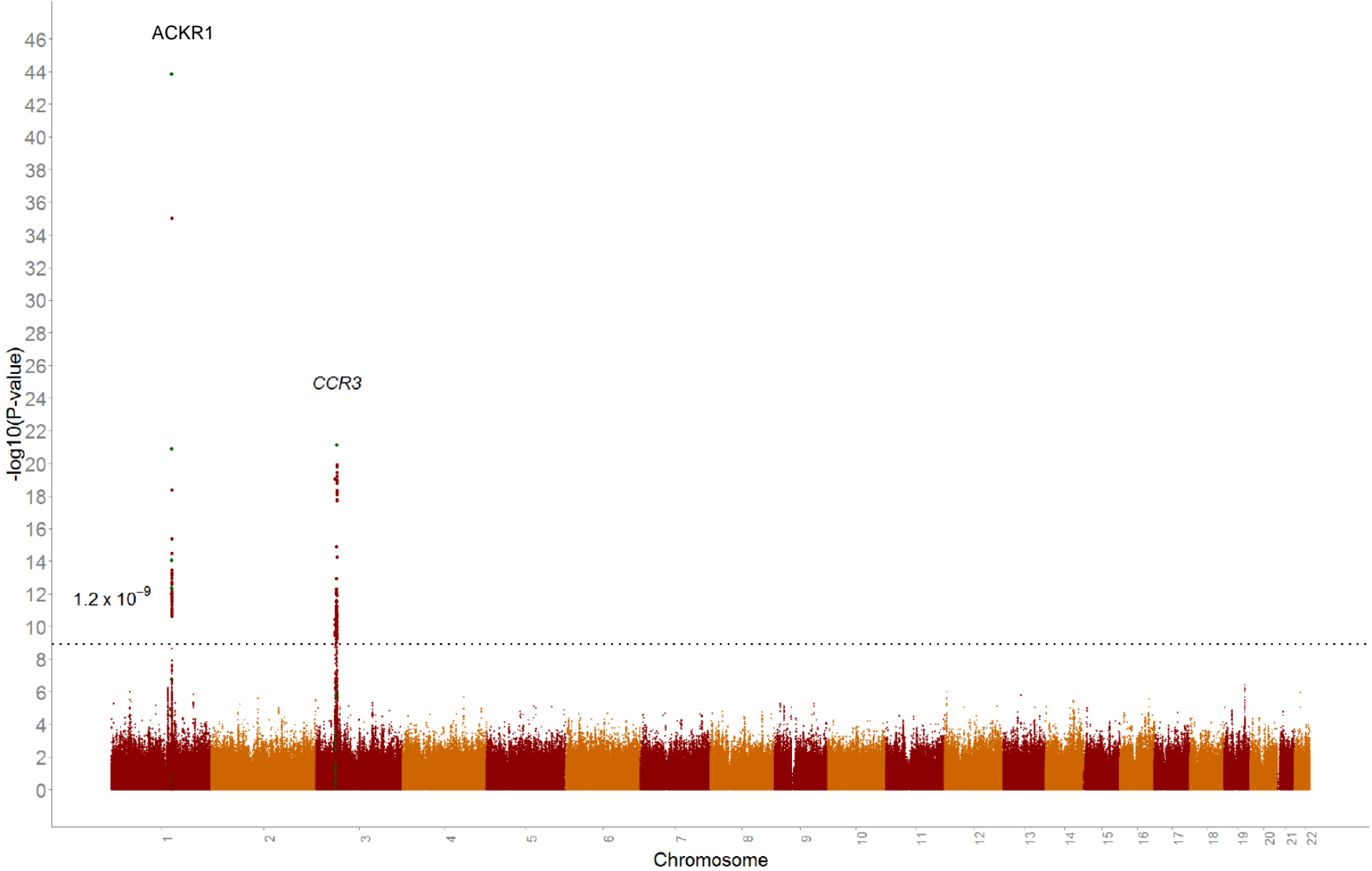
IP10



Manhattan plot for interferon gamma-induced protein 10 (CXCL10).

Figure S26

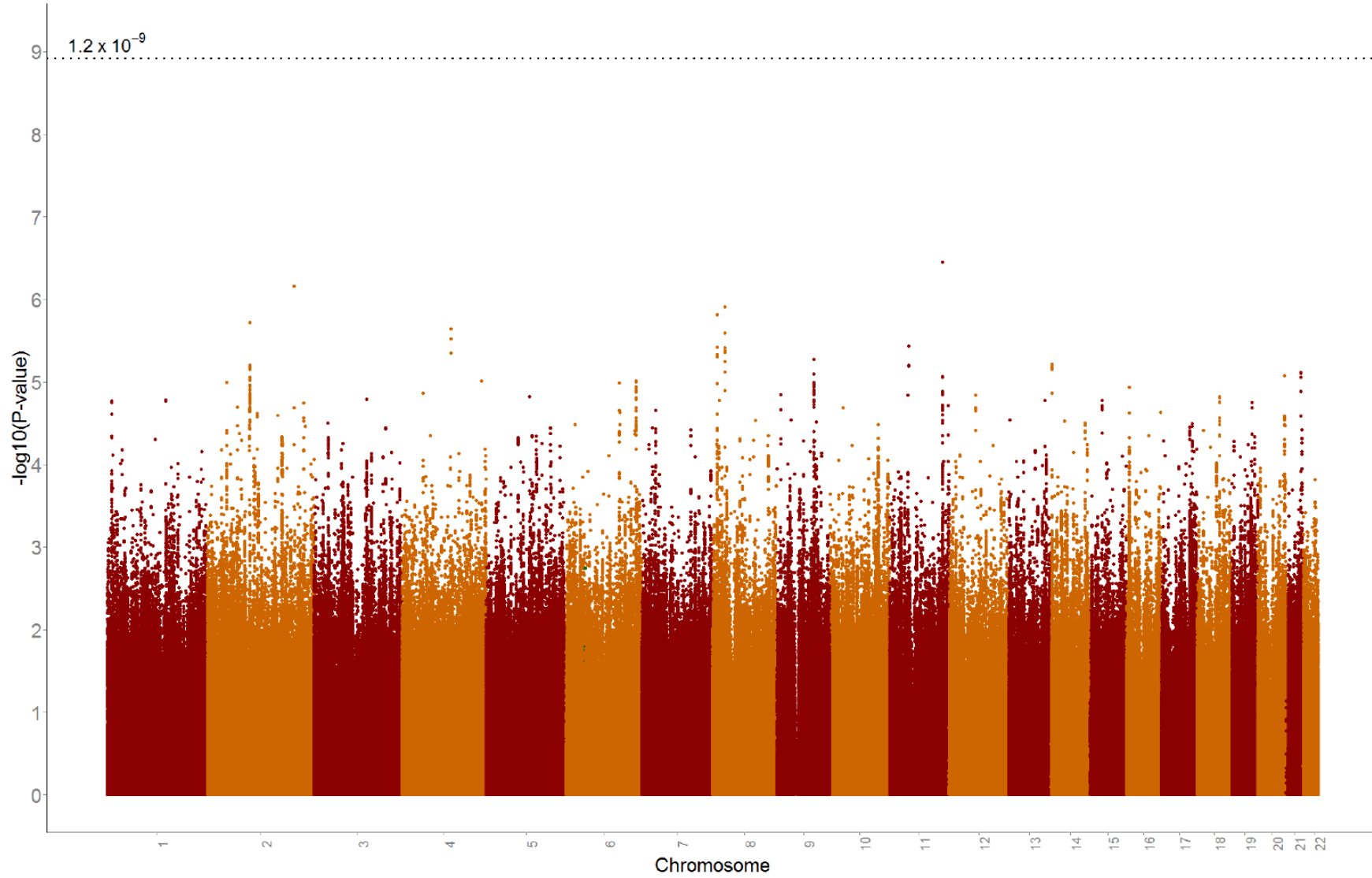
MCP1



Manhattan plot for monocyte chemotactic protein-1 (CCL2).

Figure S27

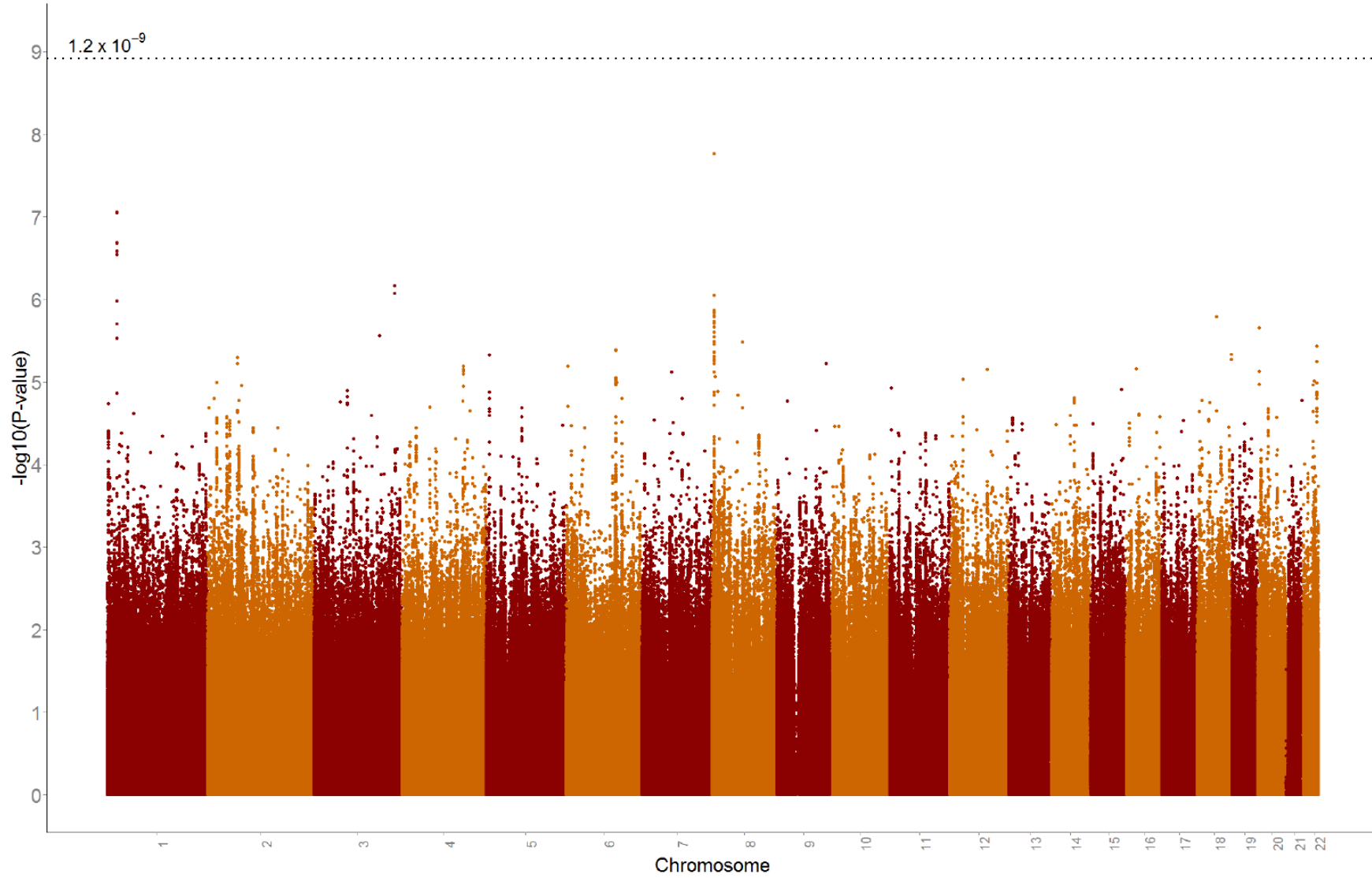
MCP3



Manhattan plot for monocyte specific chemokine 3 (CCL7).

Figure S28

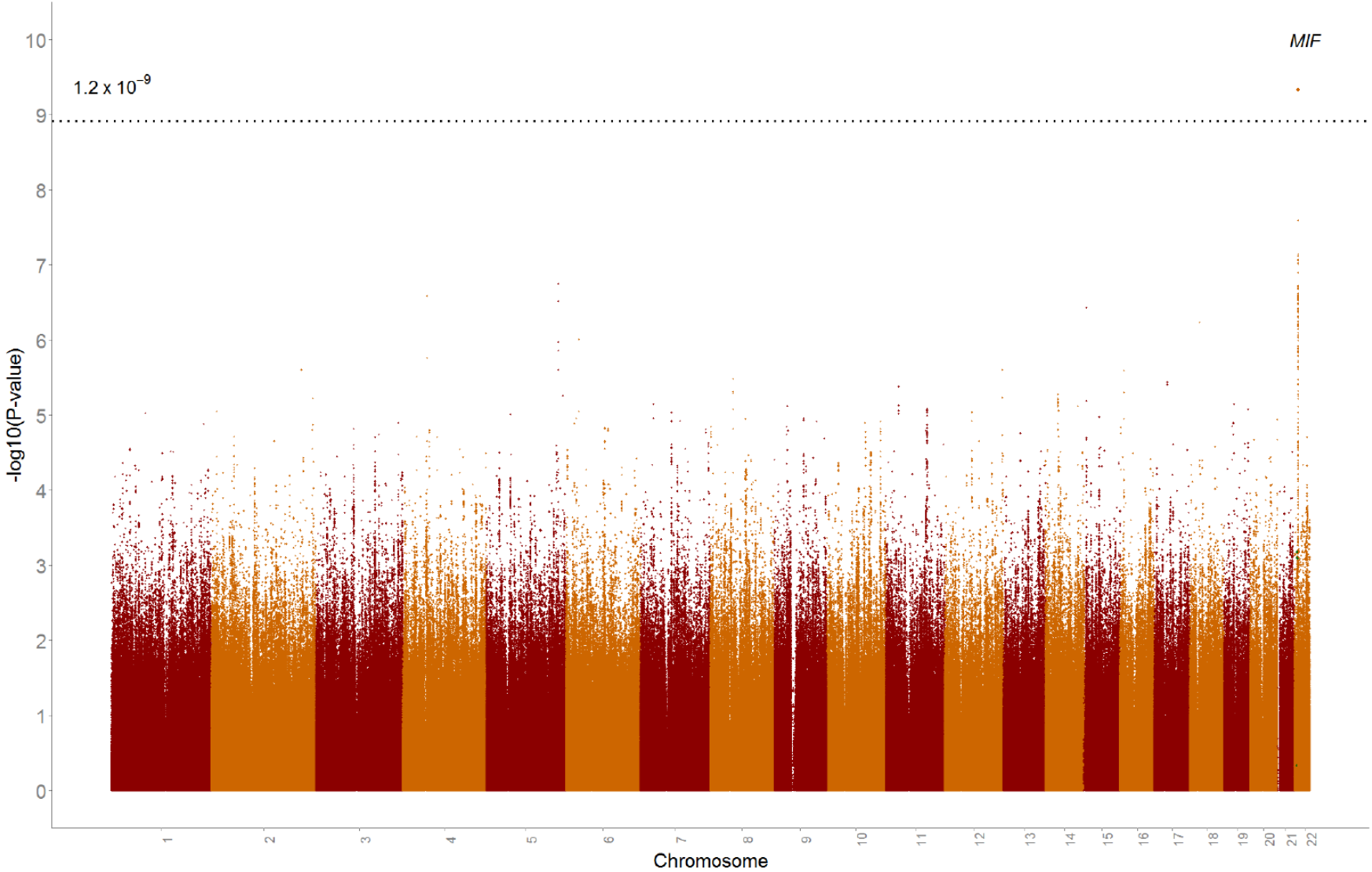
MCSF



Manhattan plot for macrophage colony-stimulating factor (MCSF).

Figure S29

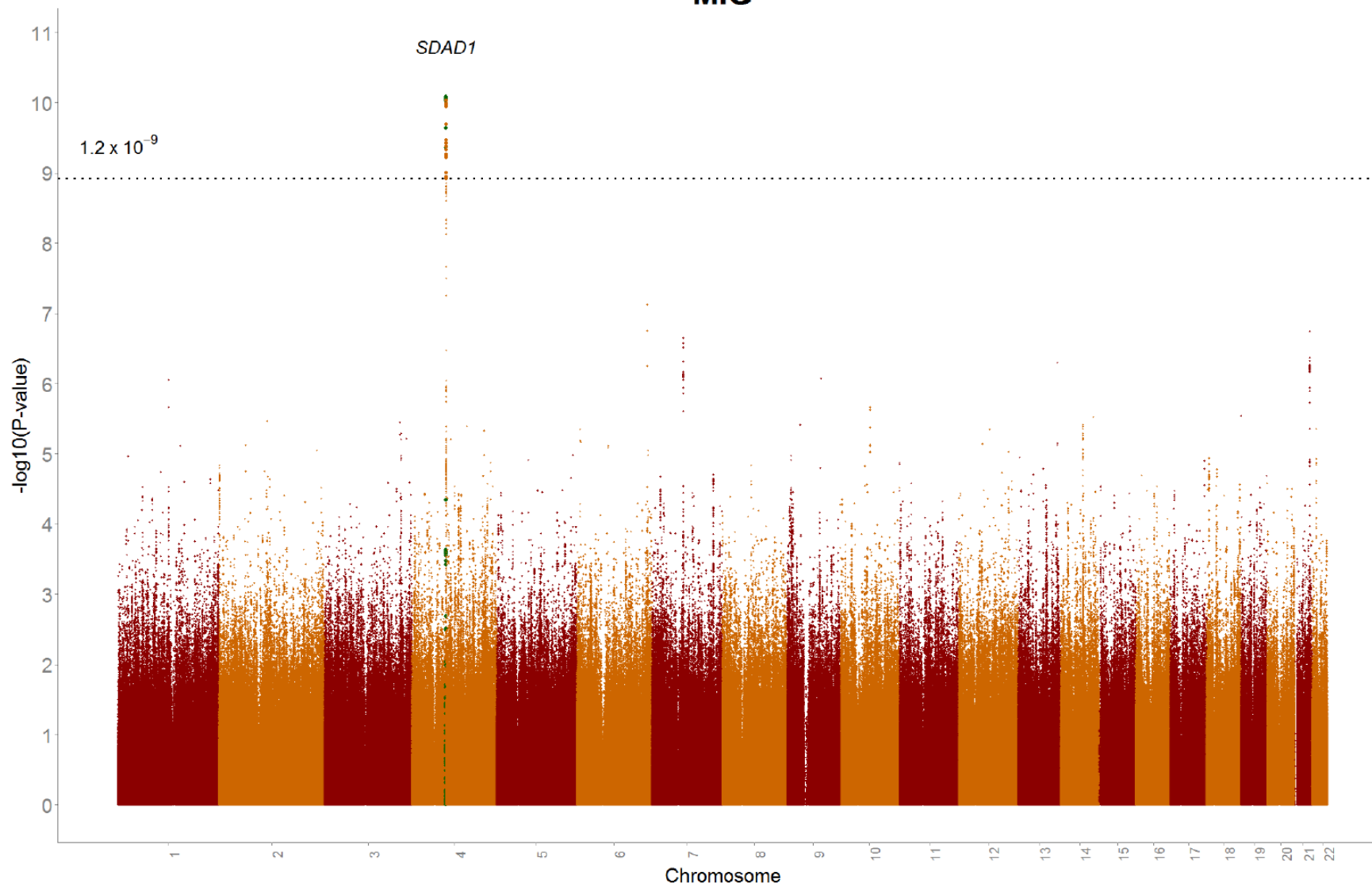
MIF



Manhattan plot for macrophage migration inhibitory factor (glycosylation-inhibiting factor).

Figure S30

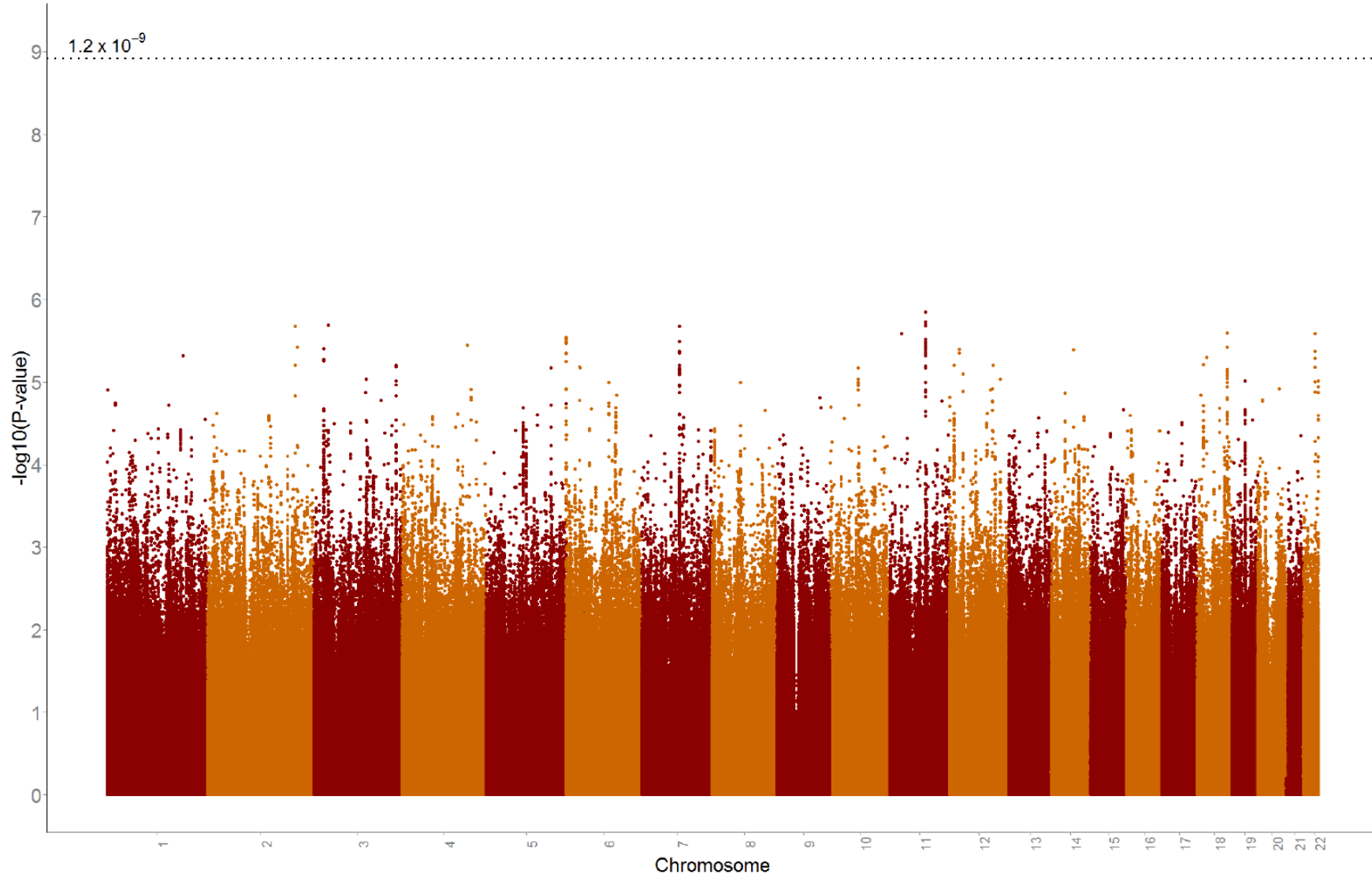
MIG



Manhattan plot for monokine induced by interferon-gamma (CXCL9).

Figure S31

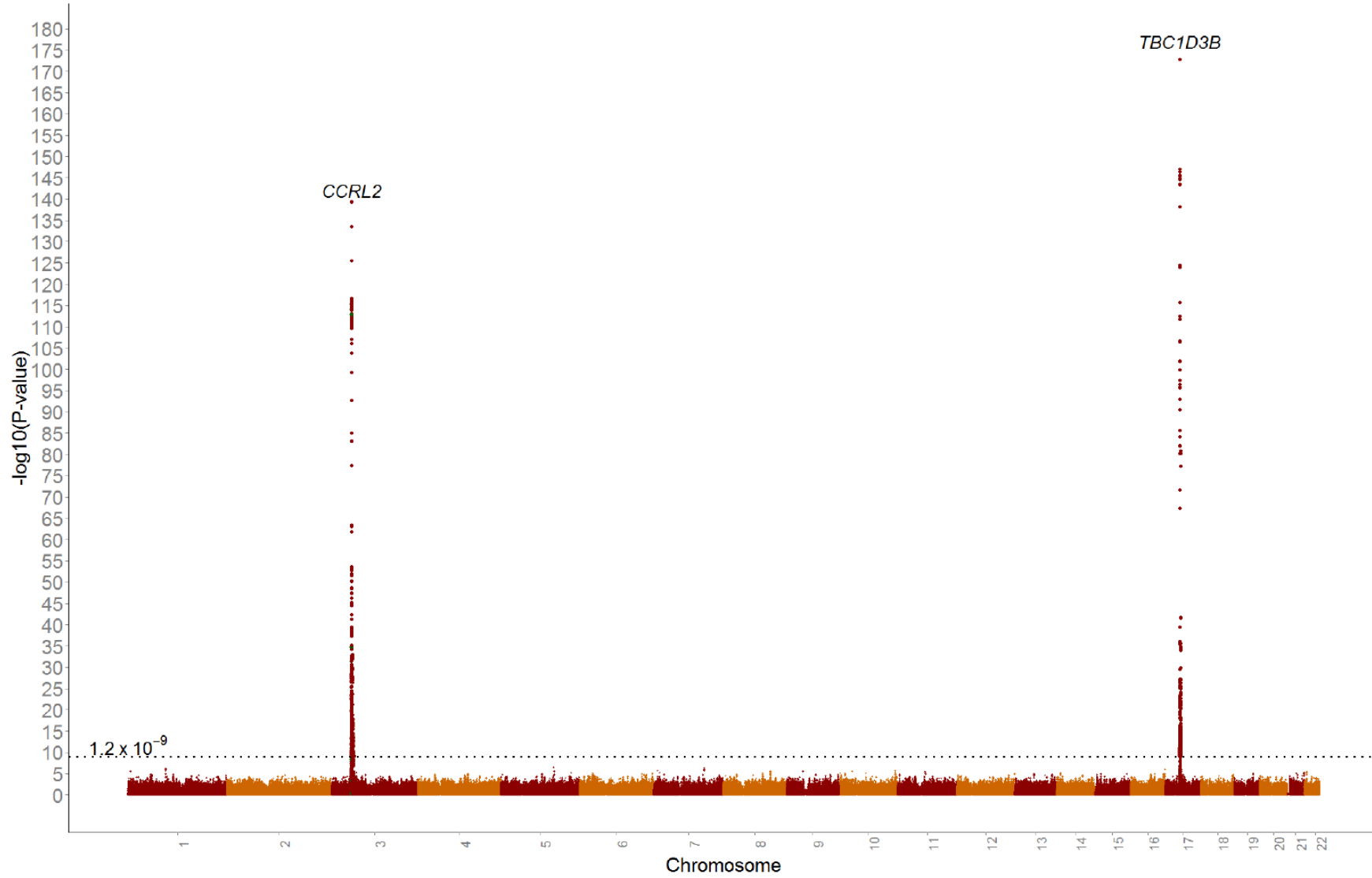
MIP1a



Manhattan plot for macrophage inflammatory protein-1 α (CCL3)

Figure S32

MIP1b



Manhattan plot for macrophage inflammatory protein-1 β (MIP1b; CCL4).

Figure S33

PDGFbb

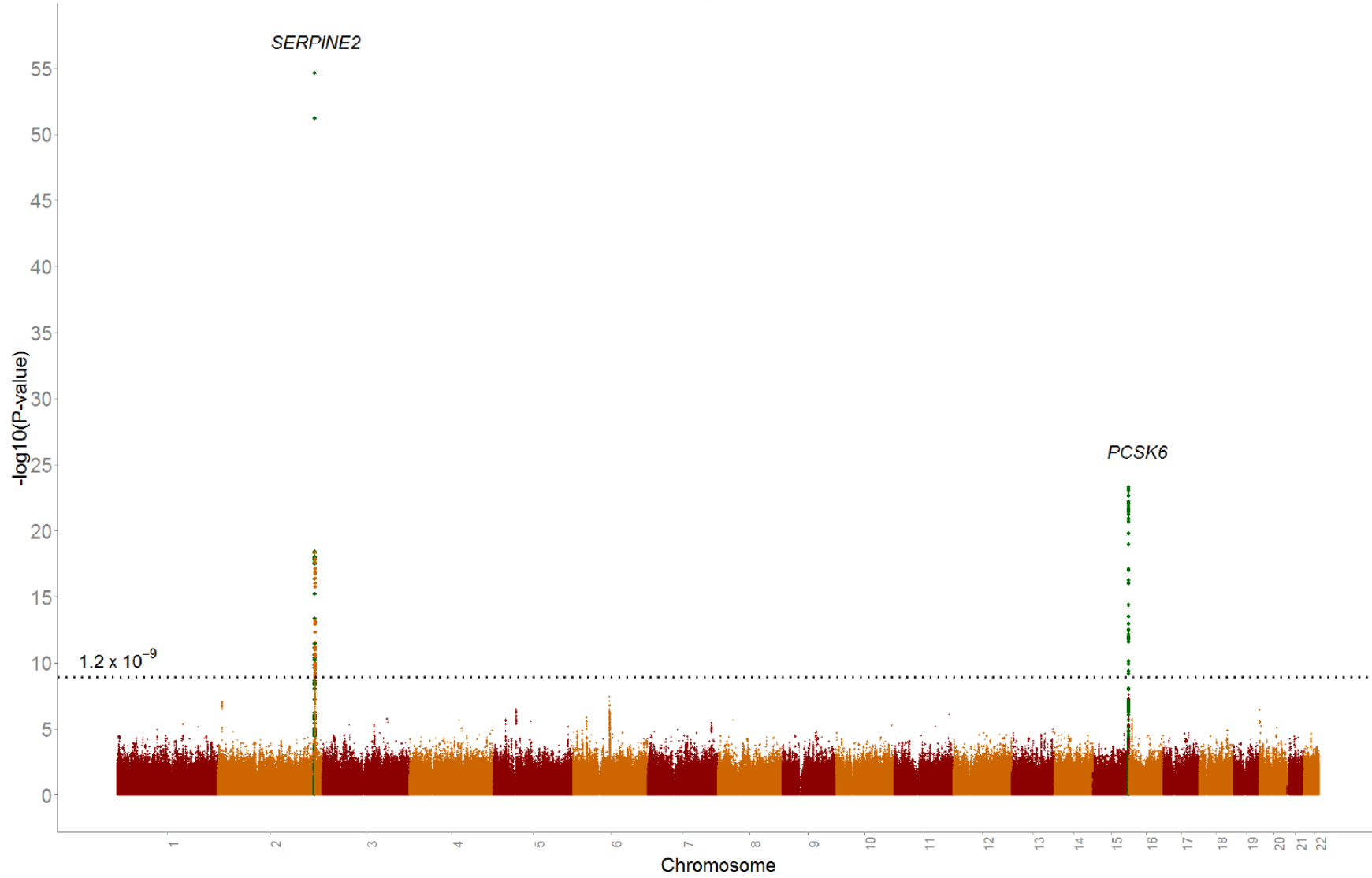


Figure S34

Manhattan plot for platelet derived growth factor BB (PDGFbb).

RANTES

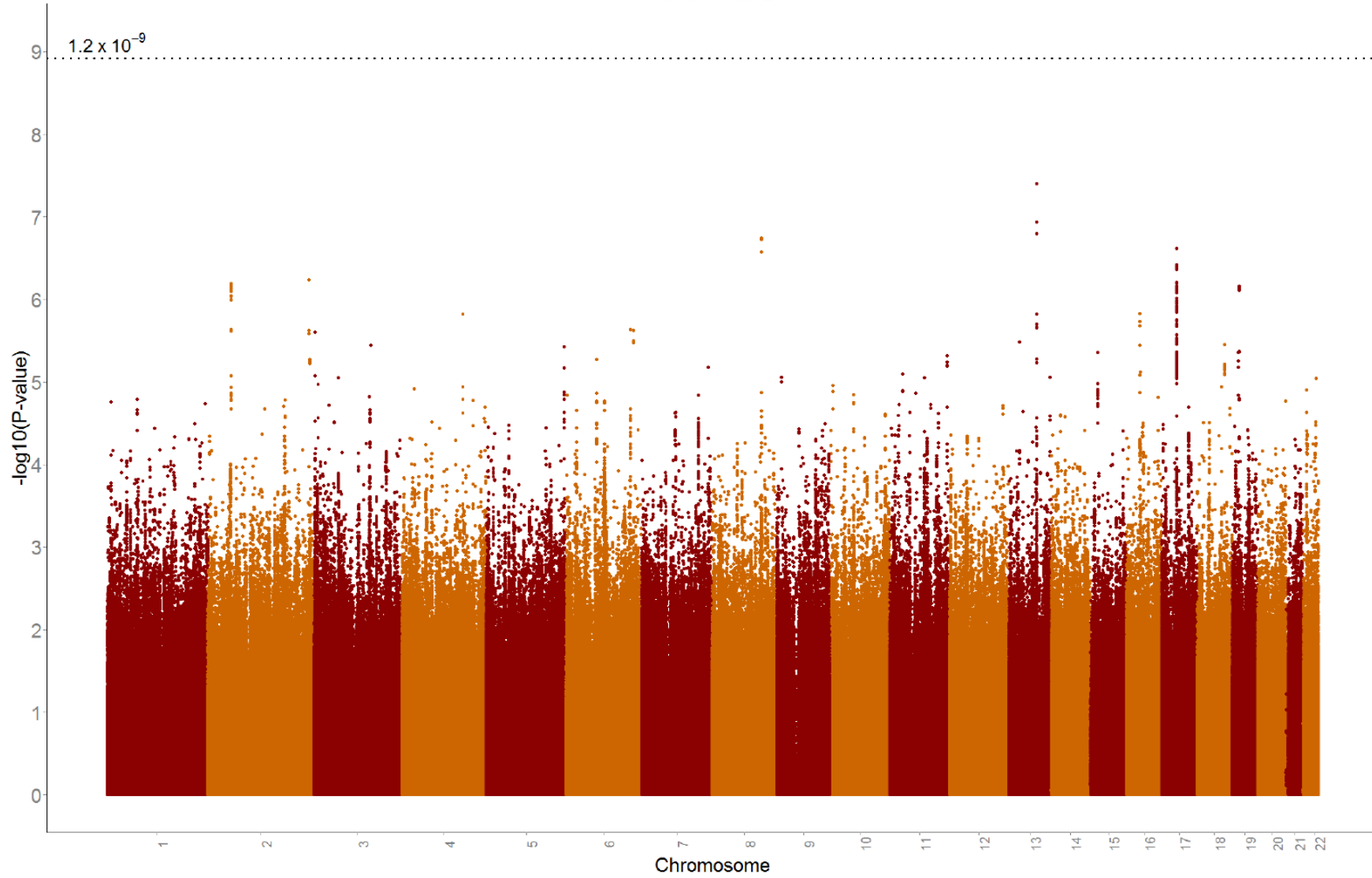
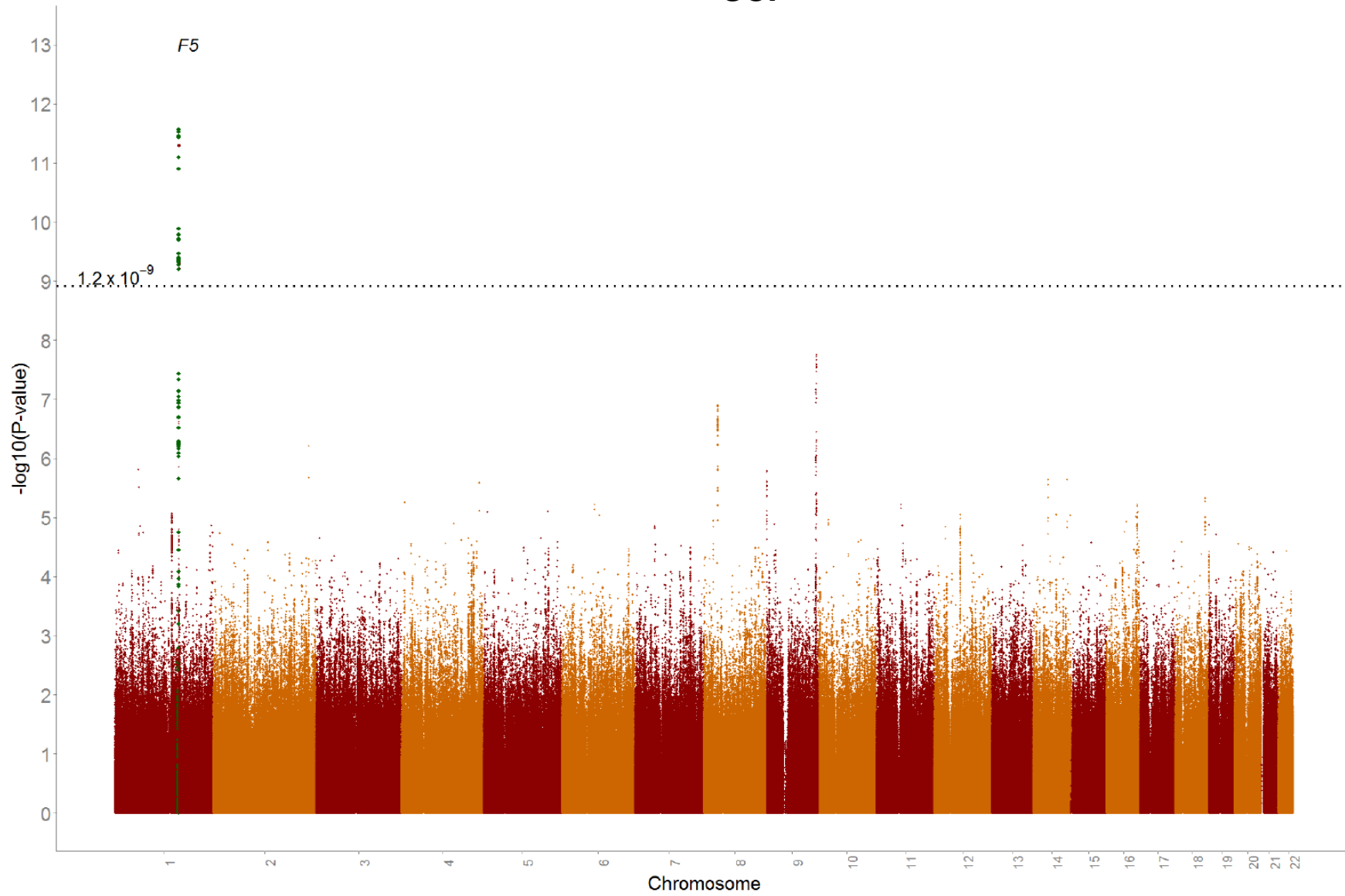


Figure S35

Manhattan plot for Regulated on Activation, Normal T Cell Expressed and Secreted (RANTES; CCL5).

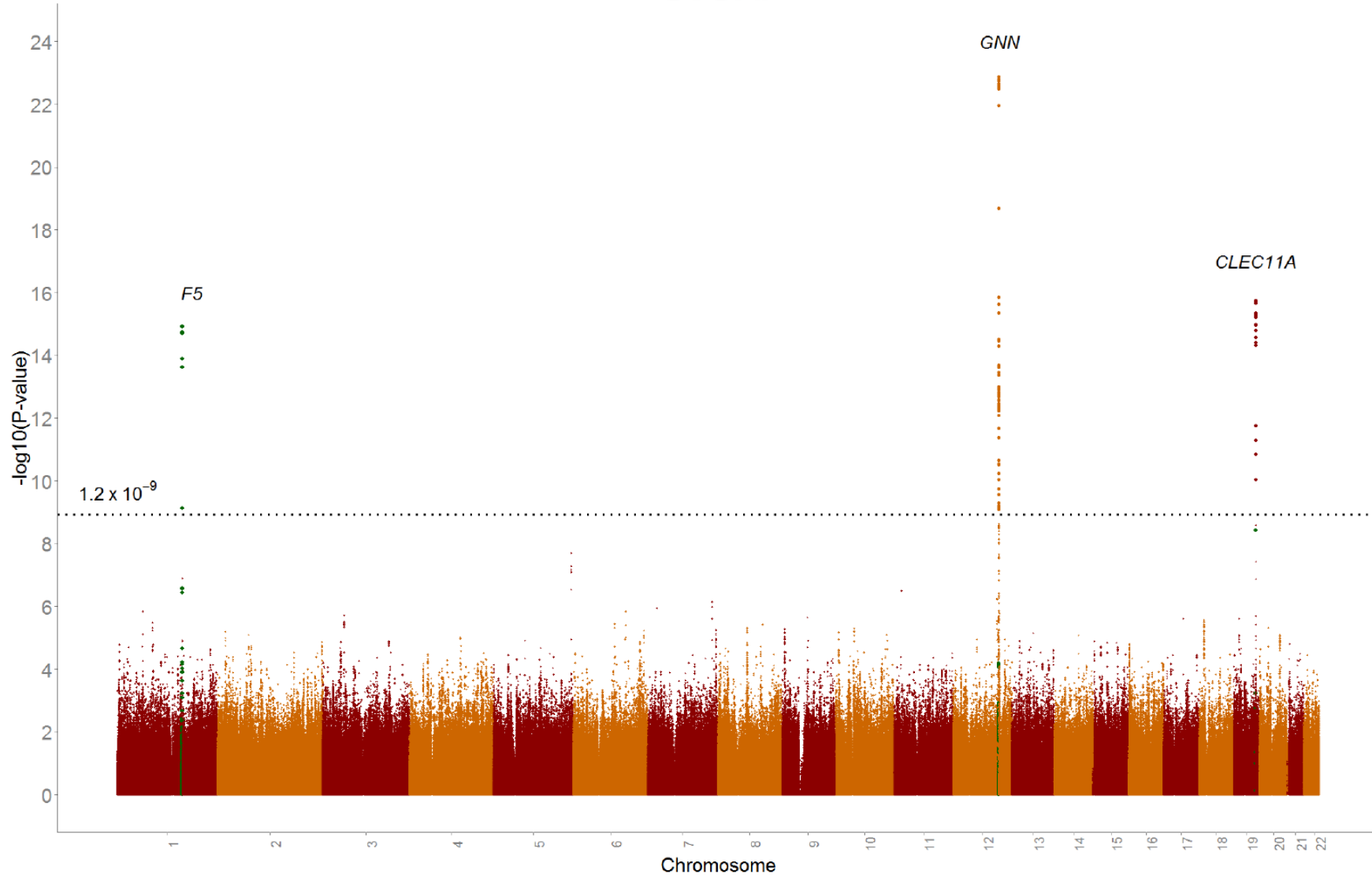
SCF



Manhattan plot for stem cell factor (SCF).

Figure S36

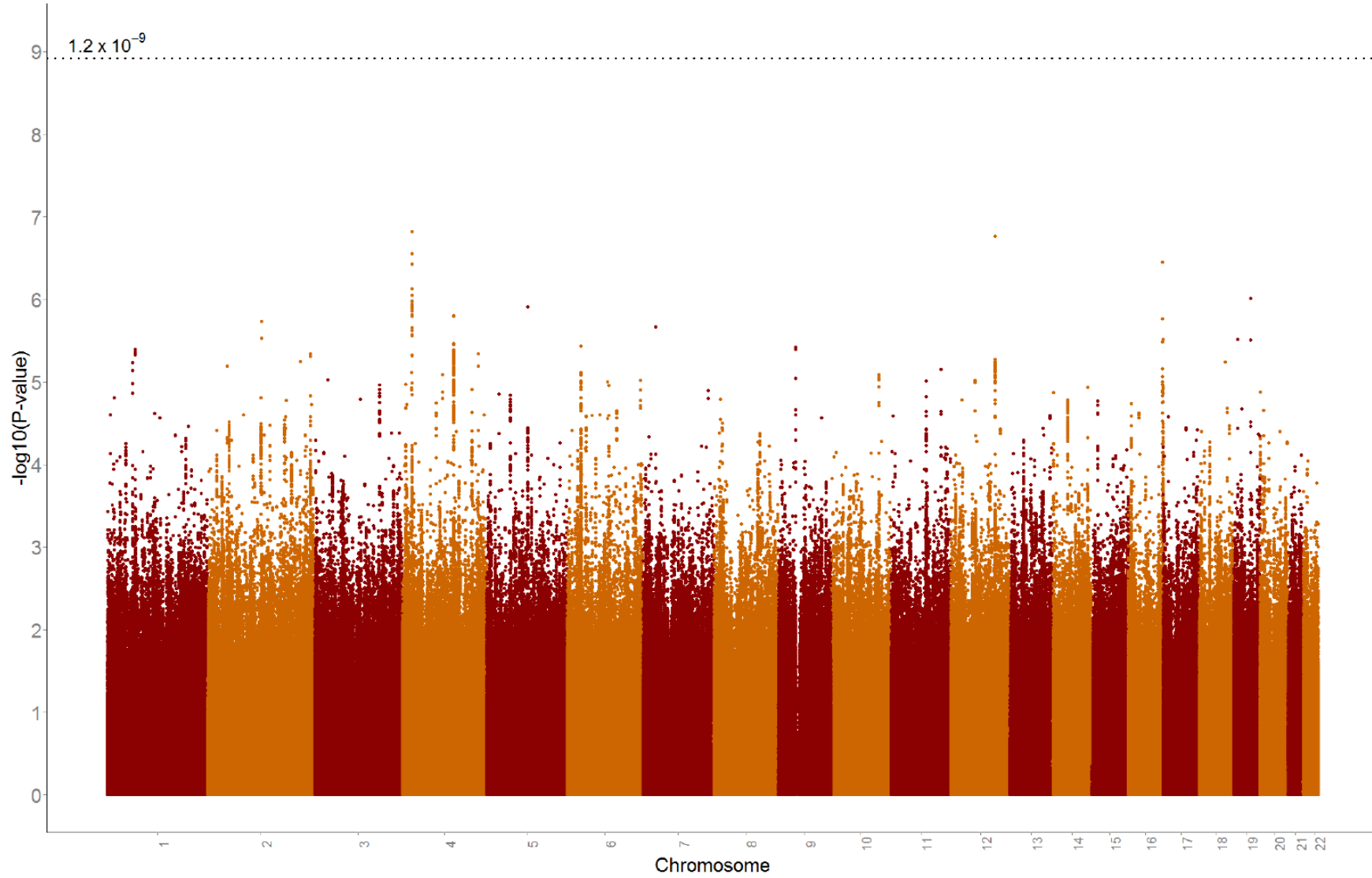
SCGFb



Manhattan plot for stem cell growth factor beta (SCGFb).

Figure S37

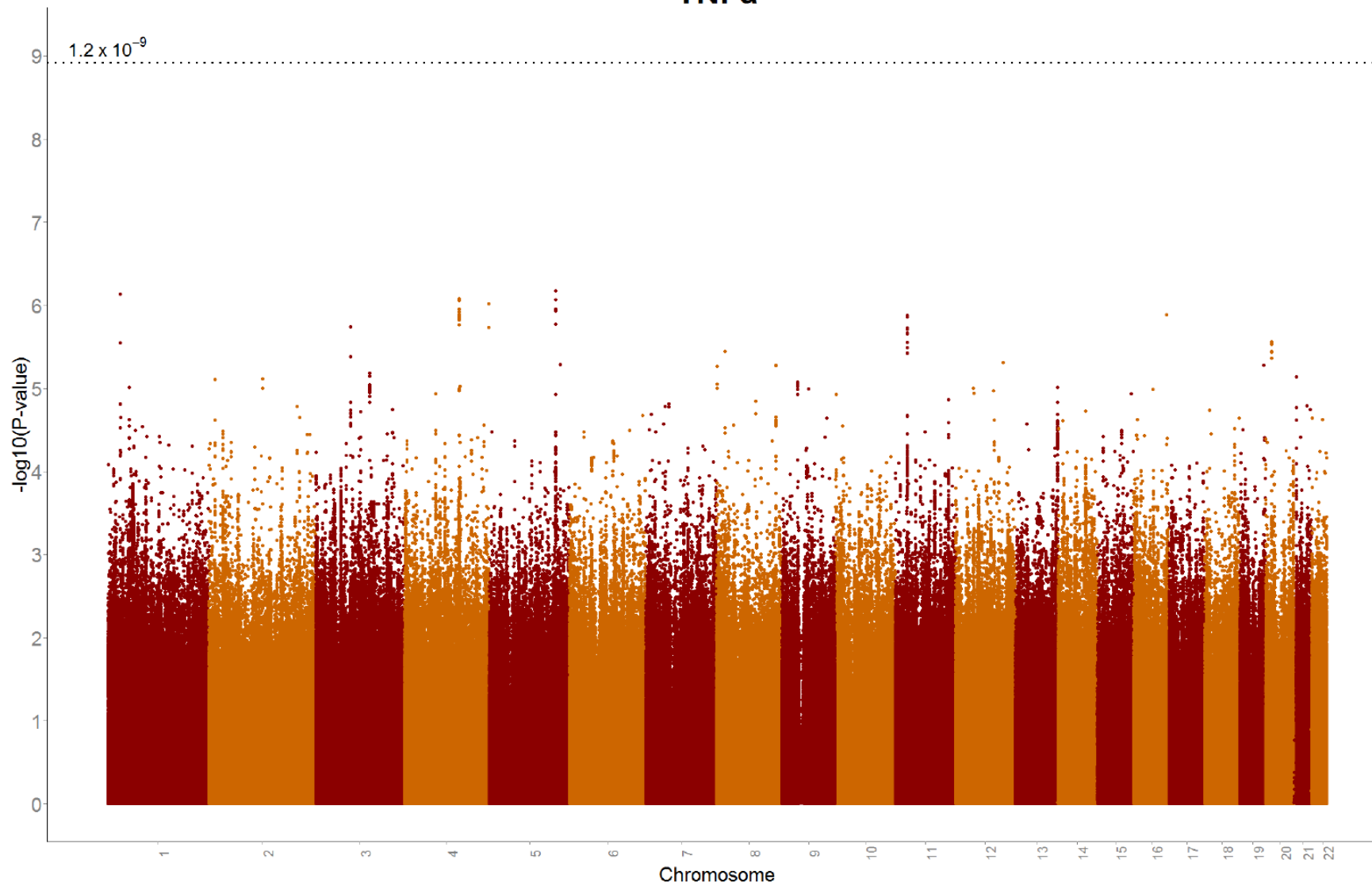
SDF1a



Manhattan plot for stromal cell-derived factor-1 alpha (SDF1a; CXCL12)

Figure S38

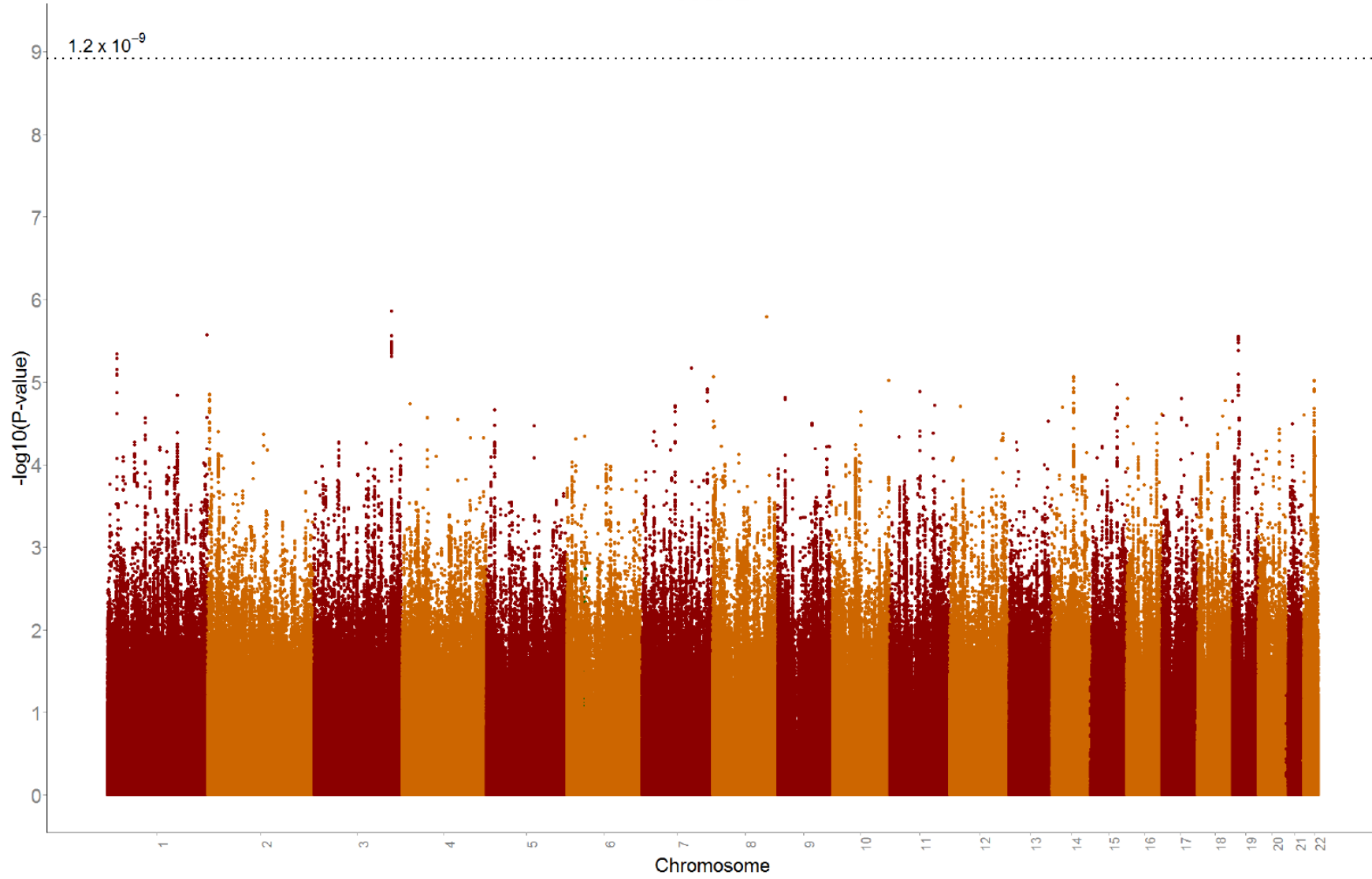
TNFa



Manhattan plot for tumor necrosis factor-alpha (TNFa).

Figure S39

TNFb



Manhattan plot for tumor necrosis factor-beta (TNFb).

Figure S40

TRAIL

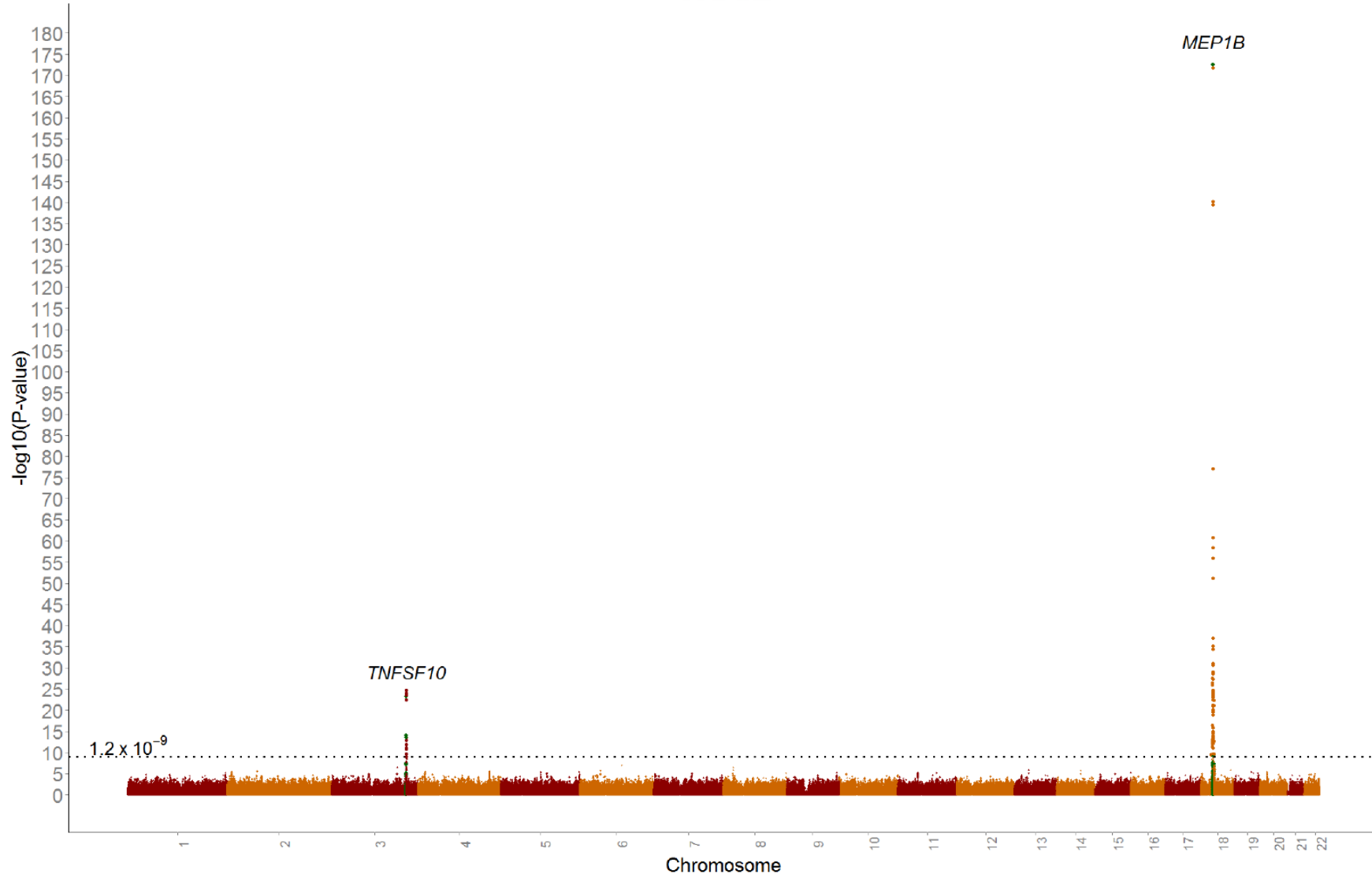


Figure S41

Manhattan plot for TNF-related apoptosis inducing ligand (TRAIL).

VEGF

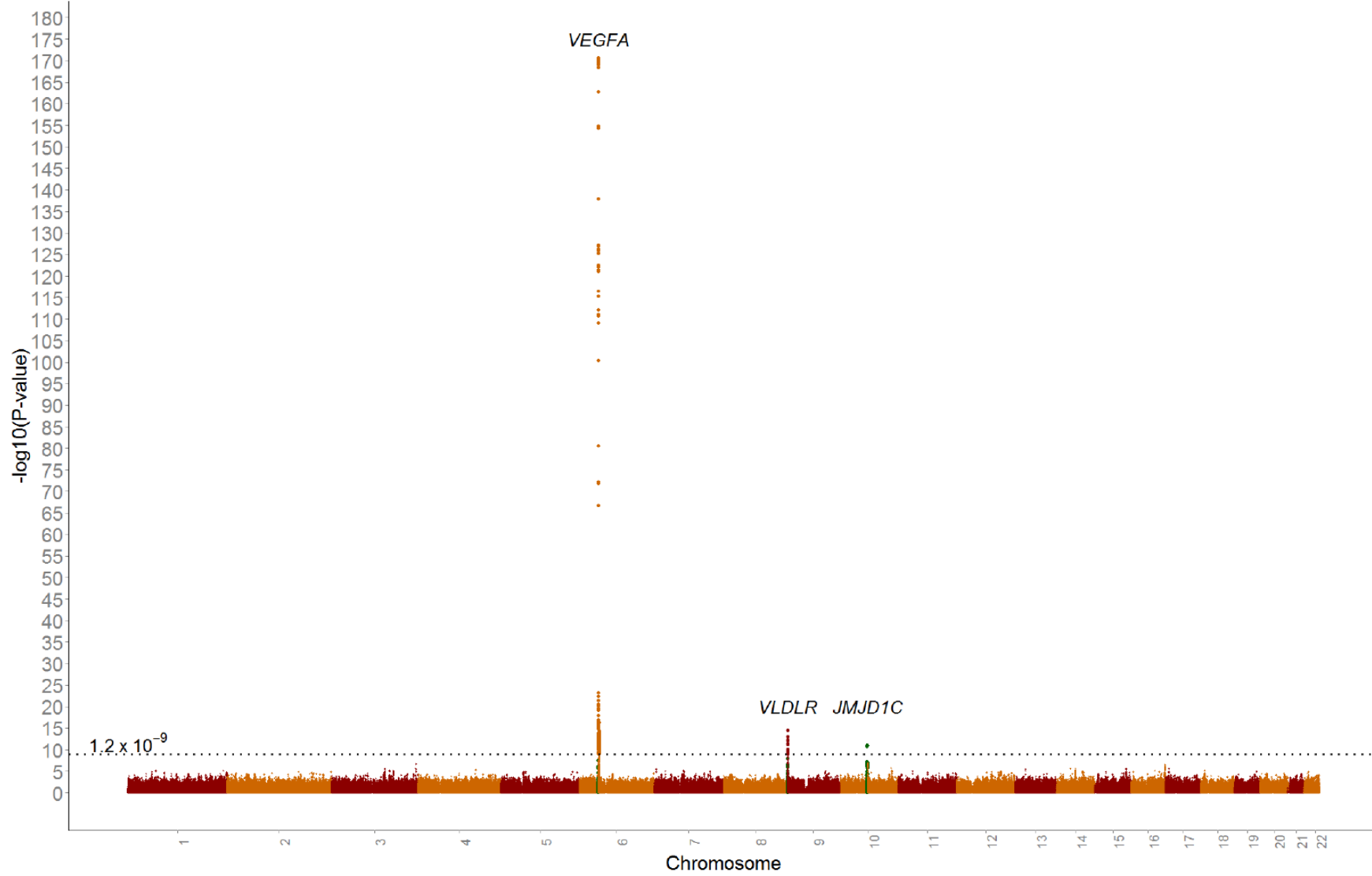


Figure S42

Manhattan plot for vascular endothelial growth factor (VEGF).

MCP1 – 1q23.2

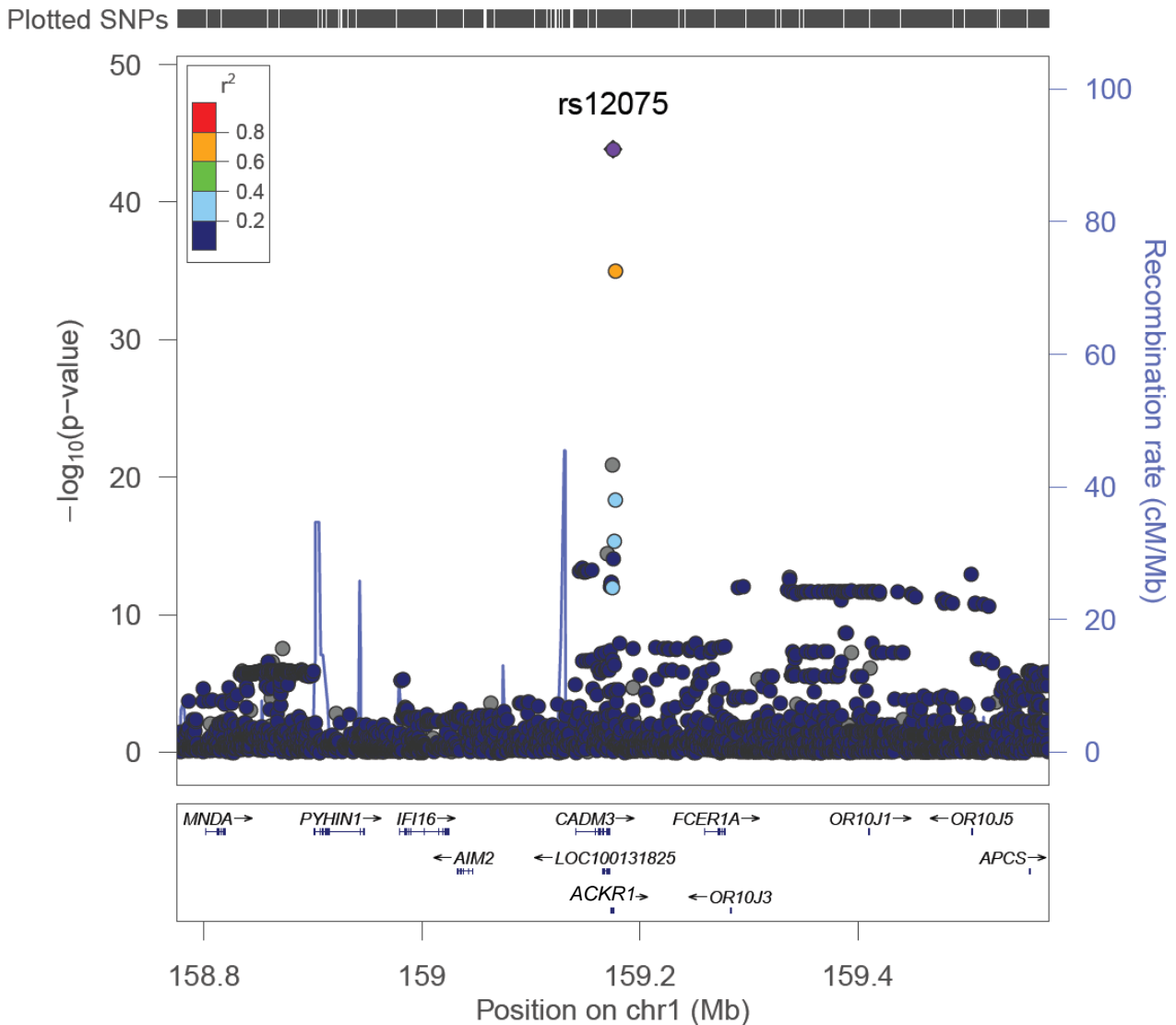


Figure S43 Locus Zoom plot from 1q23.2. The associations are for monocyte chemotactic protein-1 (MCP1; CCL2). The lead SNP is located in *ACKR1* gene and the pertinent variant alters binding properties of MCP1 to the receptor.

SCGFb – 1q24.2

Plotted SNPs

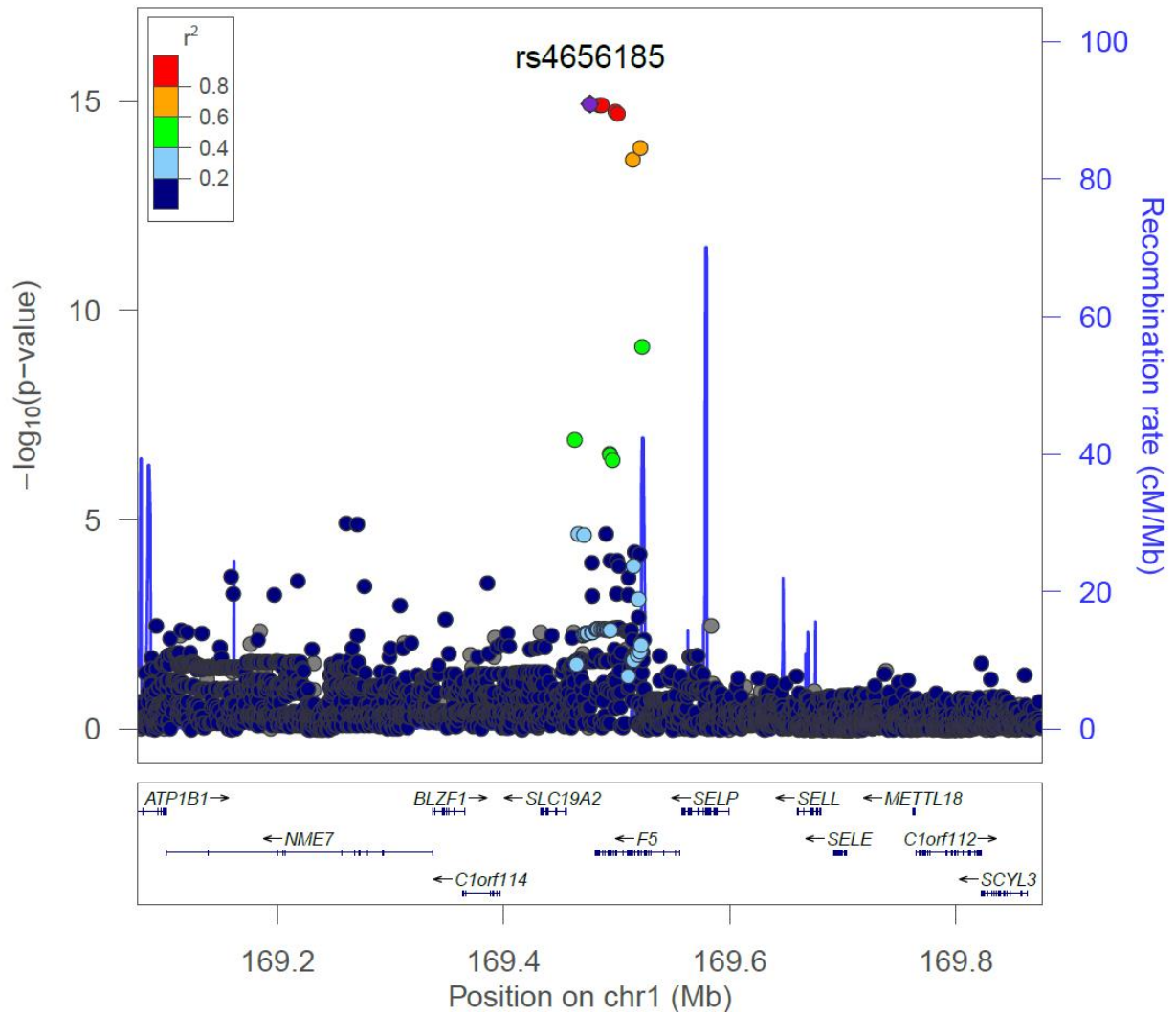


Figure S44 Locus Zoom plot for stem cell factor beta (SCGFb) from 1q24.2.

IL-18 – 2p22.3

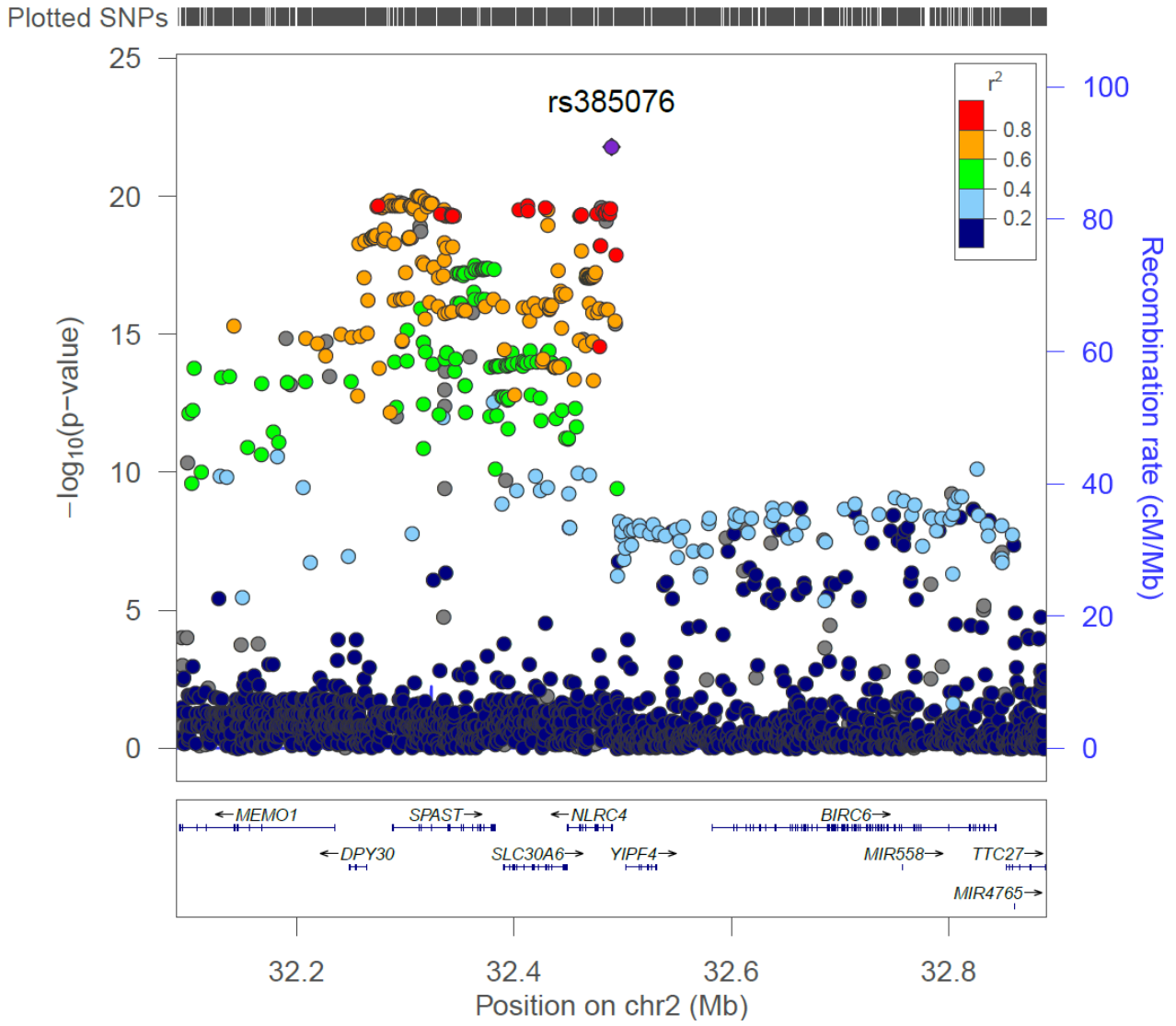


Figure S45 Locus Zoom plot for interleukin-18 (IL-18) from 2p22.5.

PDGFbb - 2q36.1

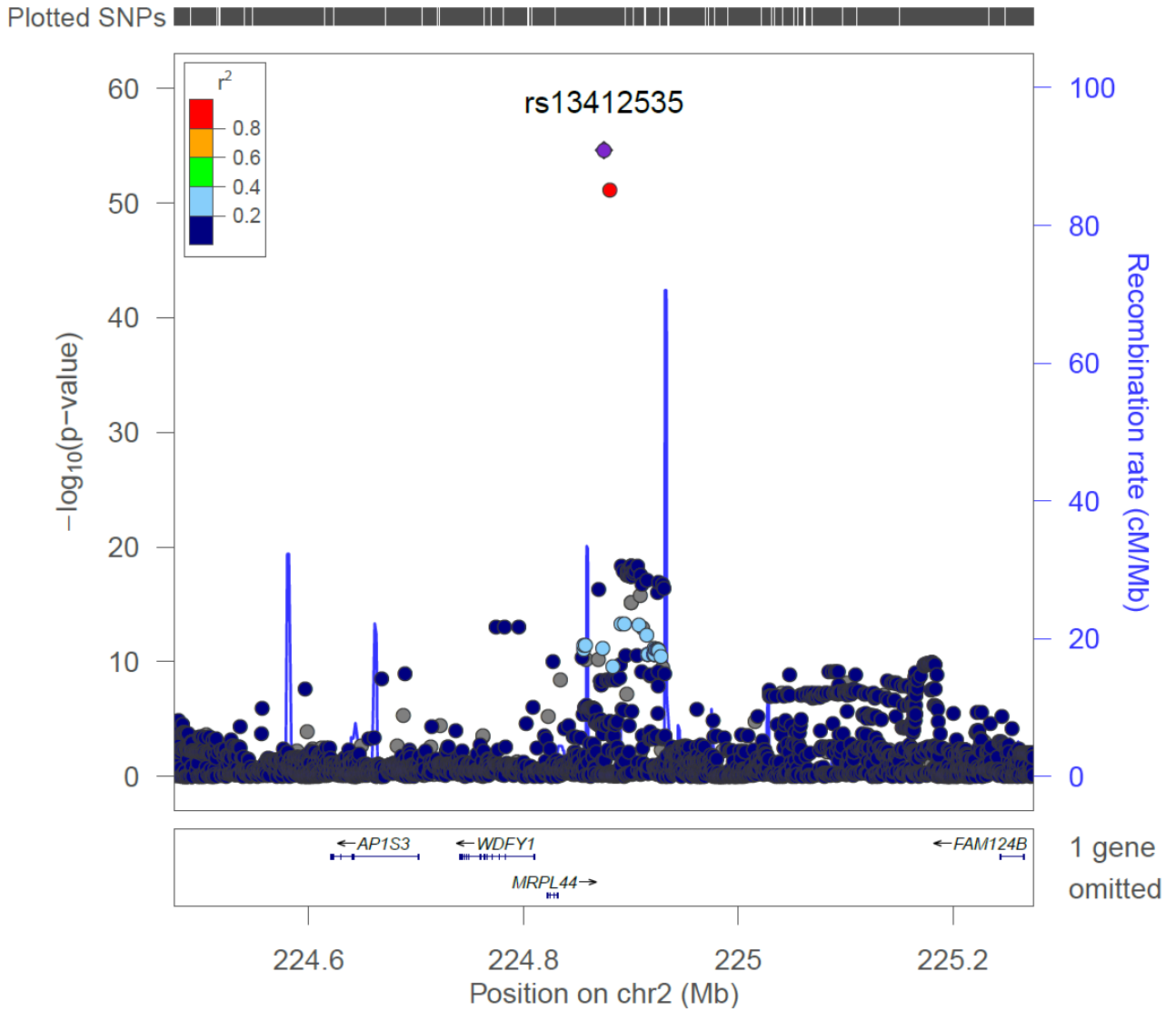


Figure S46 Locus Zoom plot for platelet derived growth factor BB (PDGFbb) from 2q36.1.

Eotaxin - 3p22.1

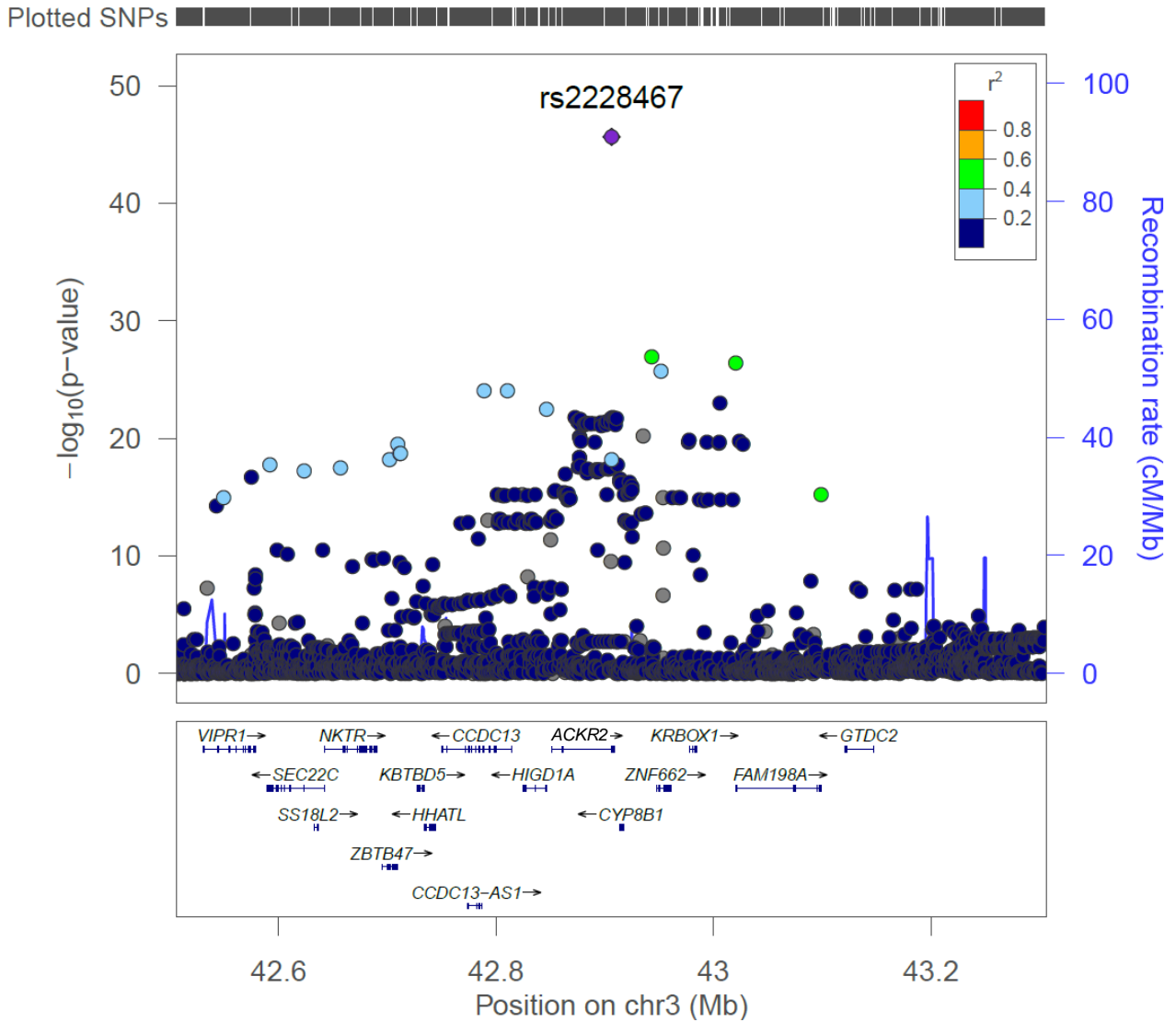


Figure S47 Locus Zoom plot for eotaxin from 3p22.1 locus.

MIP1b - 3p21.31

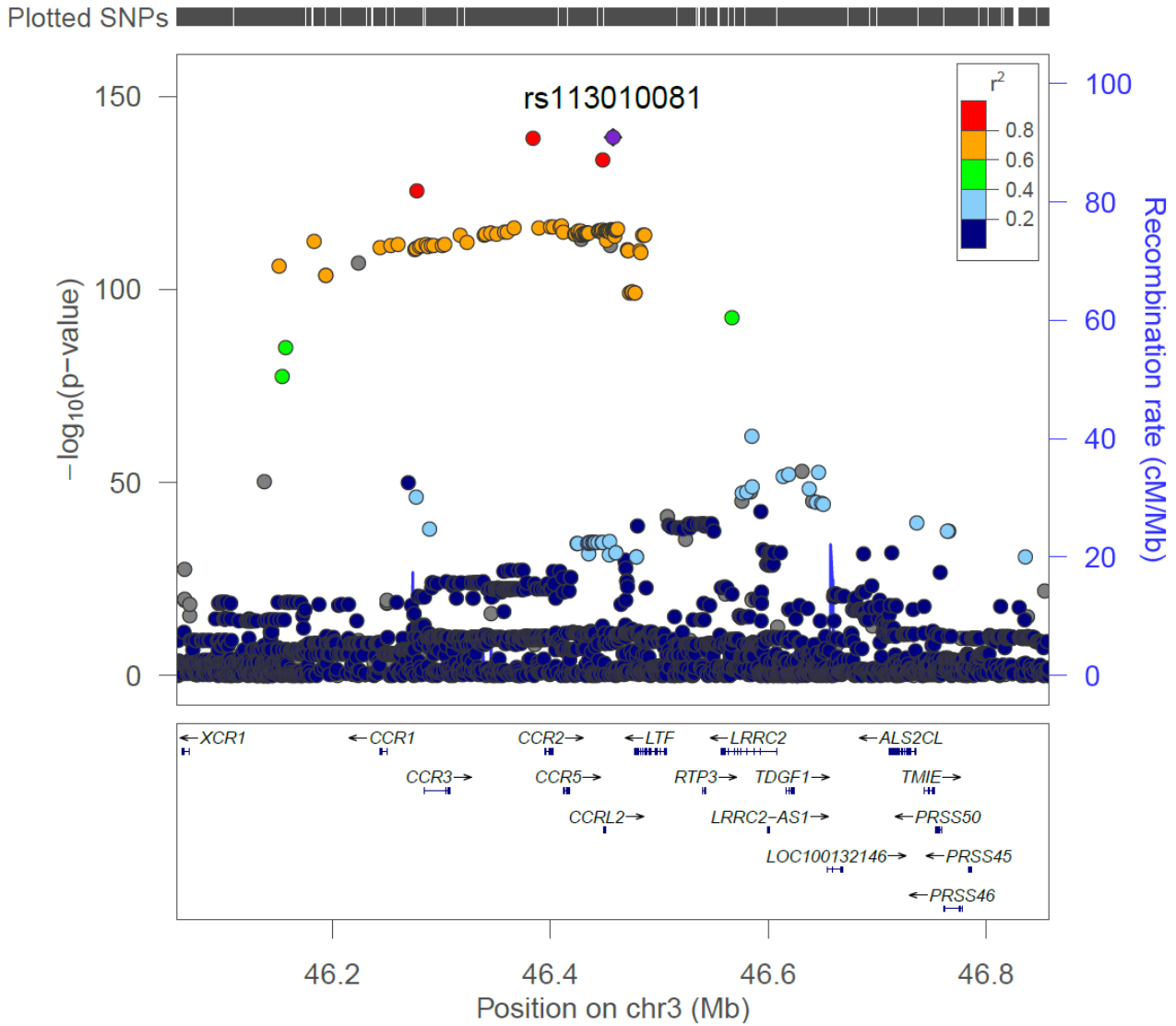


Figure S48 Locus Zoom plot for macrophage inflammatory protein-1 β (MIP1b; CCL4).

IL-17 – 3q21.1

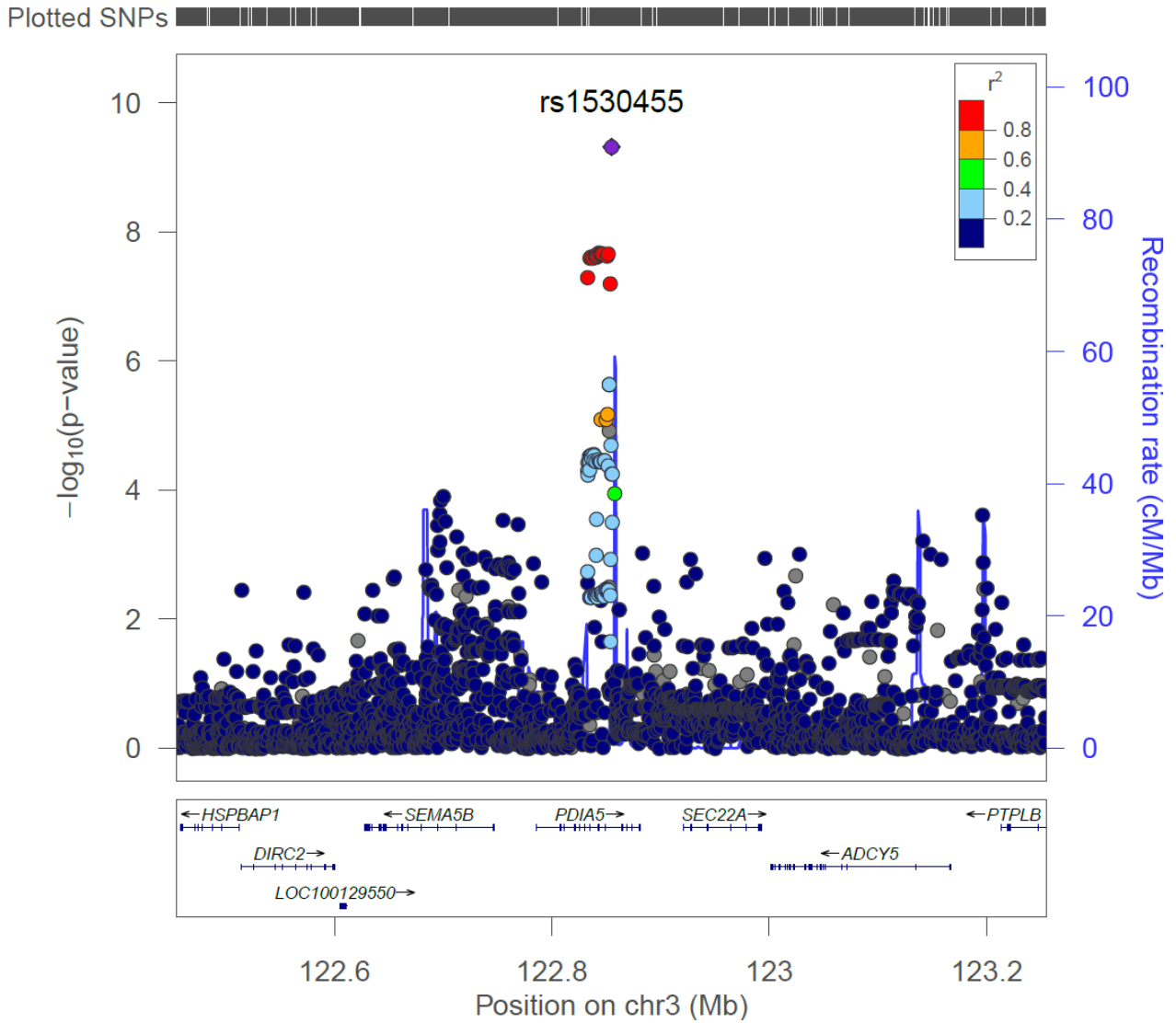


Figure S49 Locus Zoom plot for interleukin-17 (IL-17) from 3q21.1.

TRAIL - 3q26.31

Plotted SNPs

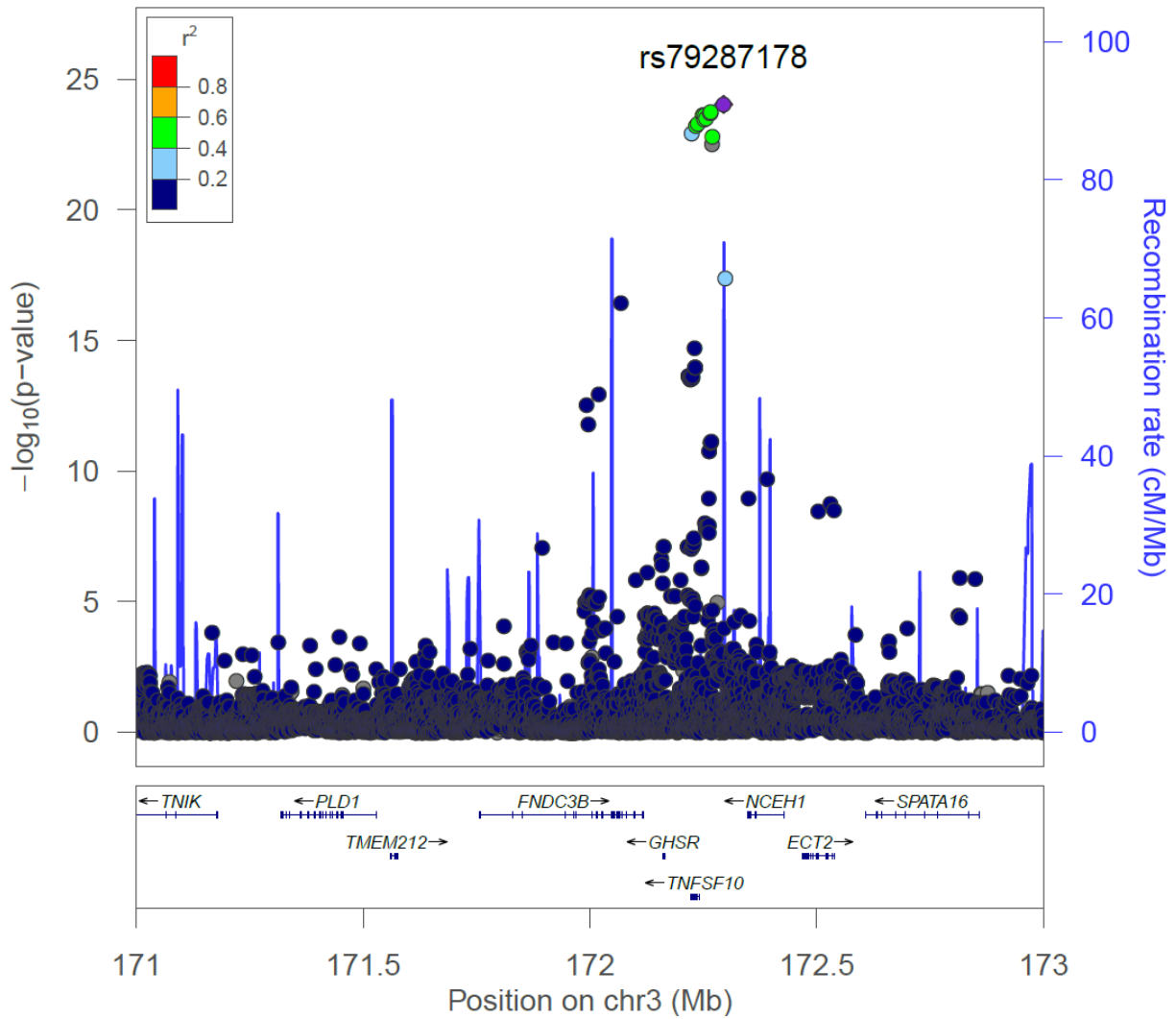


Figure S50 Locus Zoom plot for TNF-related apoptosis inducing ligand (TRAIL) from 3q26.31.

HGF - 4p16.3

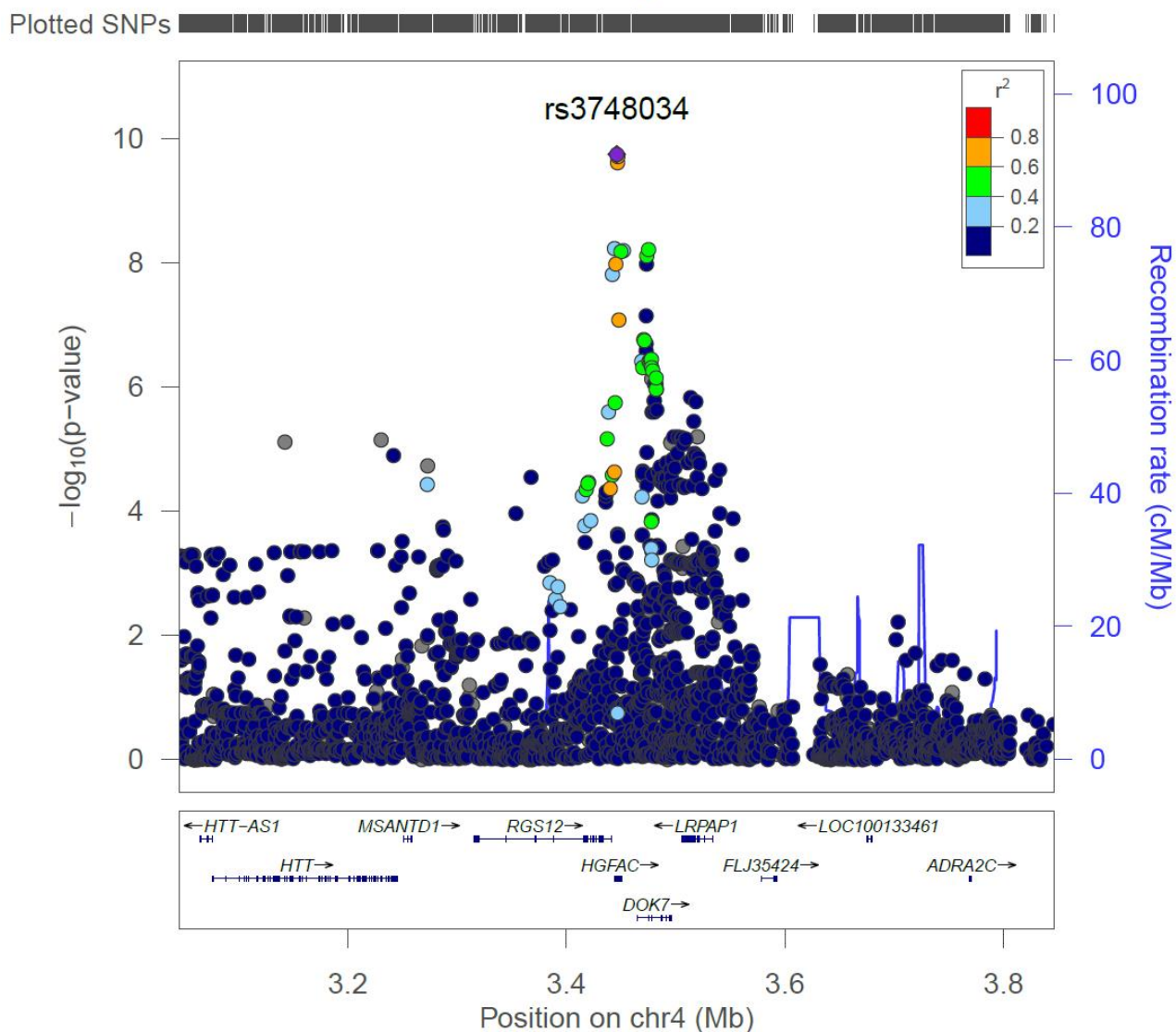


Figure S51 Locus Zoom plot for hepatocyte growth factor (HGF) from 4p16.3.

GROa - 4q13.3

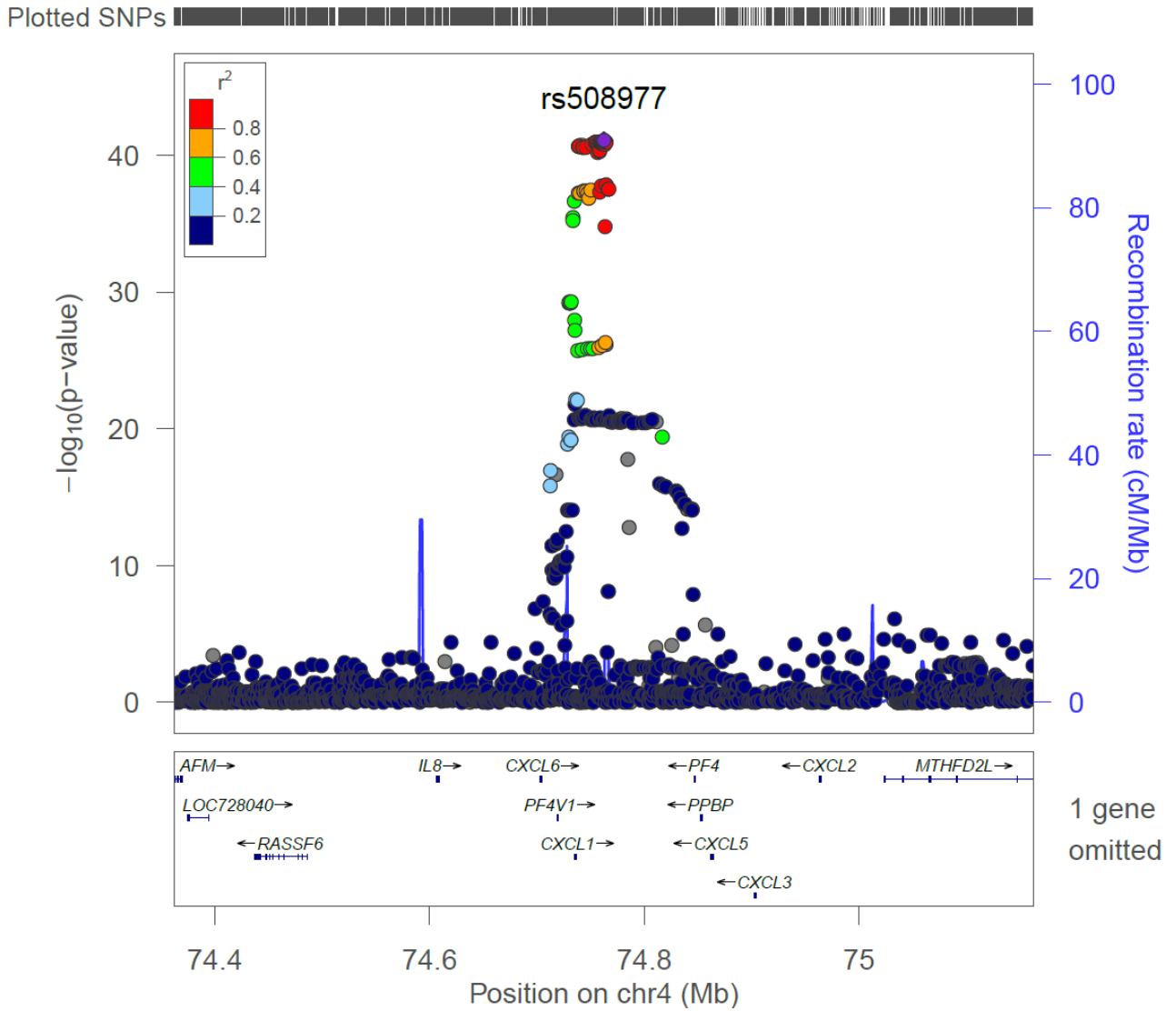


Figure S52 Locus Zoom plot for growth regulated oncogene- α (GROa; CXCL1) from 4q13.3.

IP10 – 4q21.1

Plotted SNPs

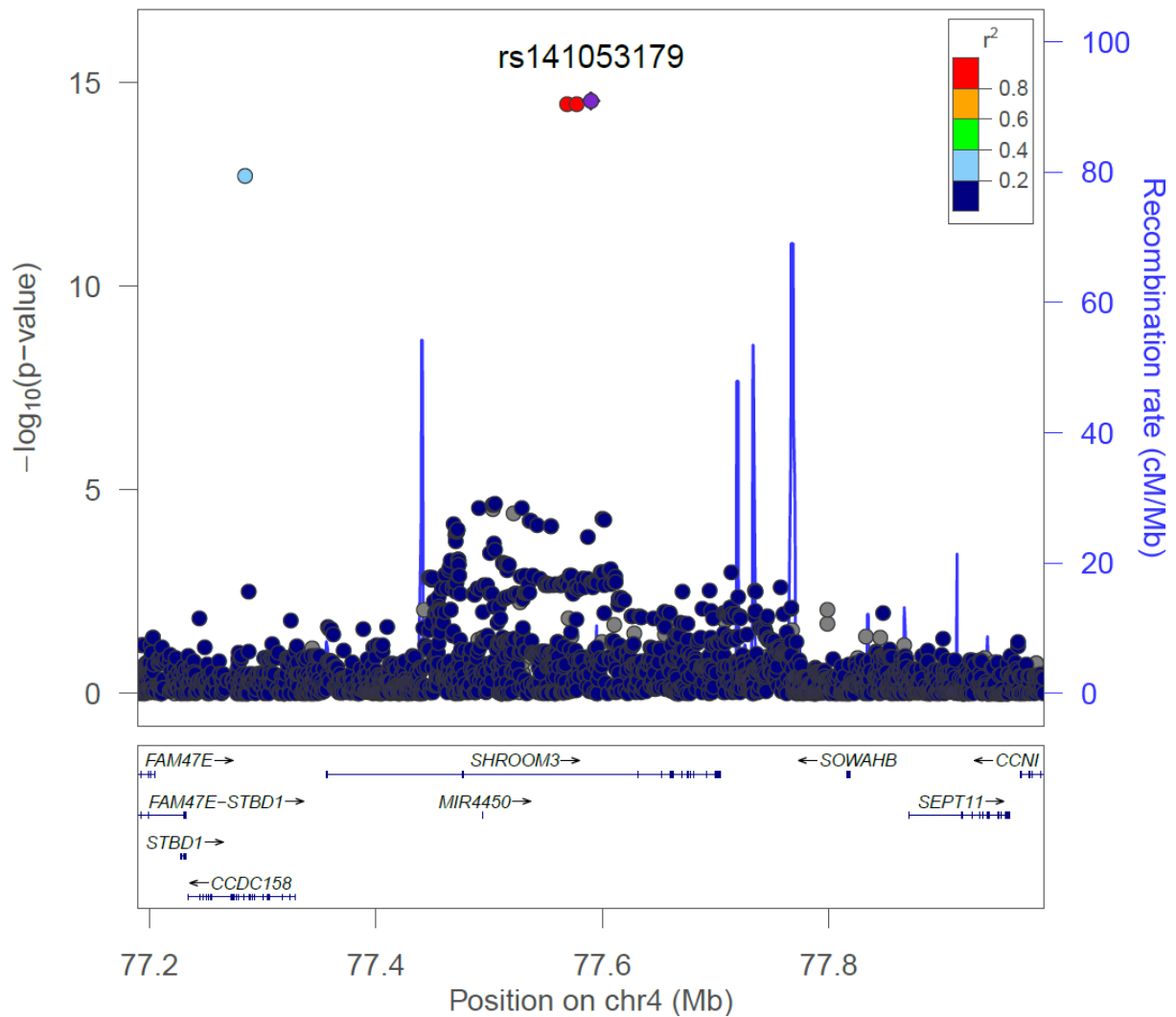


Figure S53 Locus Zoom plot for interferon gamma-induced protein 10 (IP10; CXCL10) from 4q21.1.

IL-18 – 5q13.2

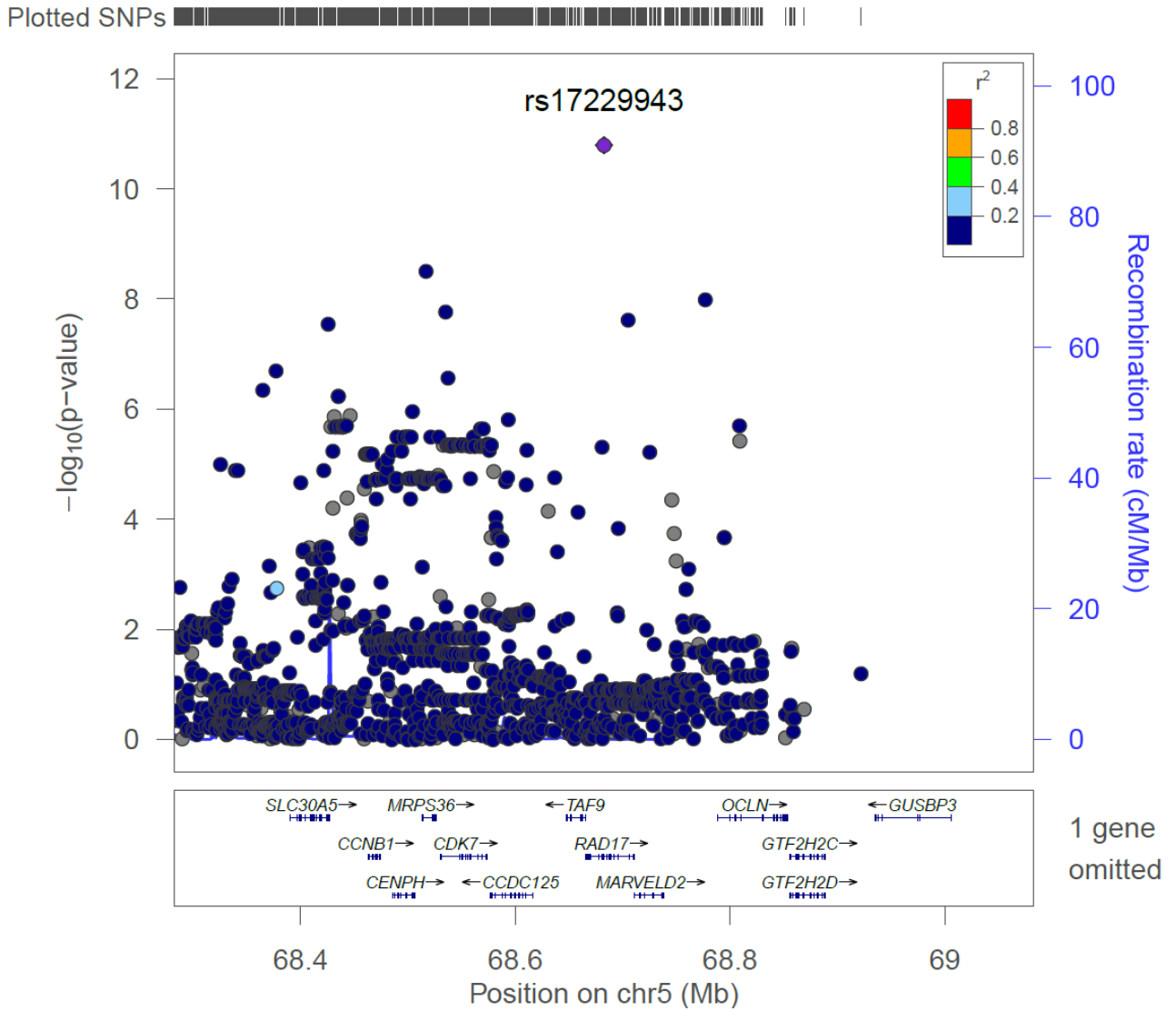


Figure S54 Locus Zoom plot for interleukin-18 (IL-18) from 5q13.2.

VEGF – 6p21.1

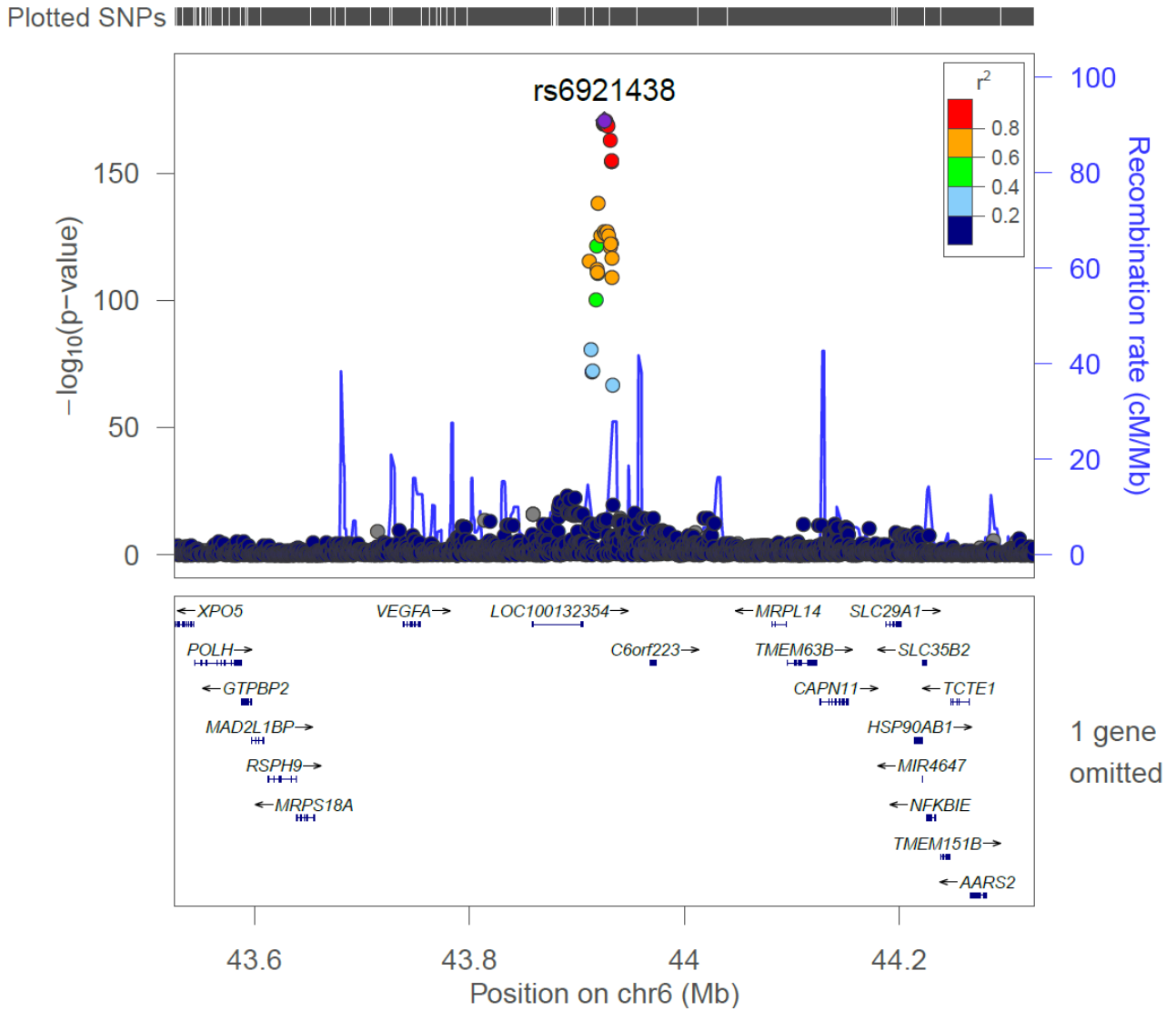


Figure S55 Locus Zoom plot for vascular endothelial growth factor (VEGF) from 6p21.1

HGF - 7q21.11

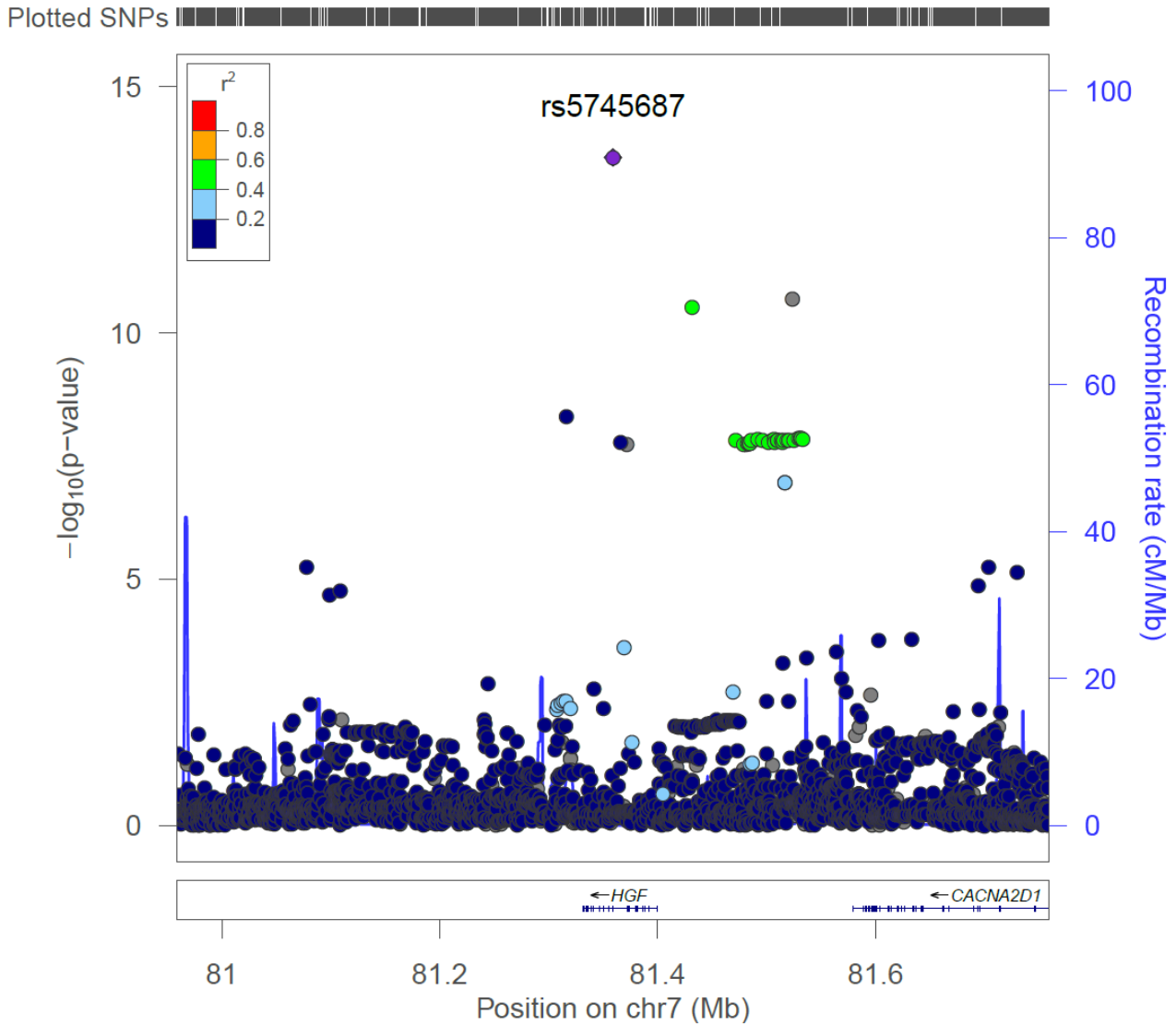


Figure S56 Locus Zoom plot for hepatocyte growth factor (HGF) from 7q21.11.

VEGF - 9p24.2

Plotted SNPs

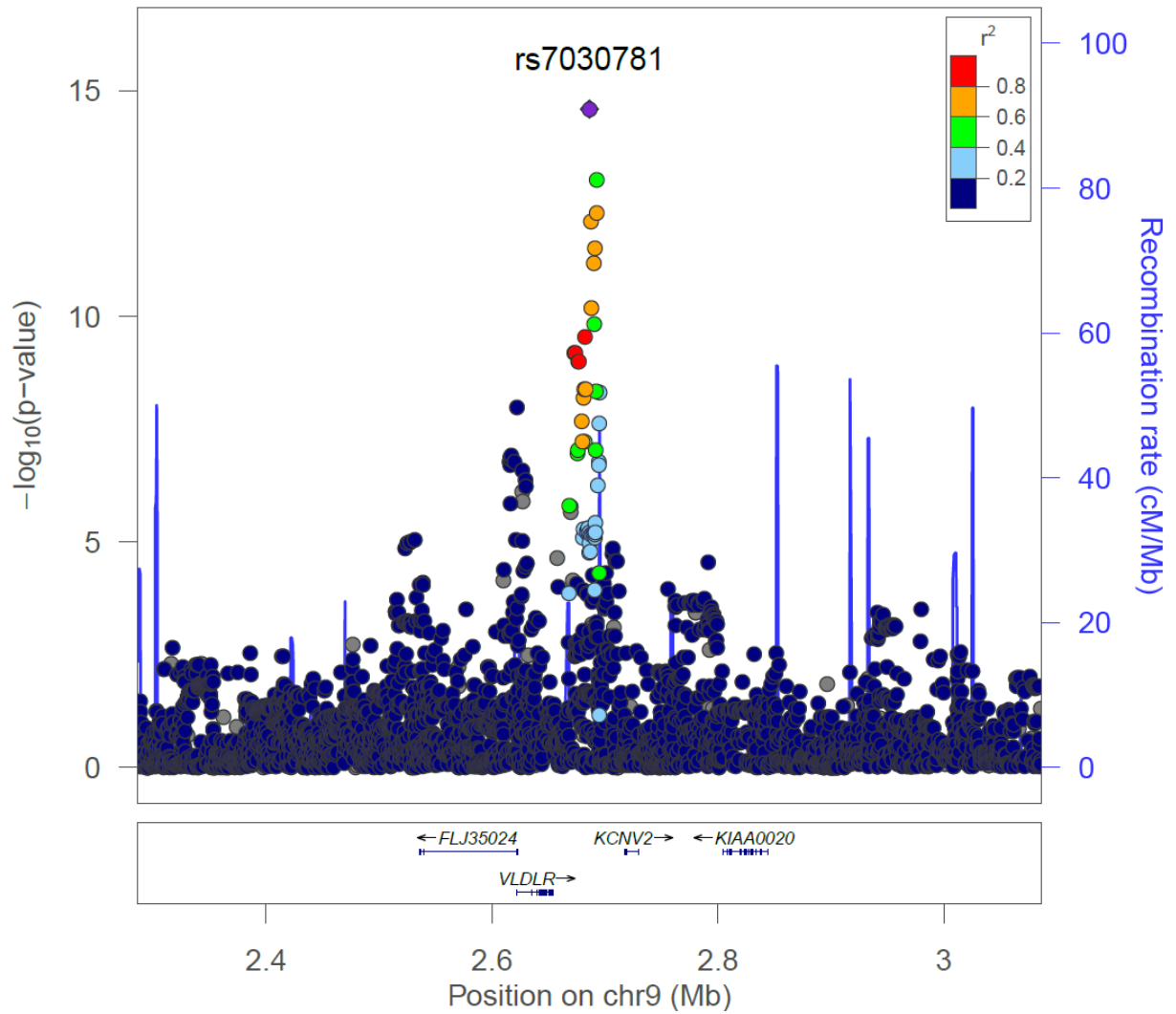


Figure S57 Locus Zoom plot for vascular endothelial growth factor (VEGF) from 9p24.2.

CTACK - 9p13.3

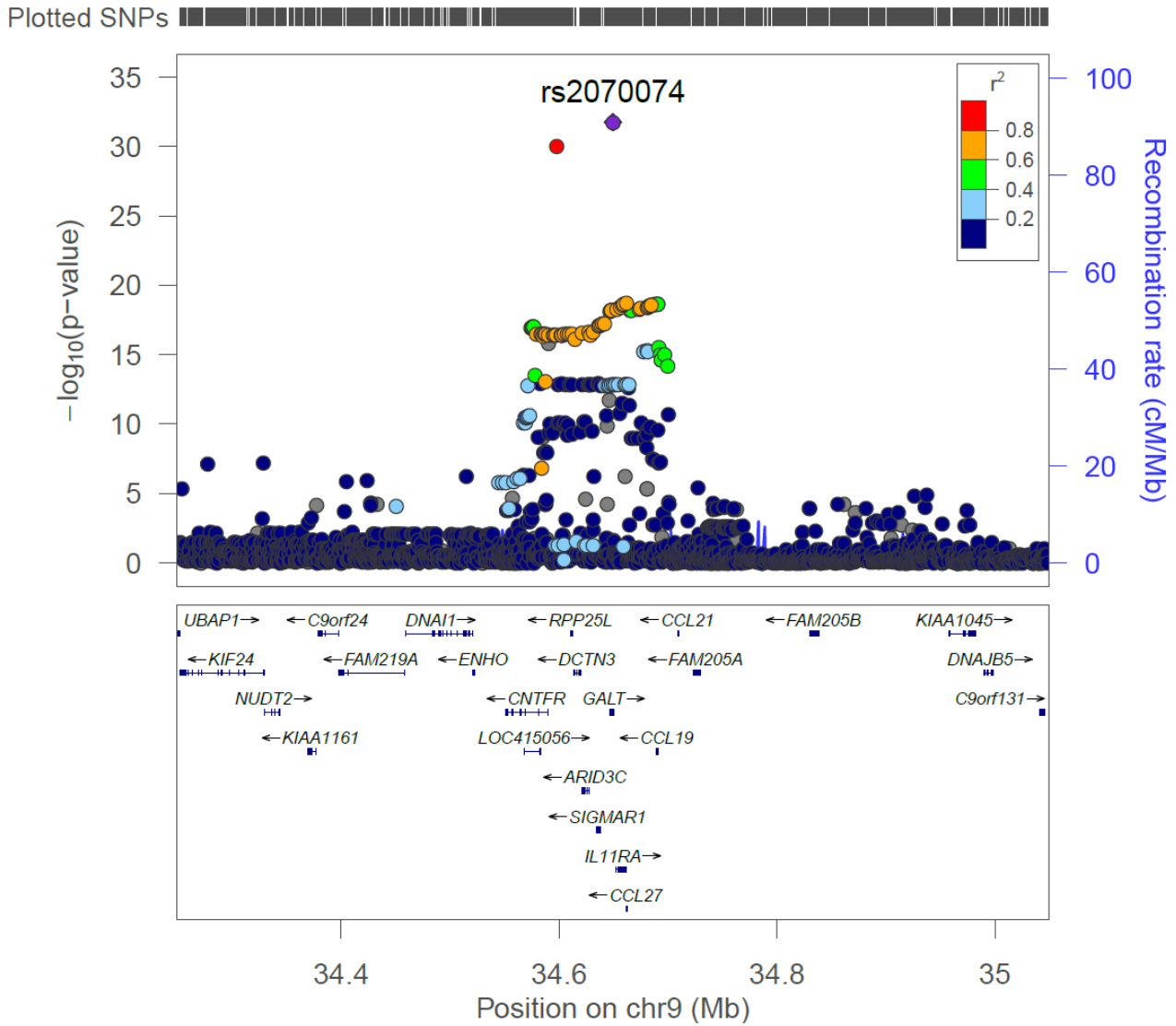


Figure S58 Locus Zoom plot for cutaneous T-cell attracting (CTACK; CCL27).

IL2ra - 10p15.1

Plotted SNPs

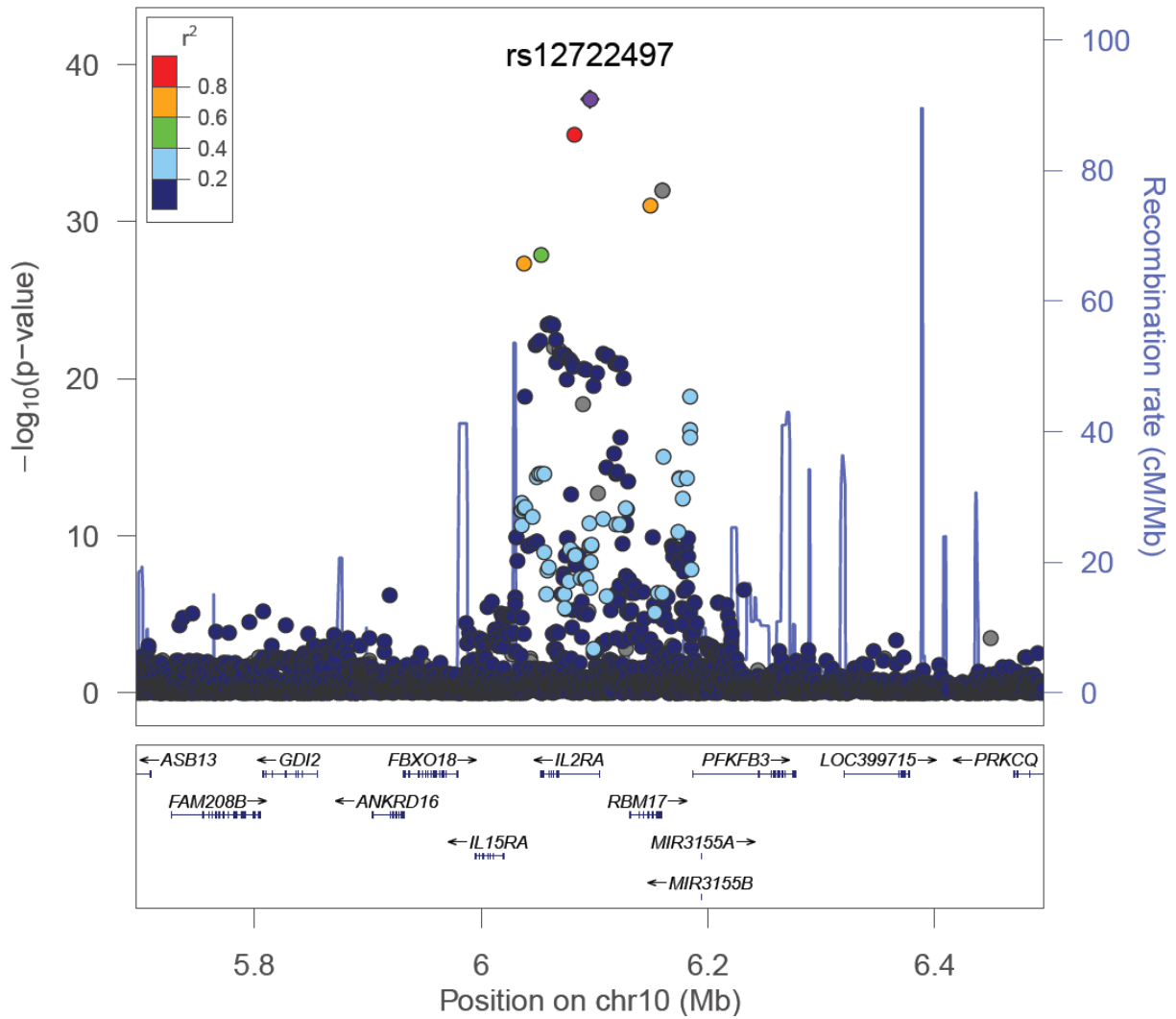


Figure S59 Locus Zoom plot for interleukin-2 receptor subunit alpha (IL2ra) from 10p15.1.

VEGF - 10q21.3

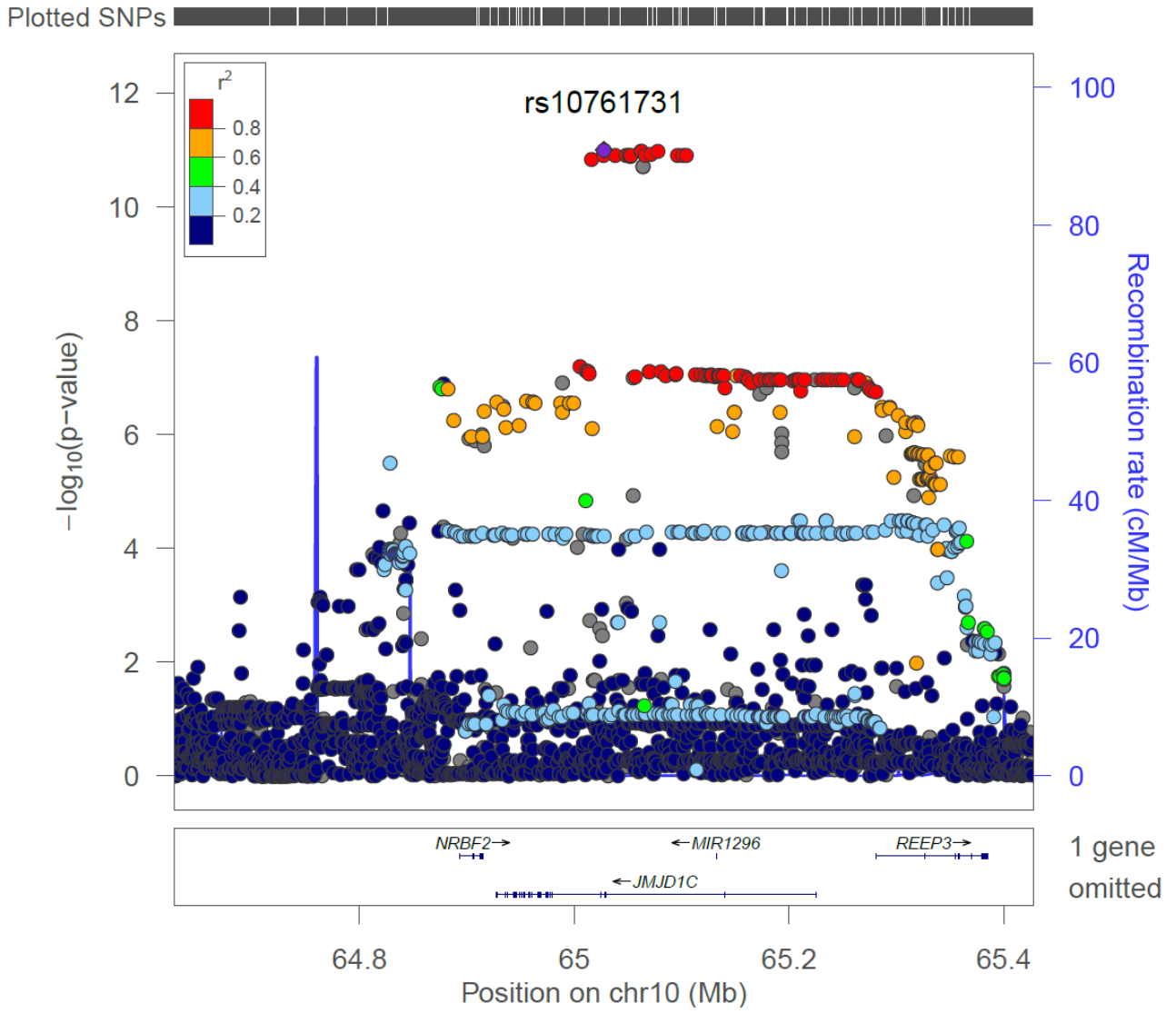


Figure S60 Locus Zoom plot for vascular endothelial growth factor (VEGF) from 10q21.3.

IL-18 – 11q23.1

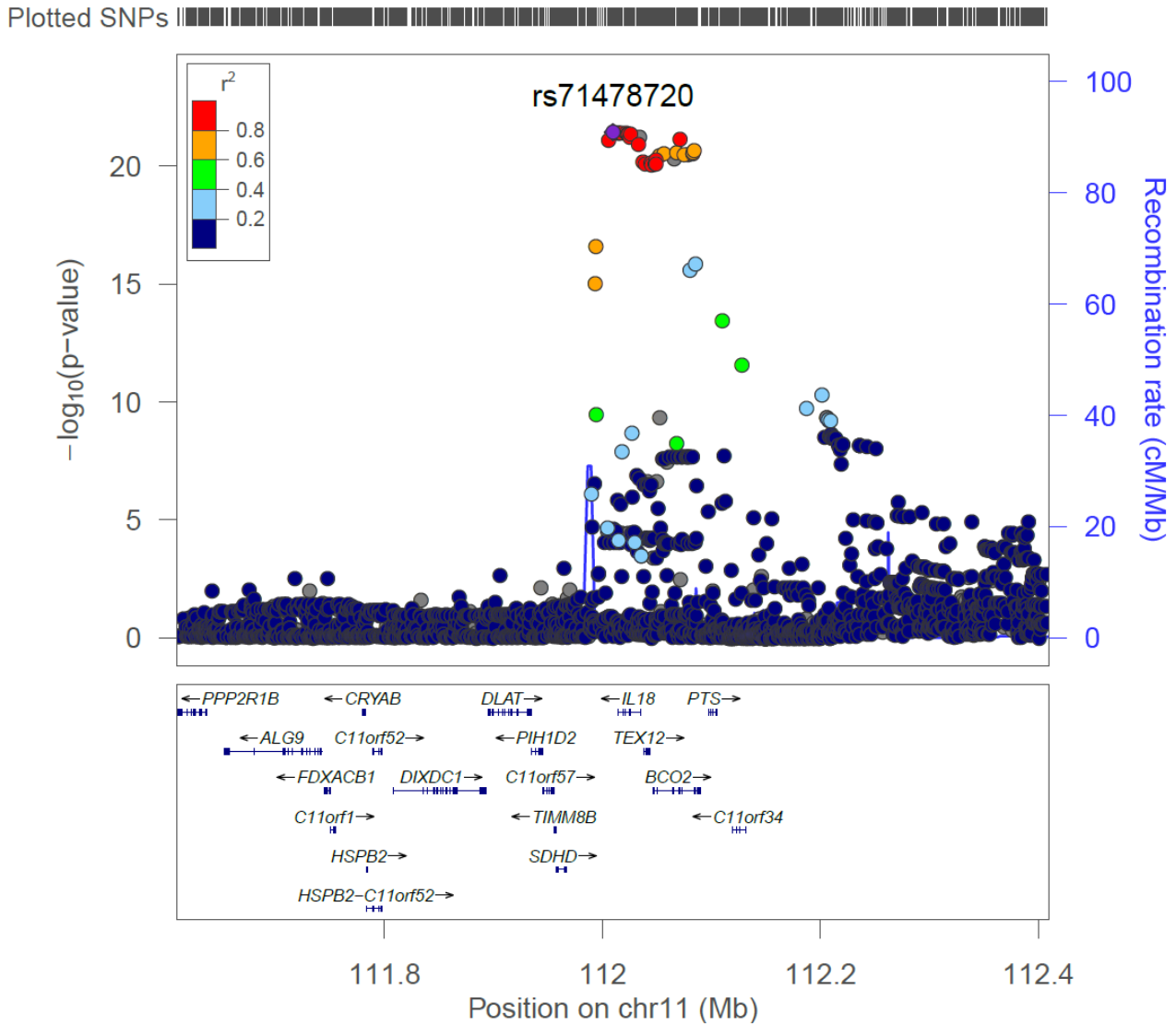


Figure S61 Locus Zoom plot for interleukin-18 (IL-18) from 11q23.1.

SCGFb – 12q23.3

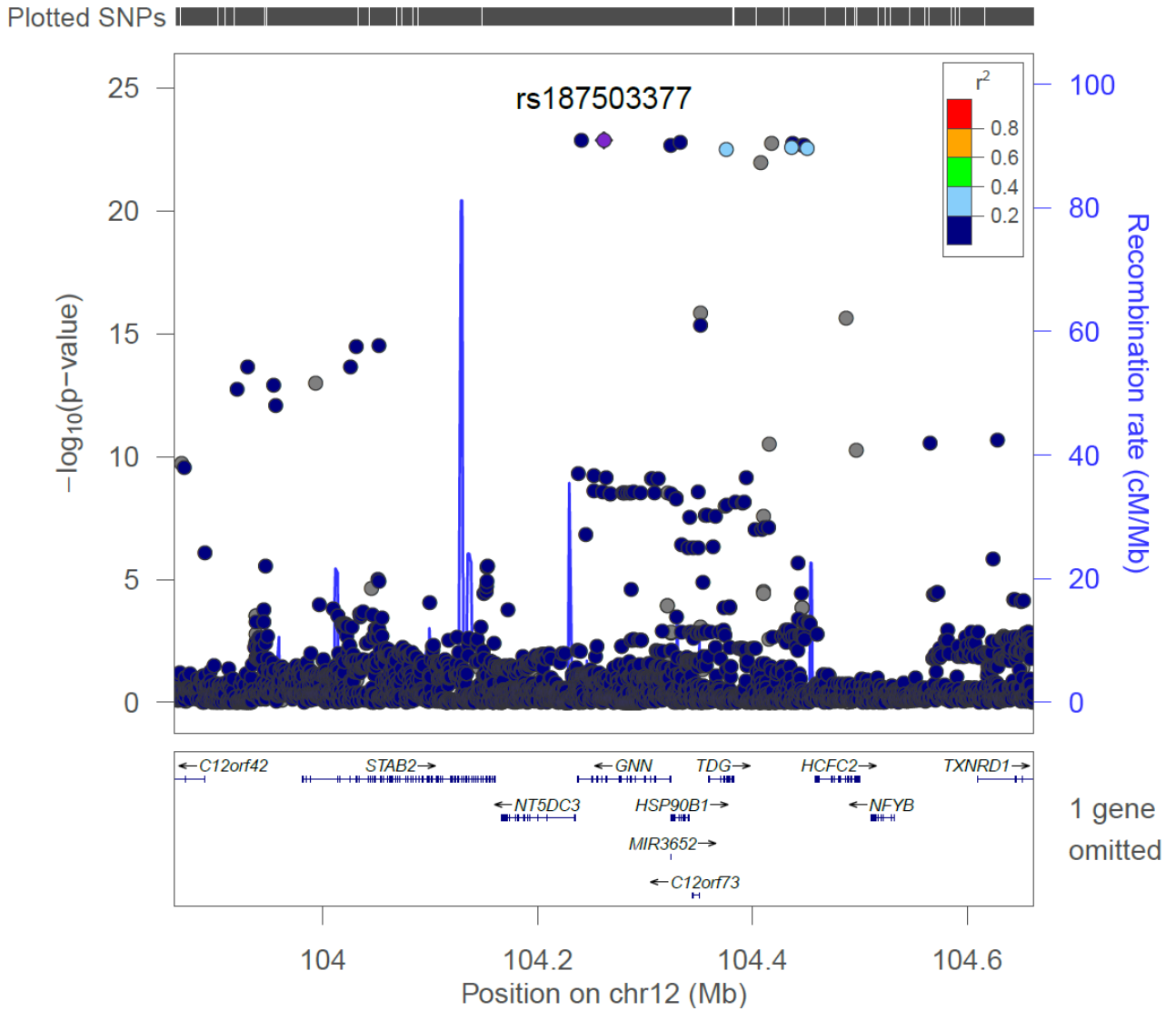


Figure S62 Locus Zoom plot for stem cell growth factor beta (SCGFb) from 12q23.3.

IL-16 – 15q25.1

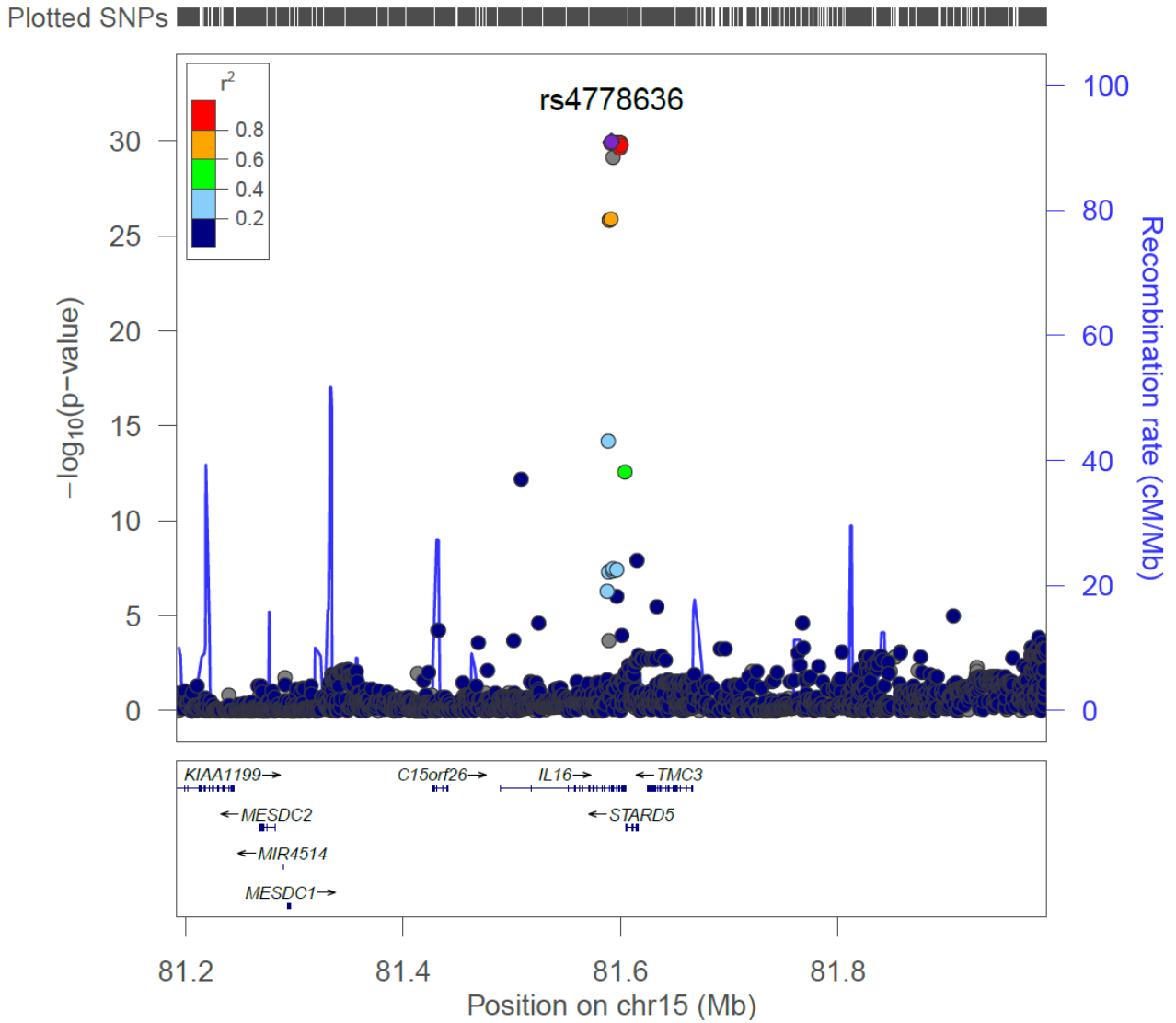


Figure S63 Locus zoom plot for interleukin-16 (IL-16) from 15q25.1.

PDGFbb – 15q26.3

Plotted SNPs

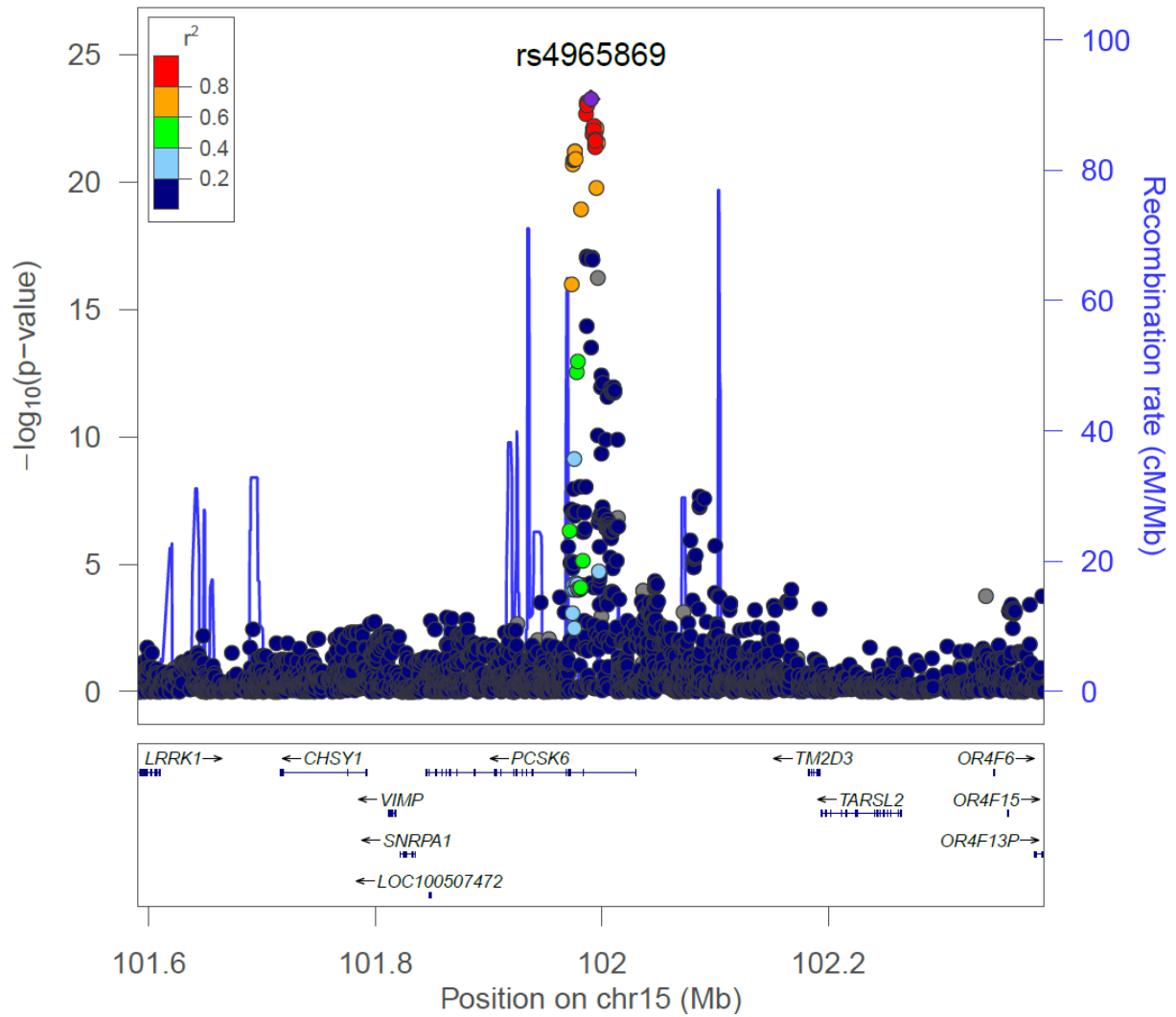


Figure S64 Locus Zoom plot for platelet derived growth factor BB (PDGFbb) from 15q26.3.

MIP1b - 17q12

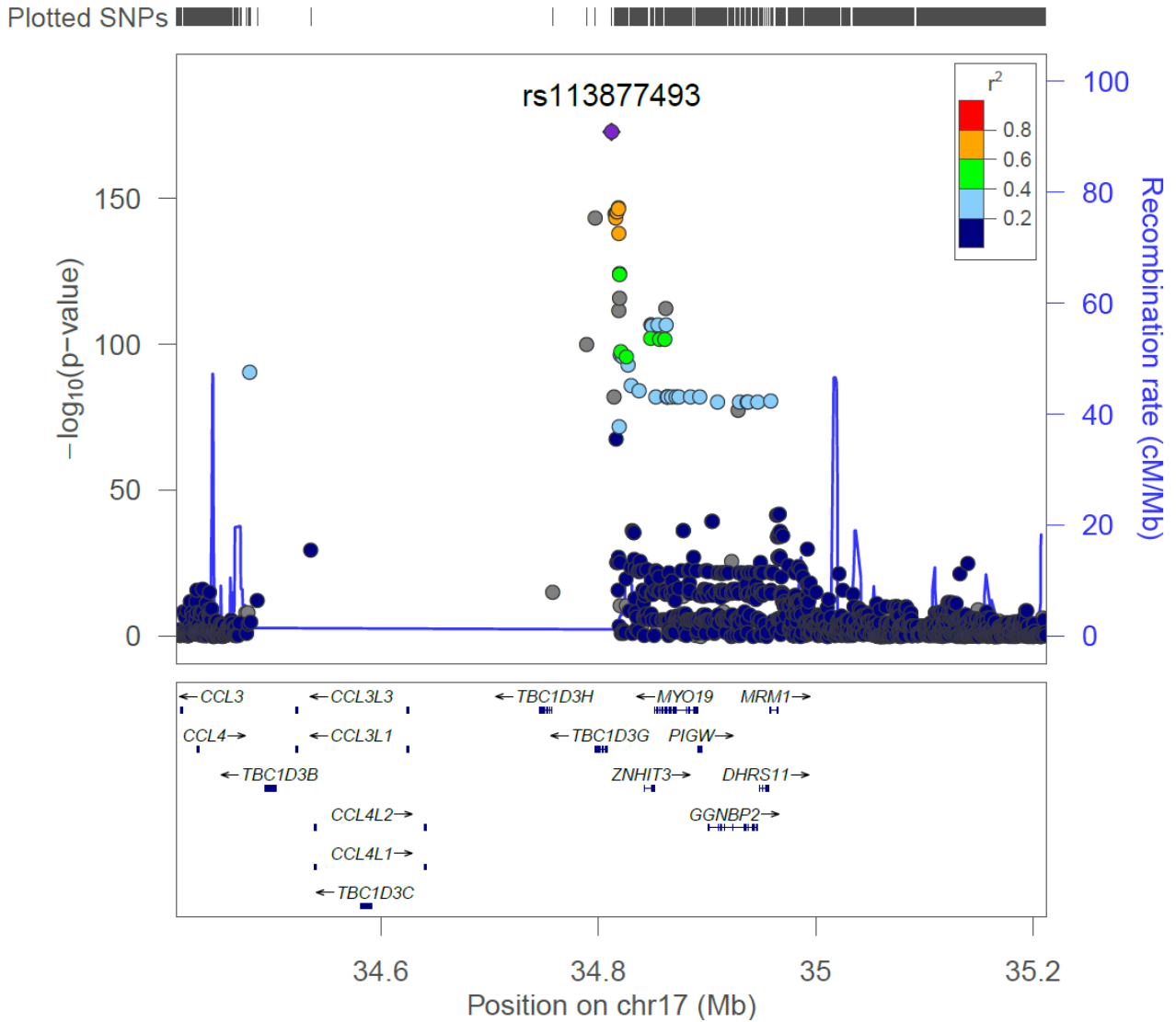


Figure S65 Locus Zoom plot from macrophage inflammatory protein-1 β (MIP1b; CCL4) from 17q12.

TRAIL - 18q12.1

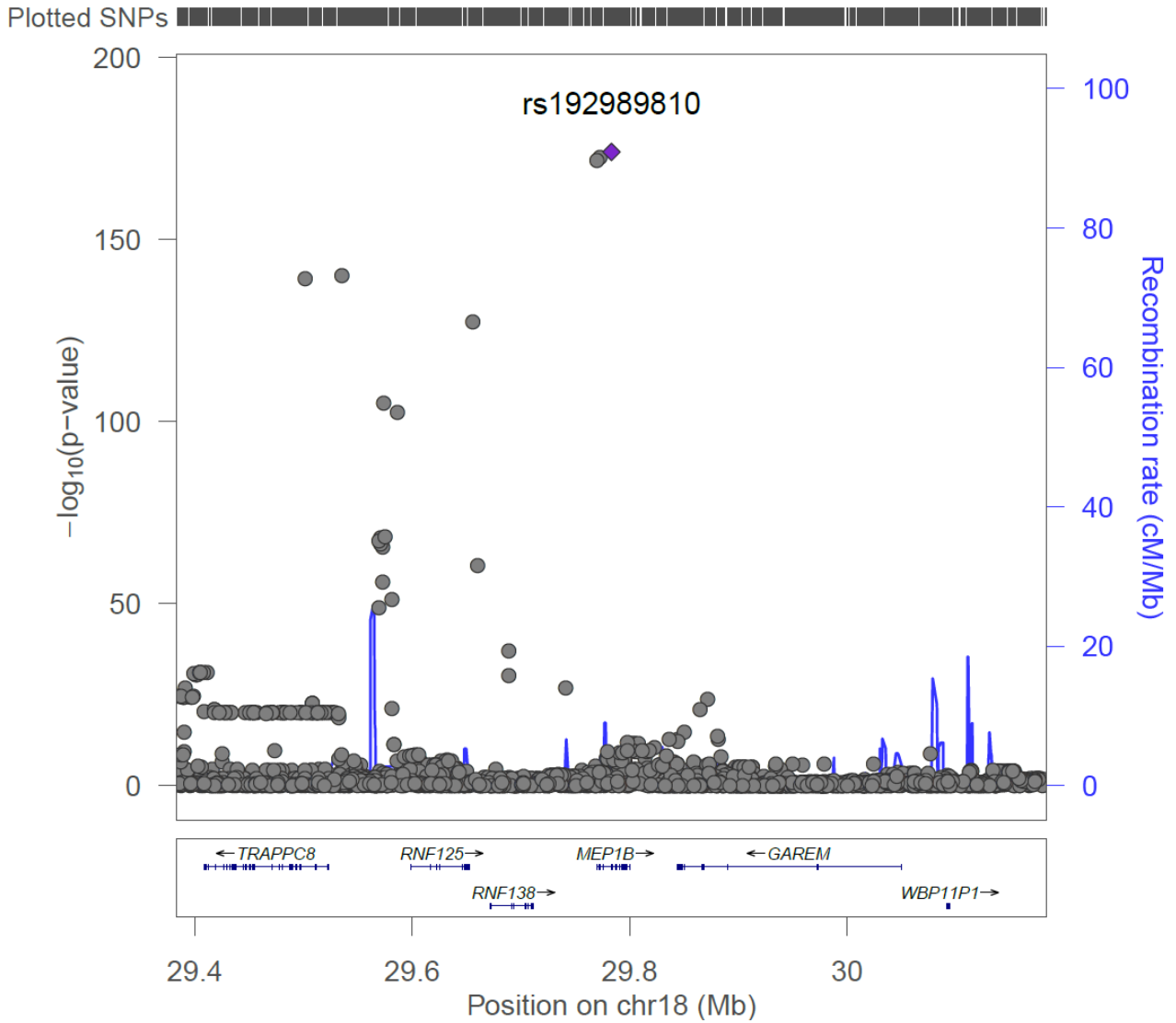


Figure S66 Locus Zoom plot for TNF-related apoptosis inducing ligand (TRAIL) from 18q12.1.

SCGFb – 19q13.33

Plotted SNPs

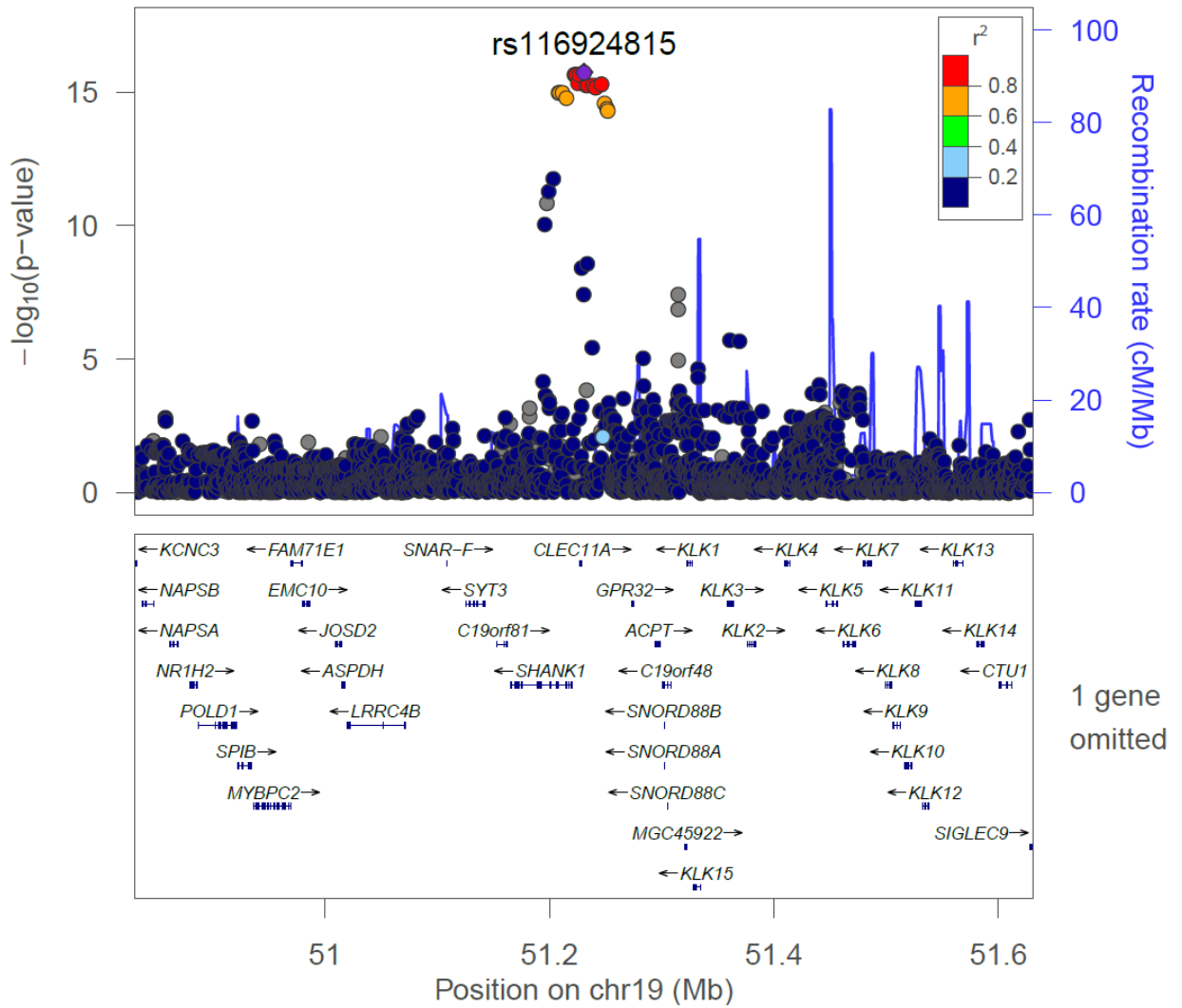


Figure S67 Locus Zoom plot for stem cell growth factor beta (SCGFb) from 19q13.33.

MIF – 22q11.23

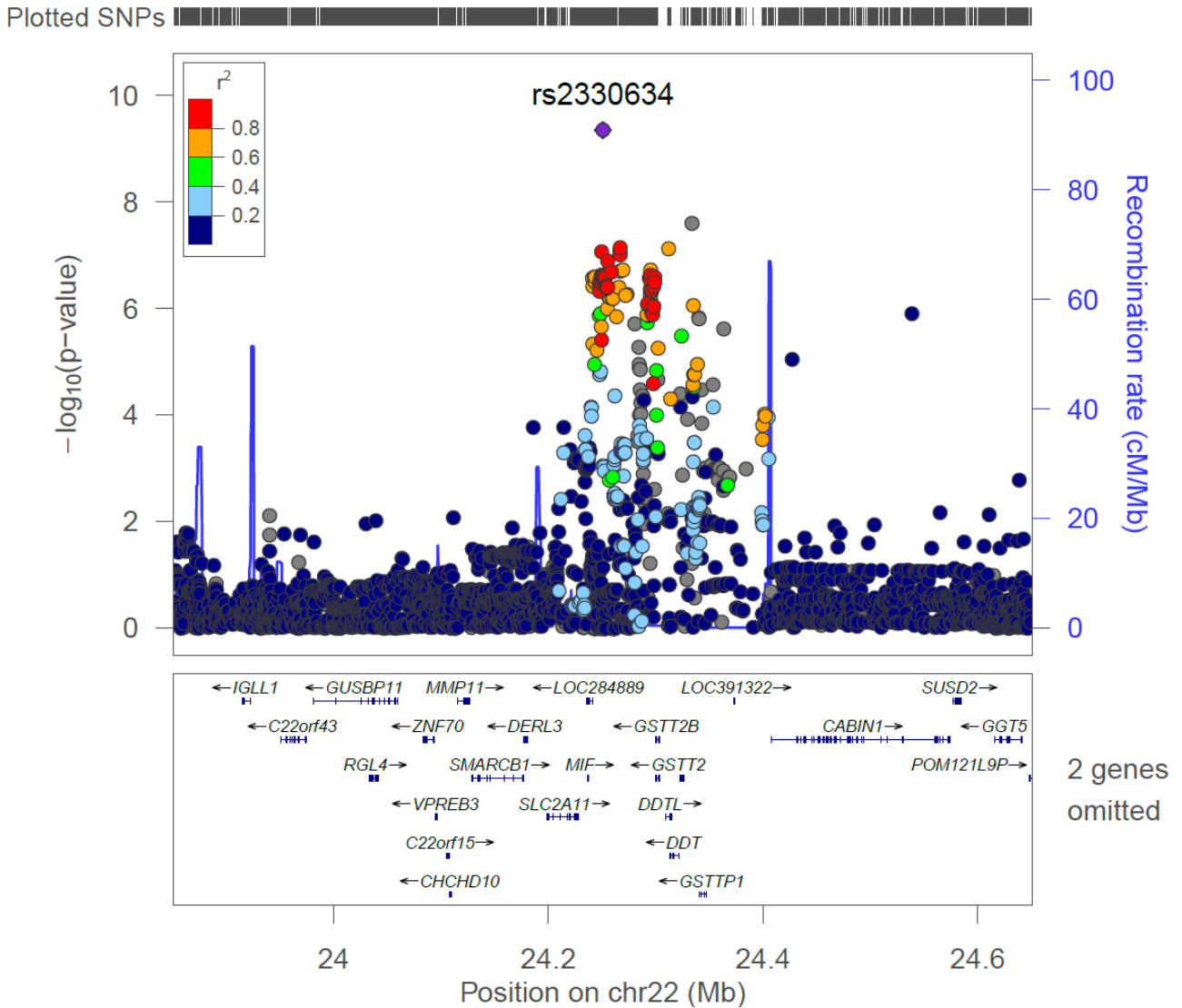


Figure S68 Locus Zoom plot for macrophage migration inhibitory factor (glycosylation-inhibiting factor; MIF) from 22q11.23.

CTACK – 22q13.31

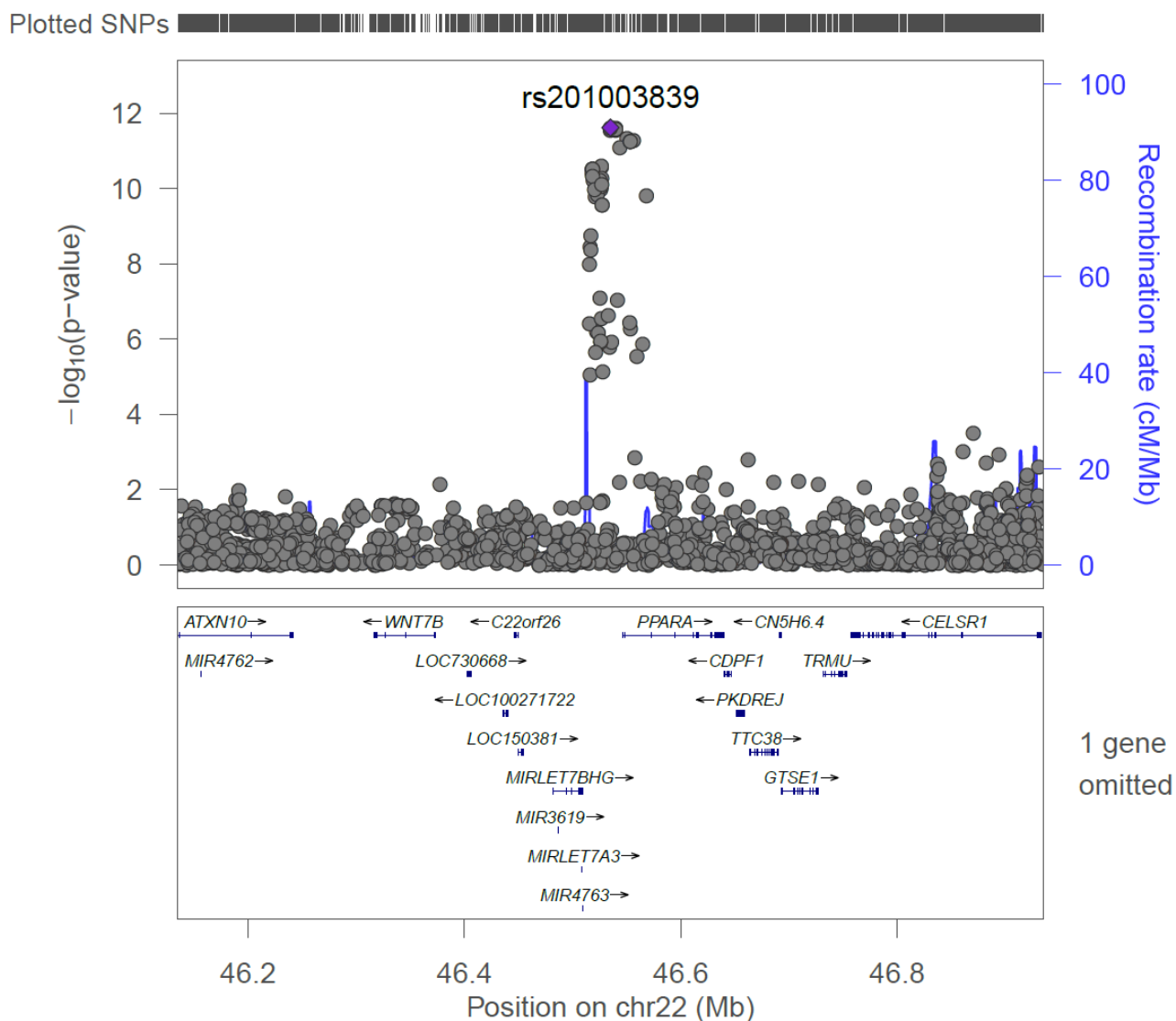


Figure S69 Locus Zoom plot for Cutaneous T-cell attracting (CTACK; CCL27) from 22q13.31.

QQ-plot for bNGF

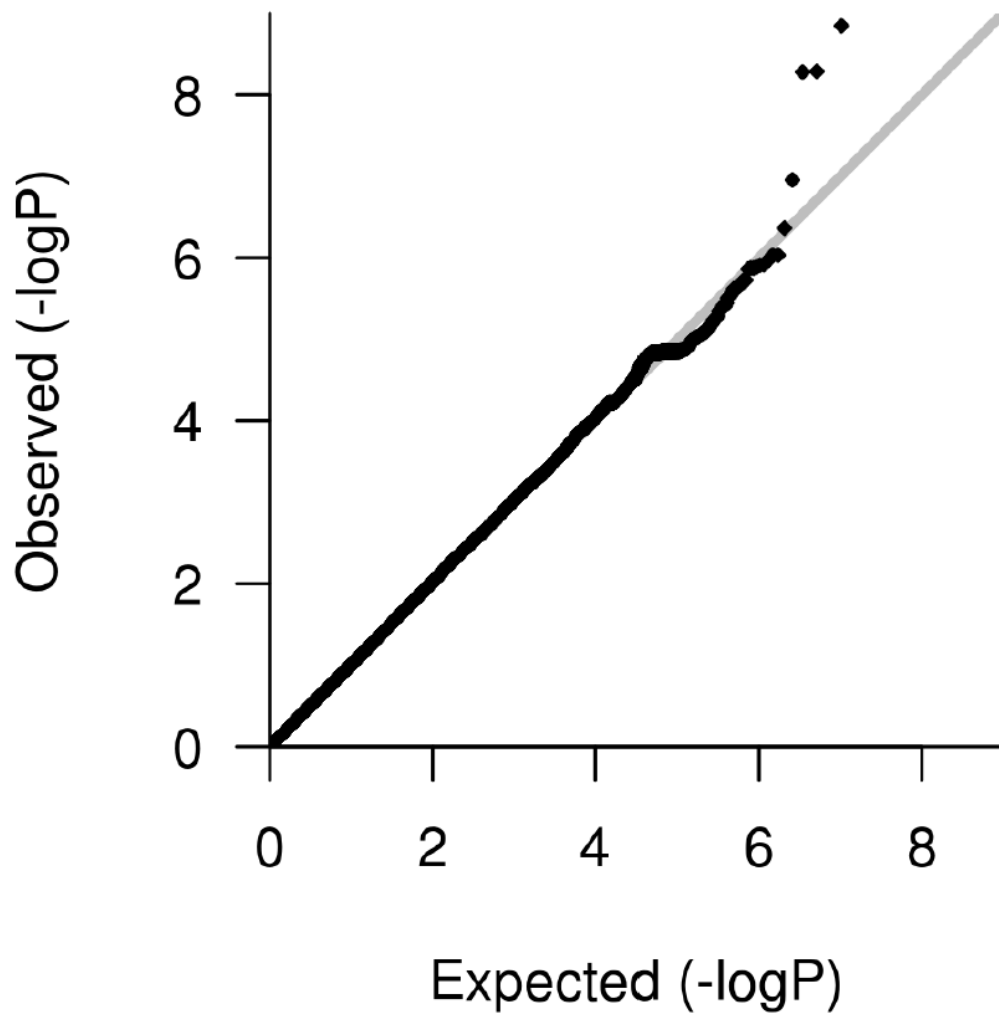


Figure S70 QQ-plot for beta nerve growth factor (bNGF).

QQ-plot for CTACK

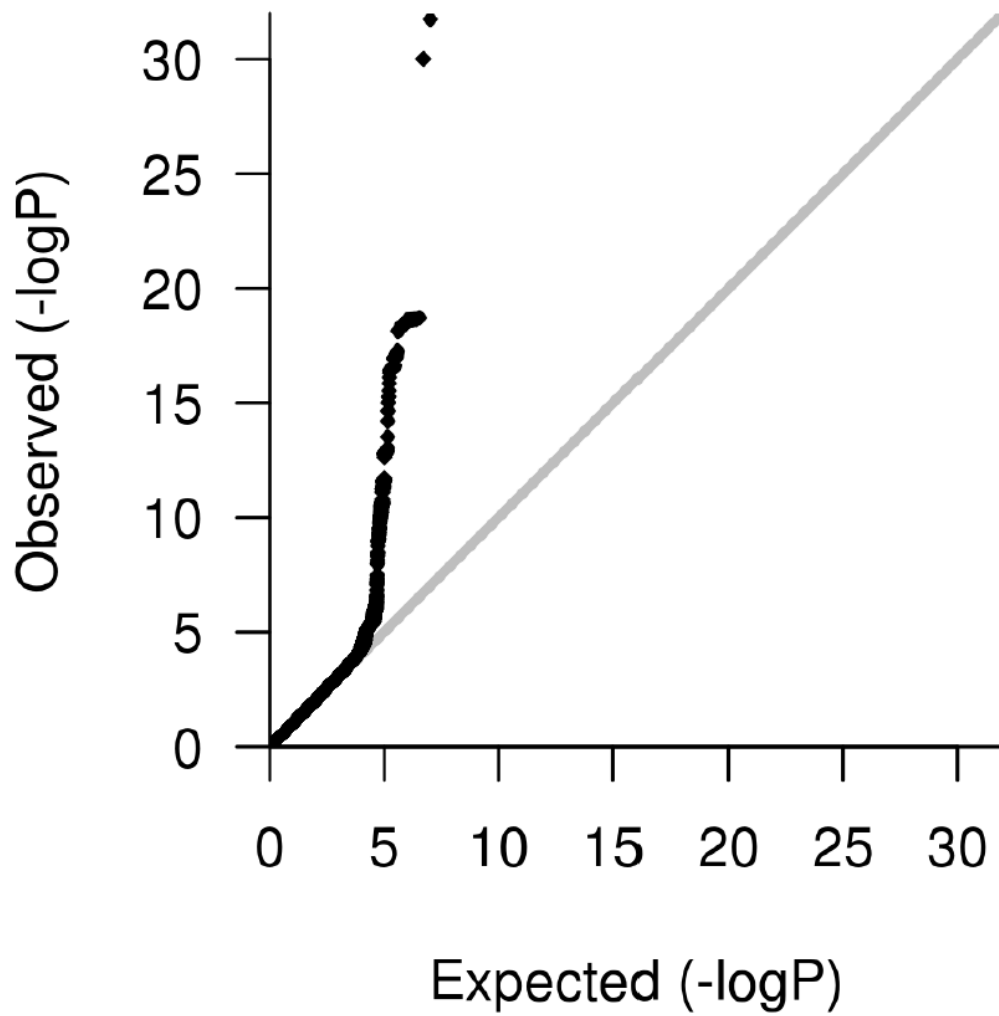


Figure S71 QQ-plot for cutaneous T-cell attracting (CTACK; CCL27).

QQ-plot for Eotaxin

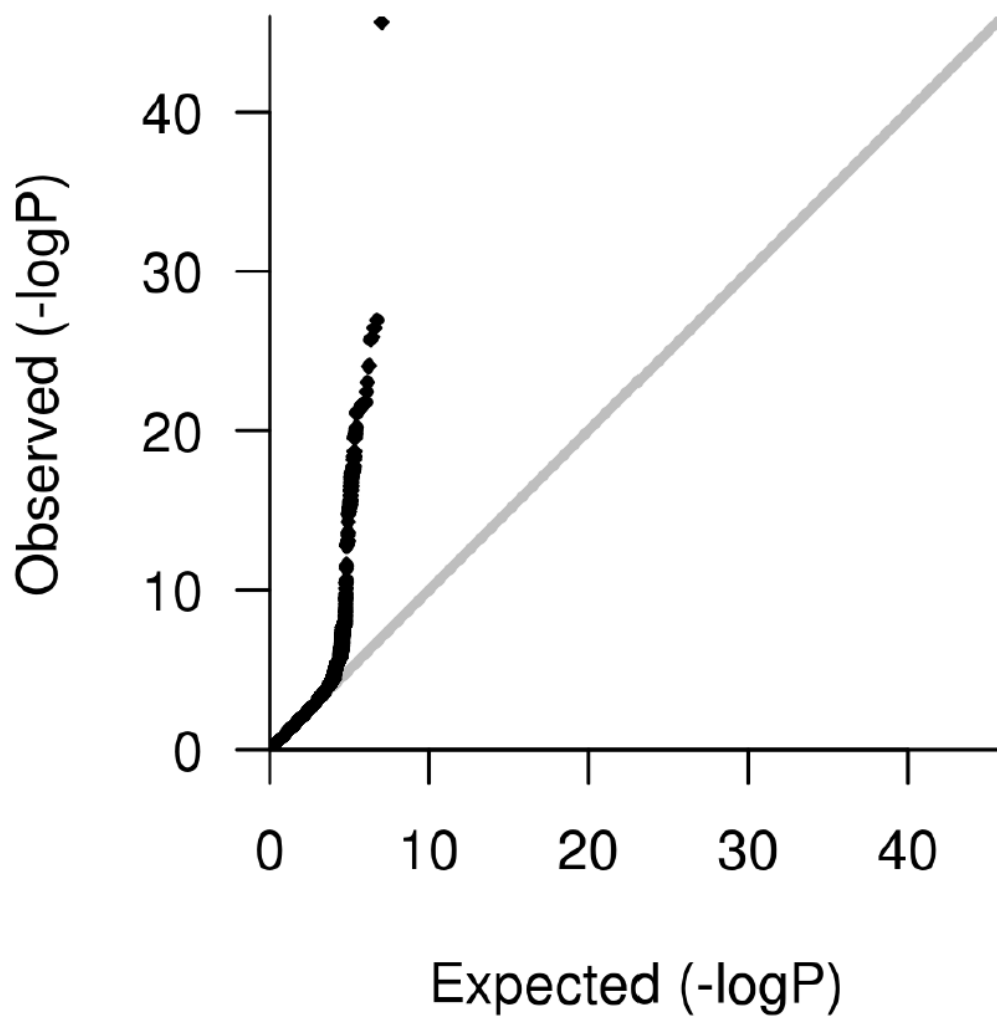


Figure S72 QQ-plot for eotaxin.

QQ-plot for FGFbasic

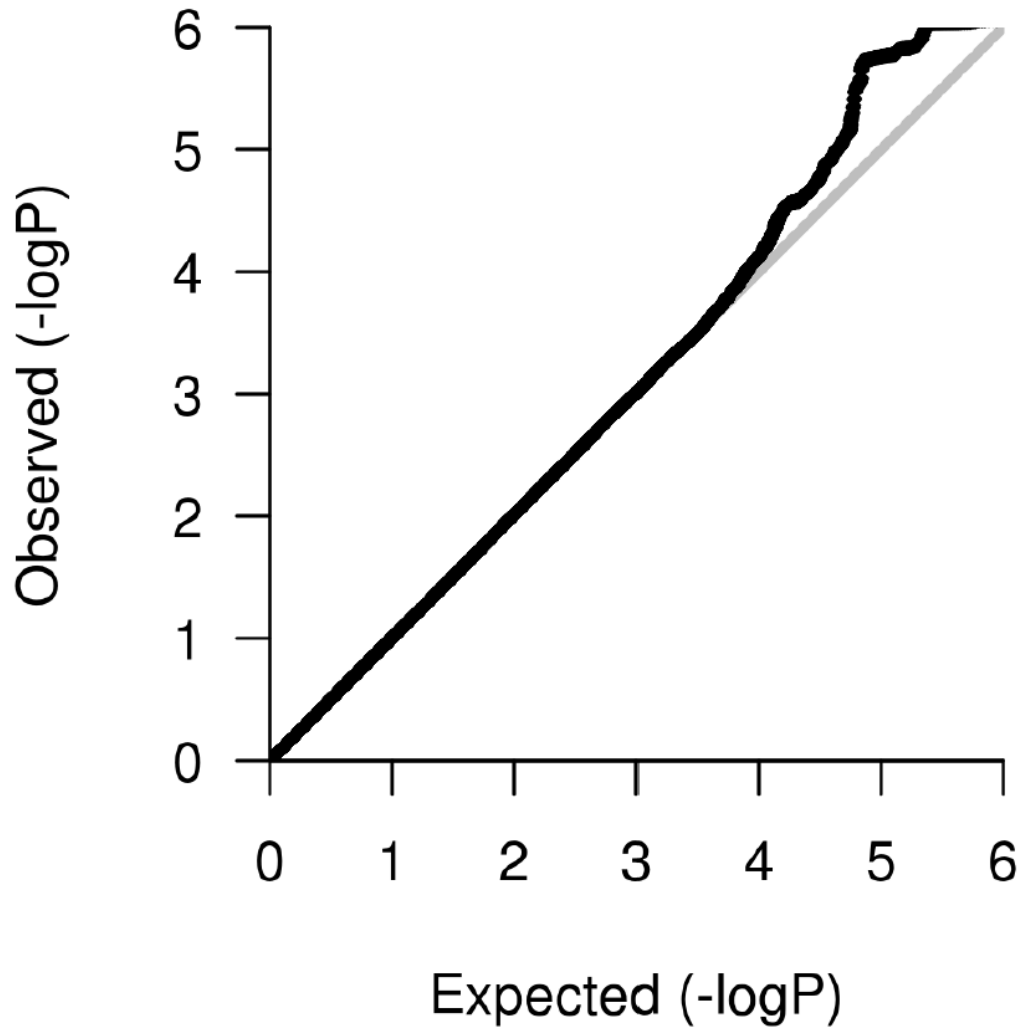


Figure S73 QQ-plot for basic fibroblast growth factor (FGFbasic).

QQ-plot for GCSF

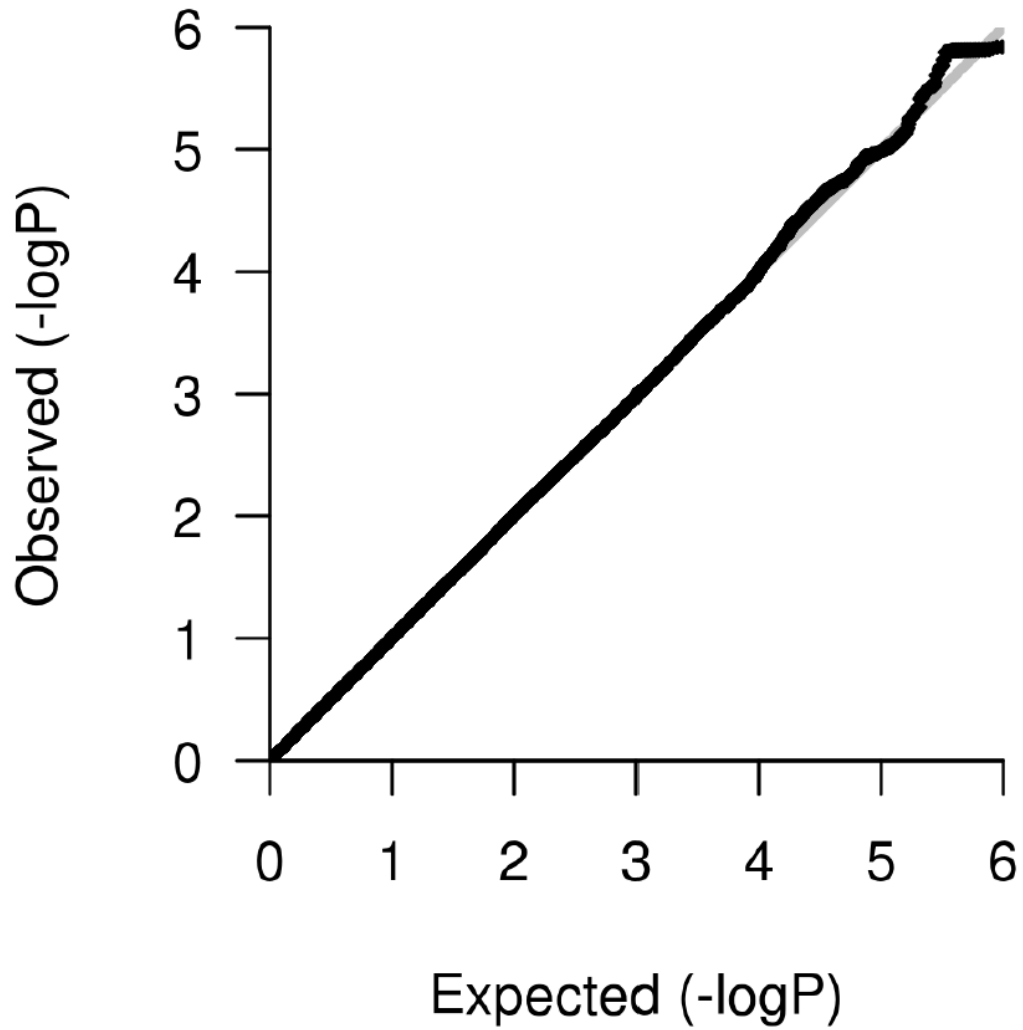


Figure S74 QQ-plot for granulocyte colony-stimulating factor (GCSF).

QQ-plot for GROa

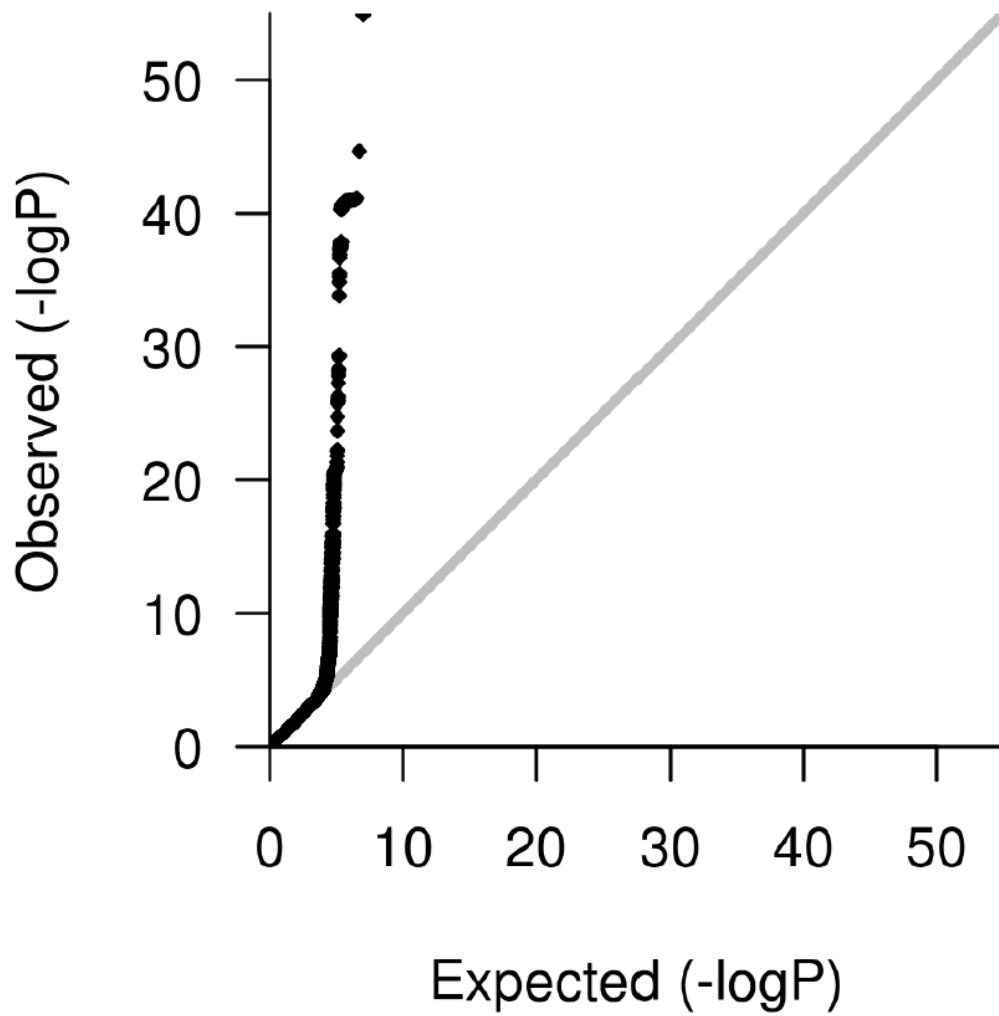


Figure S75 QQ-plot for growth regulated oncogene- α (GROa; CXCL1).

QQ-plot for HGF

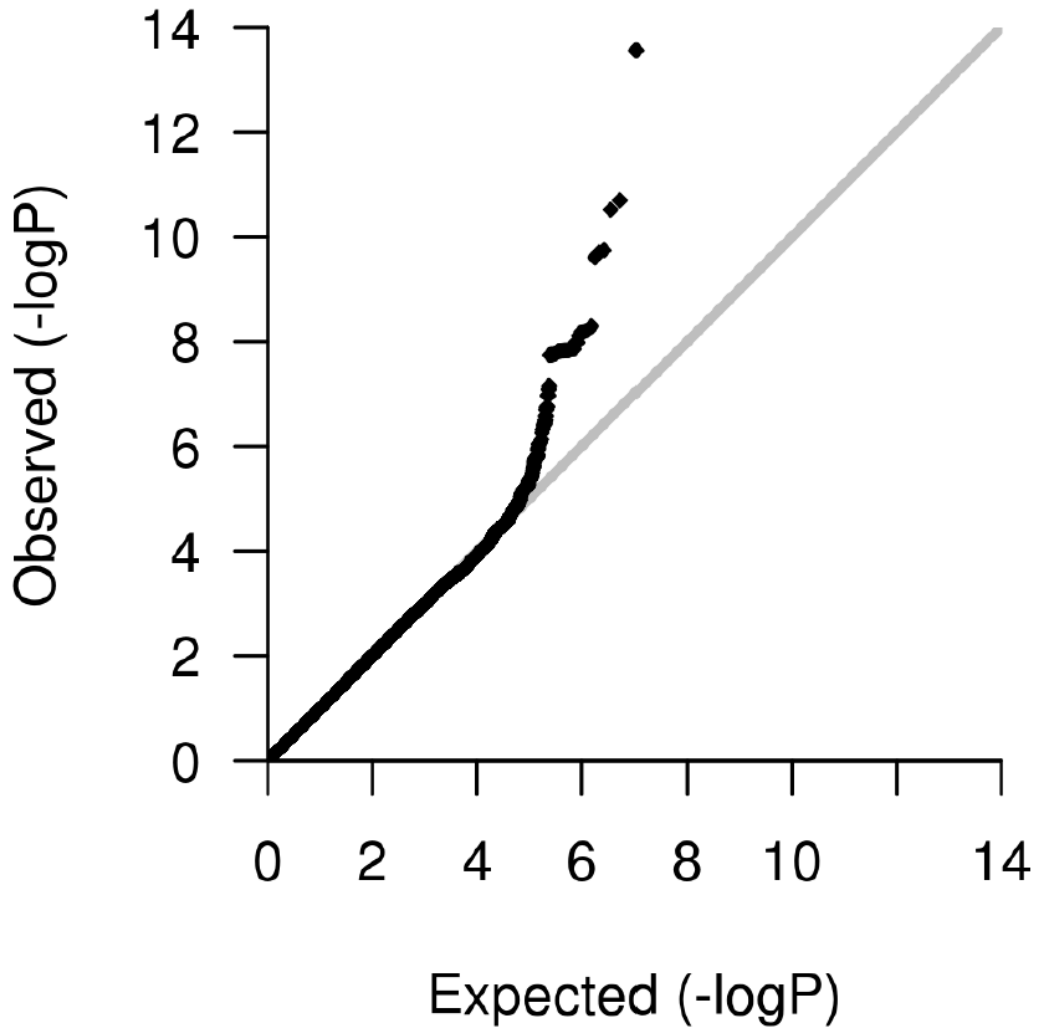


Figure S76 QQ-plot for hepatocyte growth factor (HGF).

QQ-plot for IFNg

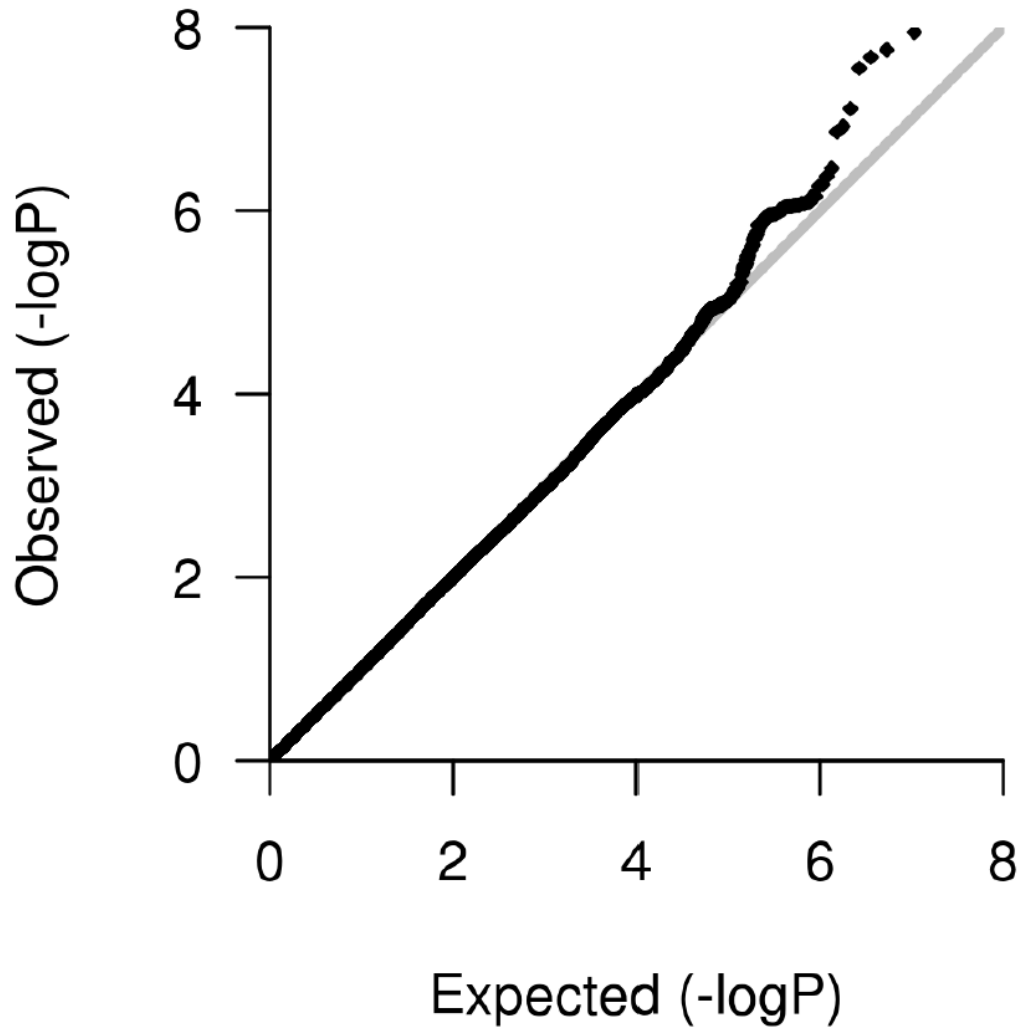


Figure S77 QQ-plot for interferon gamma (IFNg).

QQ-plot for IL-1b

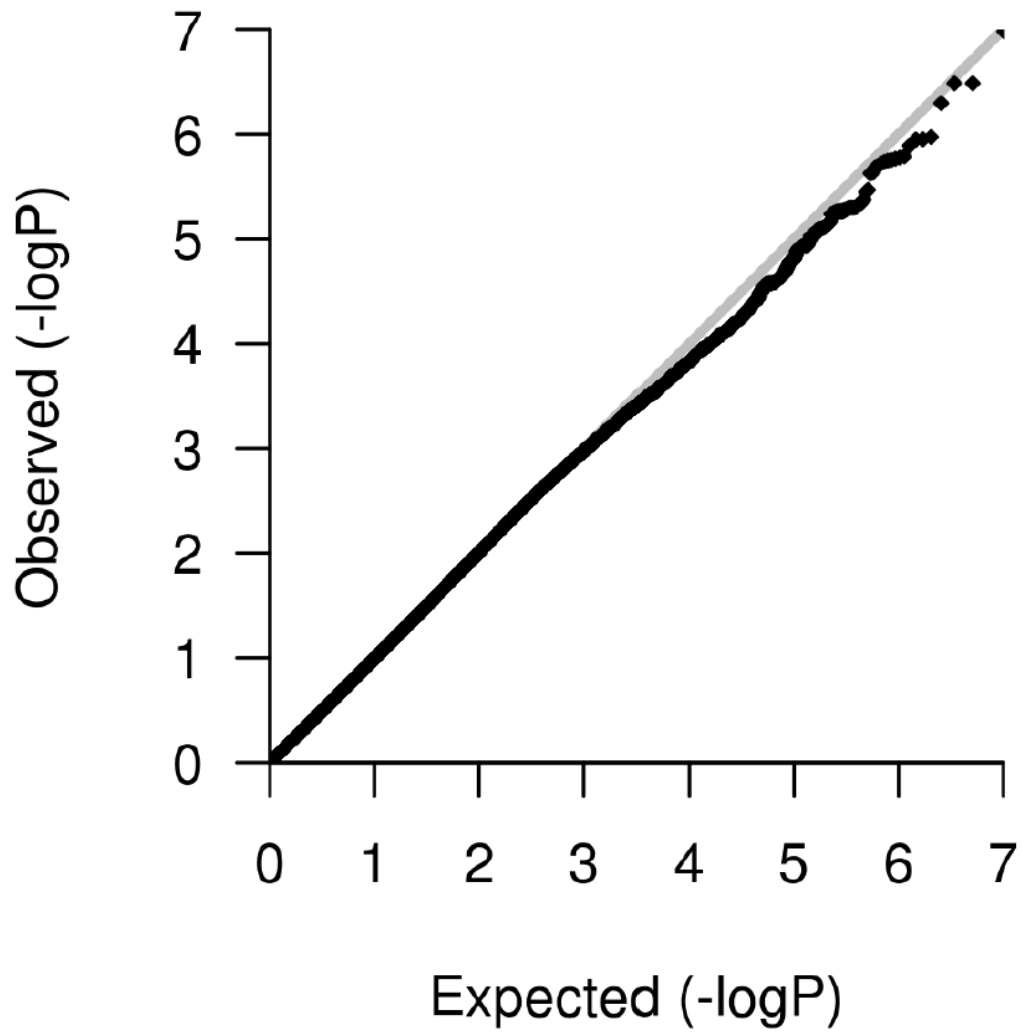


Figure S78 QQ-plot for interleukin-1-beta (IL-1b).

QQ-plot for IL1ra

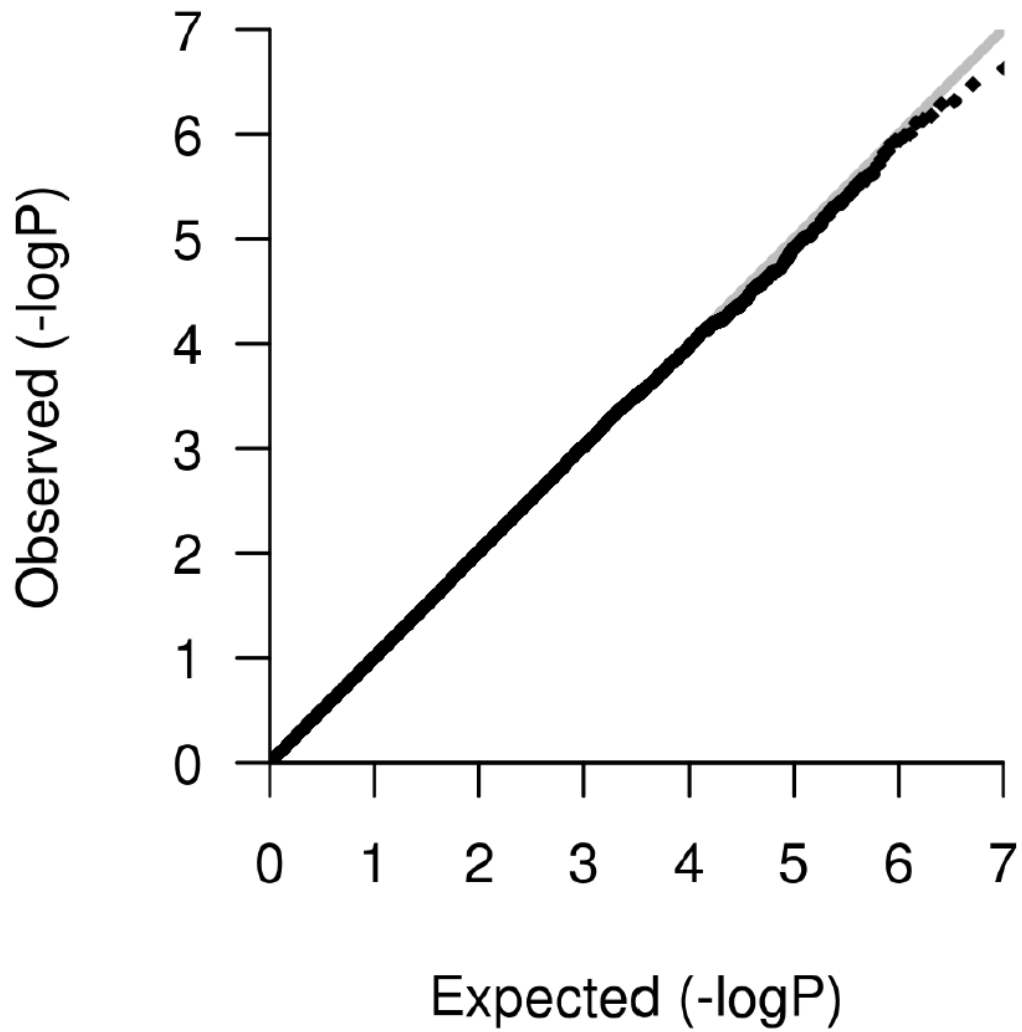


Figure S79 QQ-plot for interleukin-1 receptor antagonist (IL1ra).

QQ-plot for IL-2

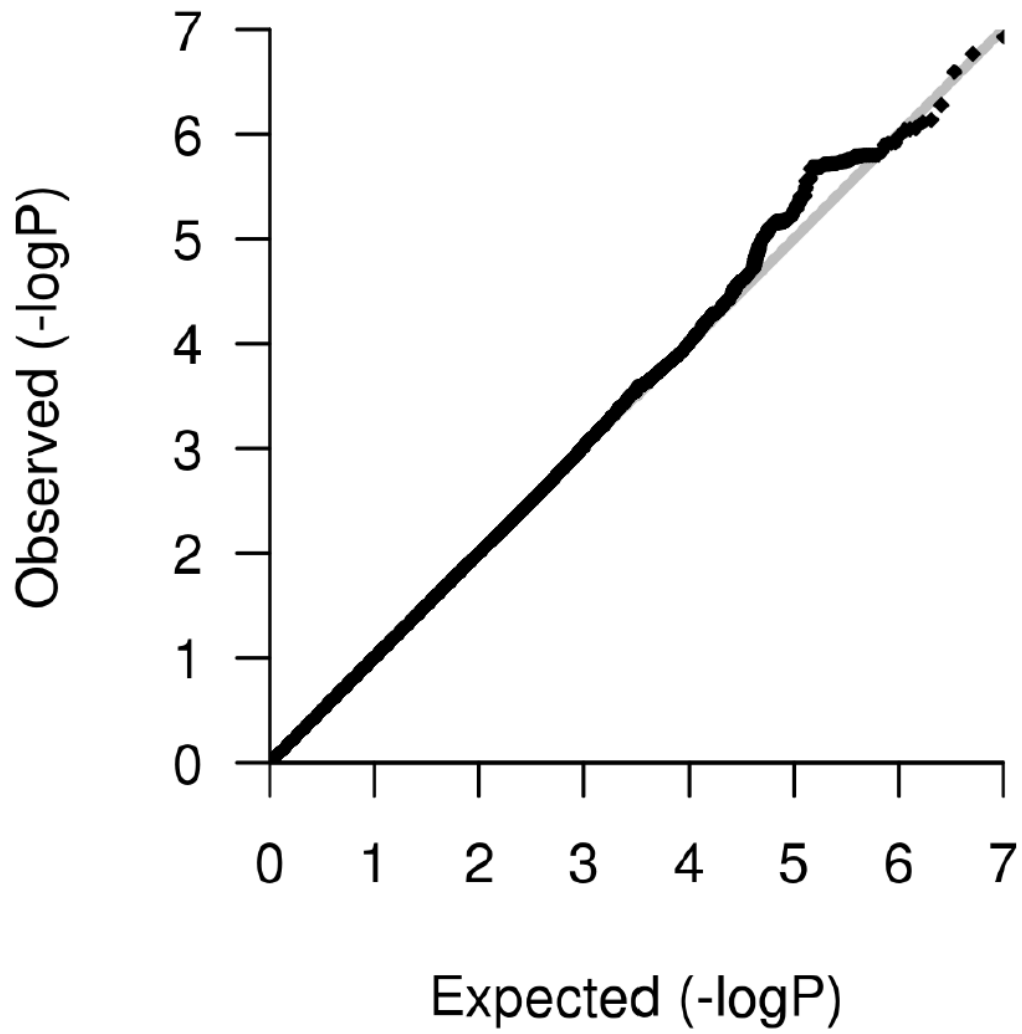


Figure S80 QQ-plot for interleukin-2 (IL-2).

QQ-plot for IL2ra

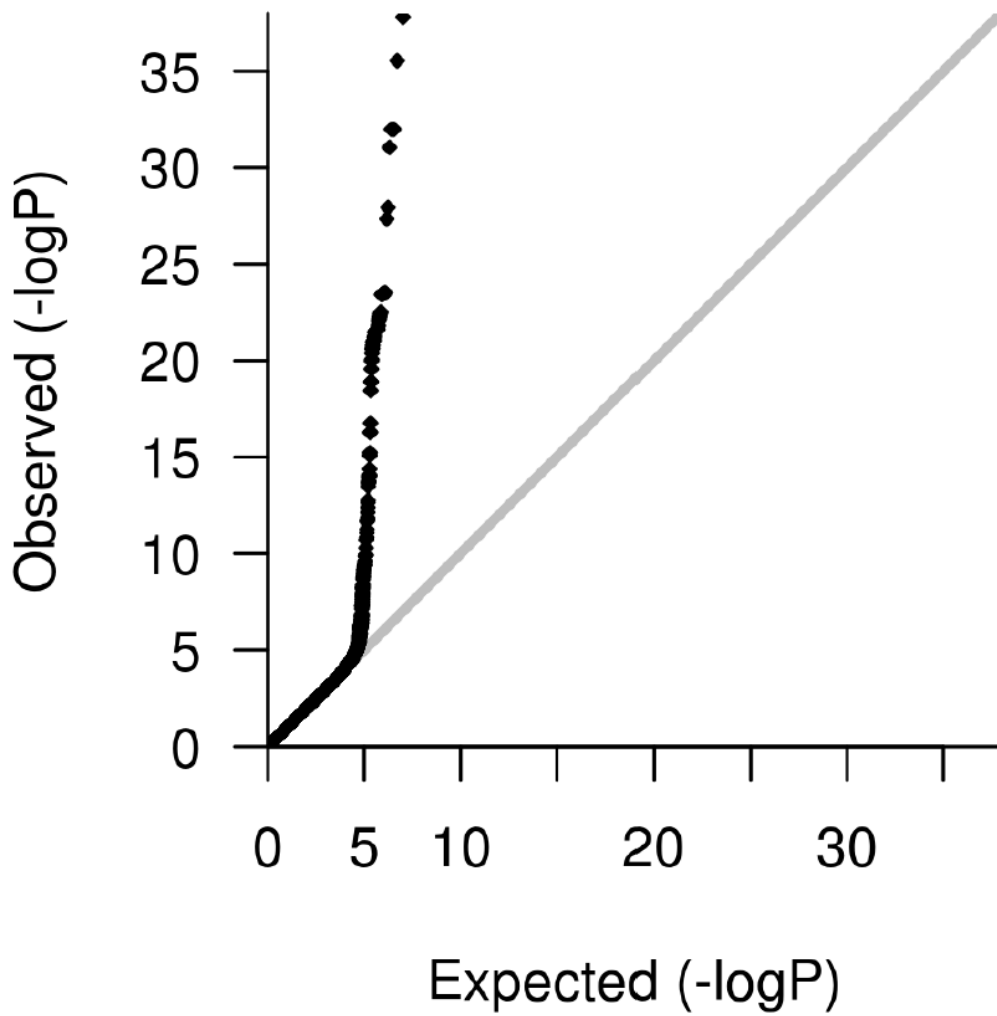


Figure S81 QQ-plot for Interleukin-2 receptor subunit alpha (IL2ra).

QQ-plot for IL-4

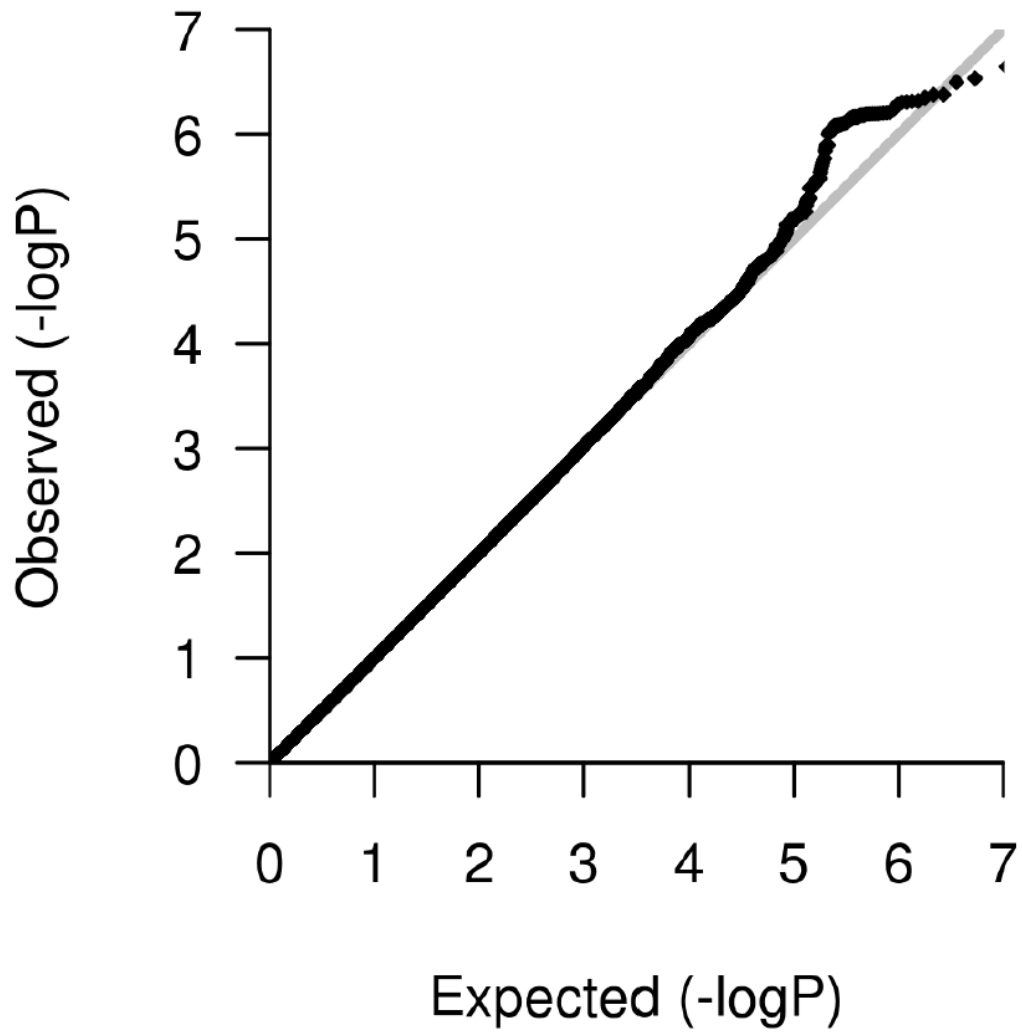


Figure S82 QQ-plot for interleukin-4 (IL-4).

QQ-plot for IL-5

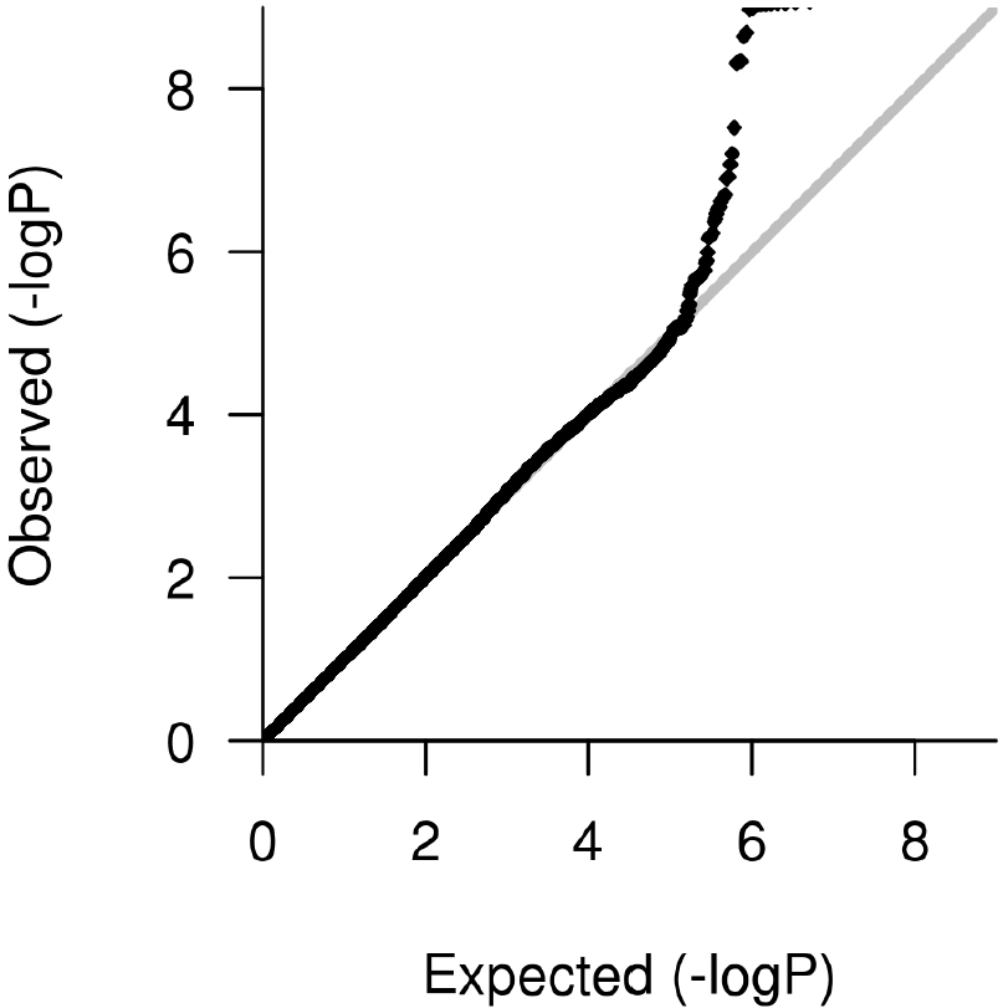


Figure S83 QQ-plot for interleukin-5 (IL-5).

QQ-plot for IL-6

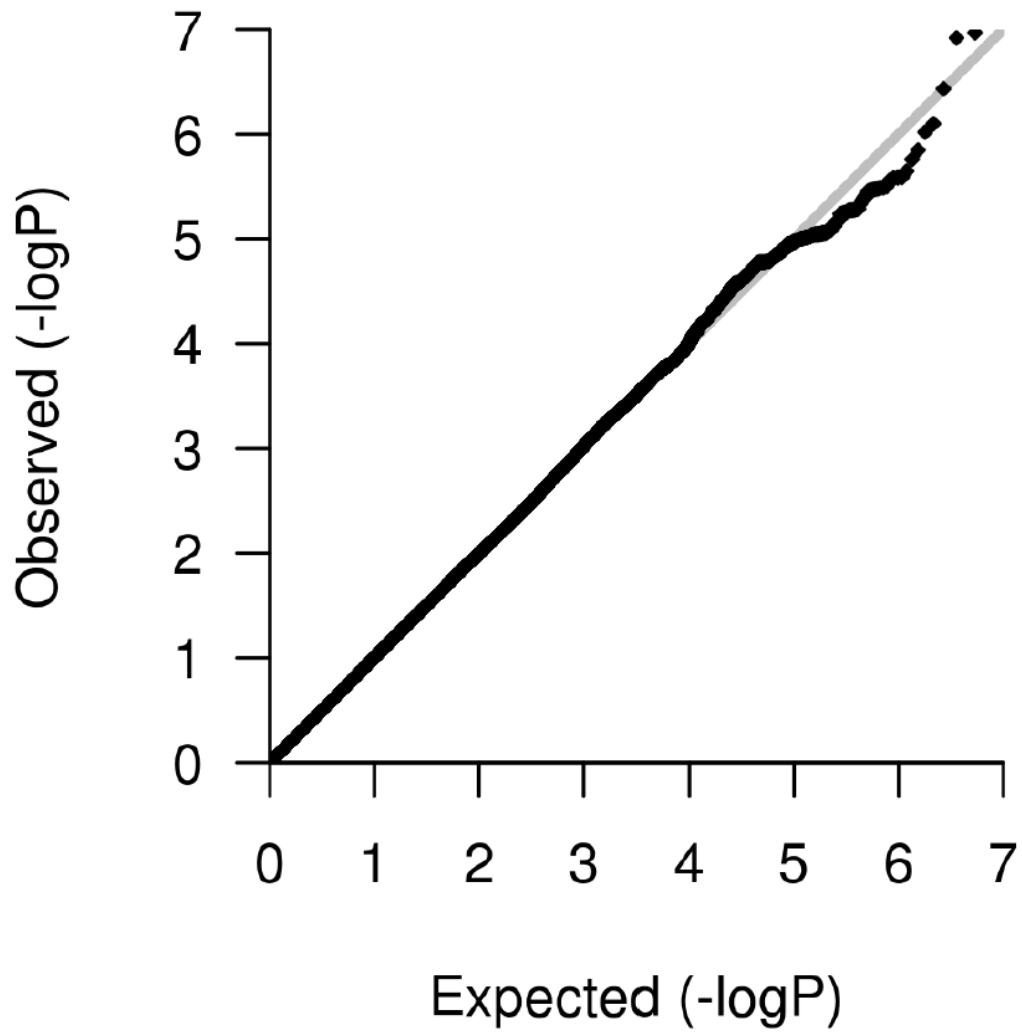


Figure S84 QQ-plot for interleukin-6 (IL-6).

QQ-plot for IL-7

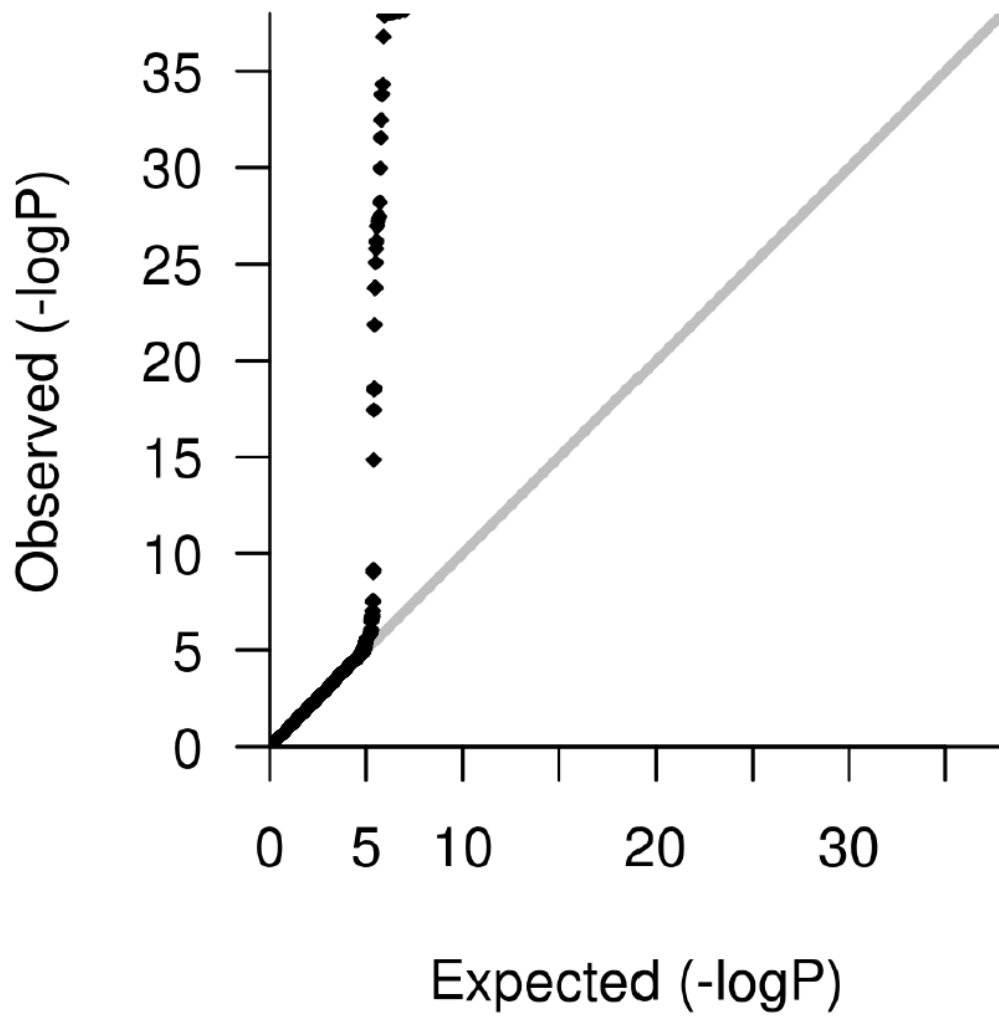


Figure S85 QQ-plot for interleukin-7 (IL-7).

QQ-plot for IL-8

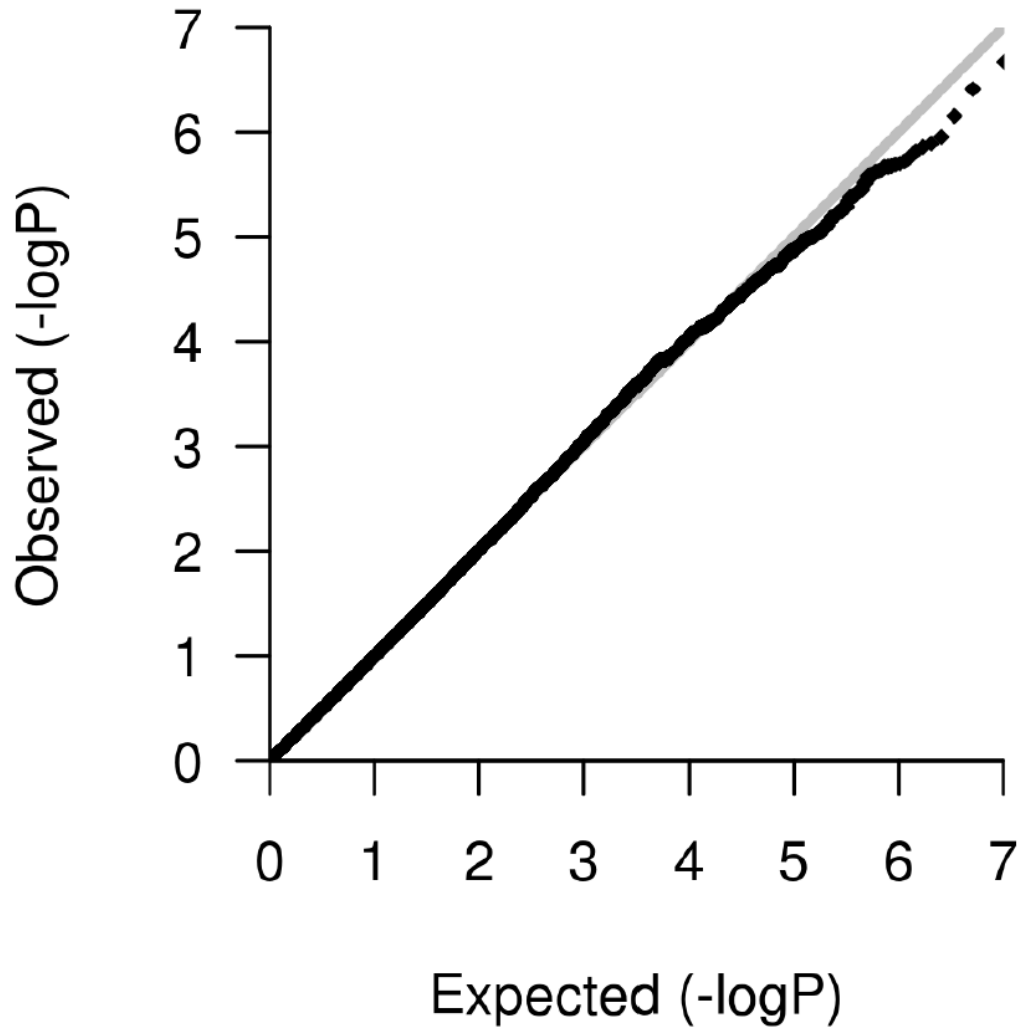


Figure S86 QQ-plot for interleukin-8 (IL-8).

QQ-plot for IL-9

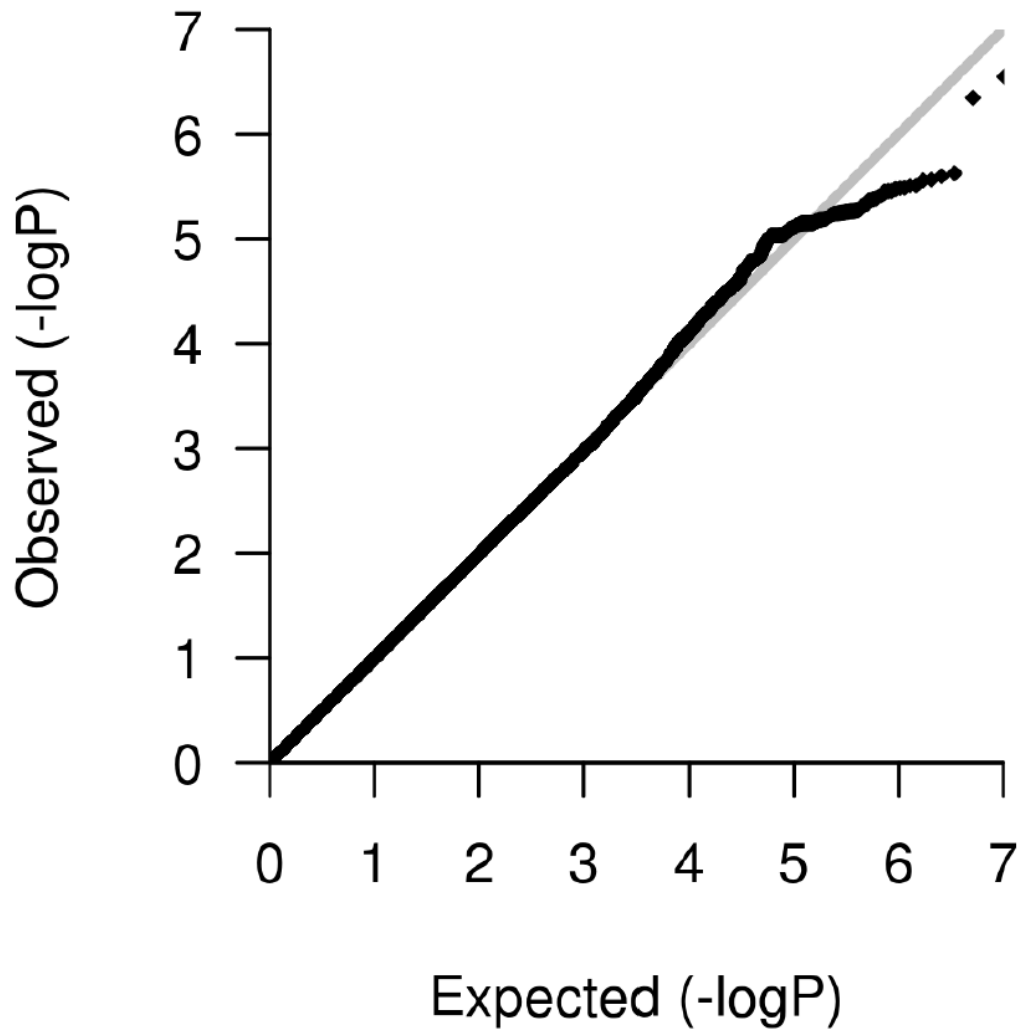


Figure S87 QQ-plot for interleukin-9 (IL-9).

QQ-plot for IL-10

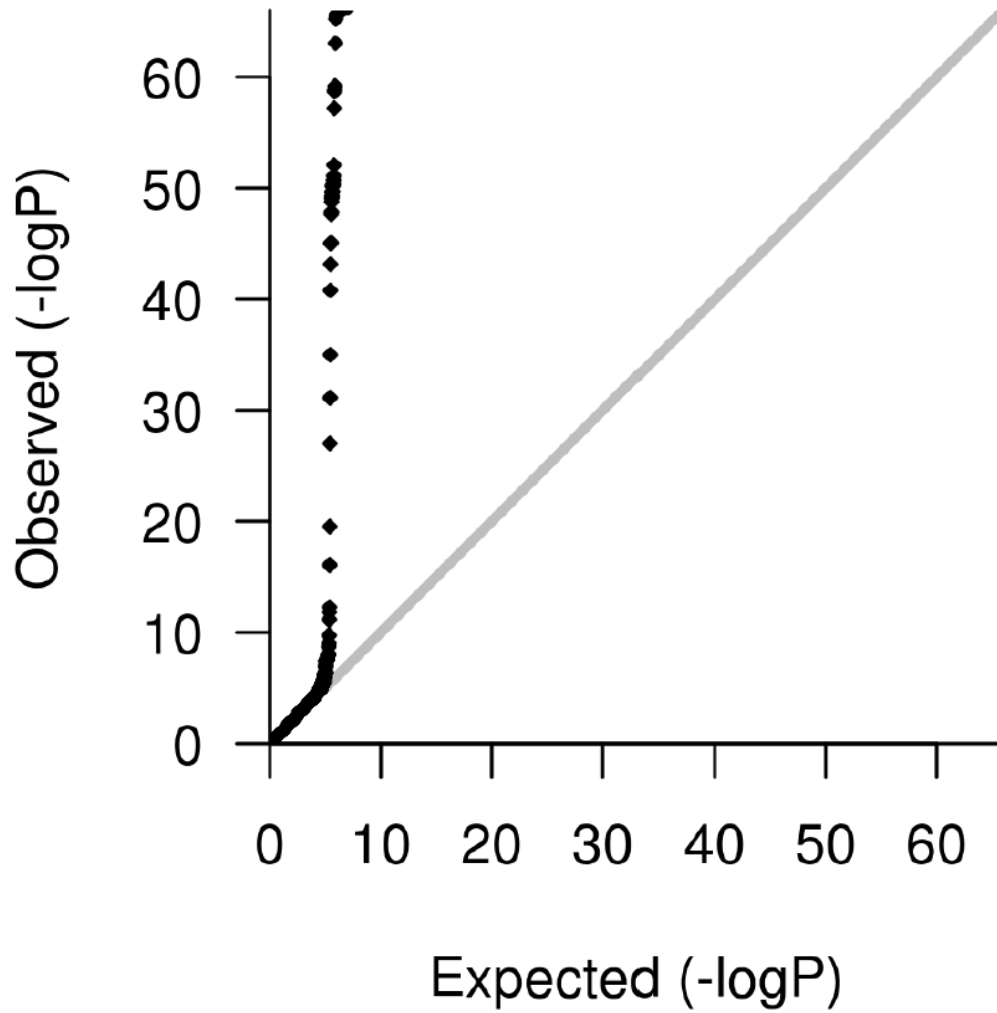


Figure S88 QQ-plot for interleukin-10 (IL-10).

QQ-plot for IL-12p70

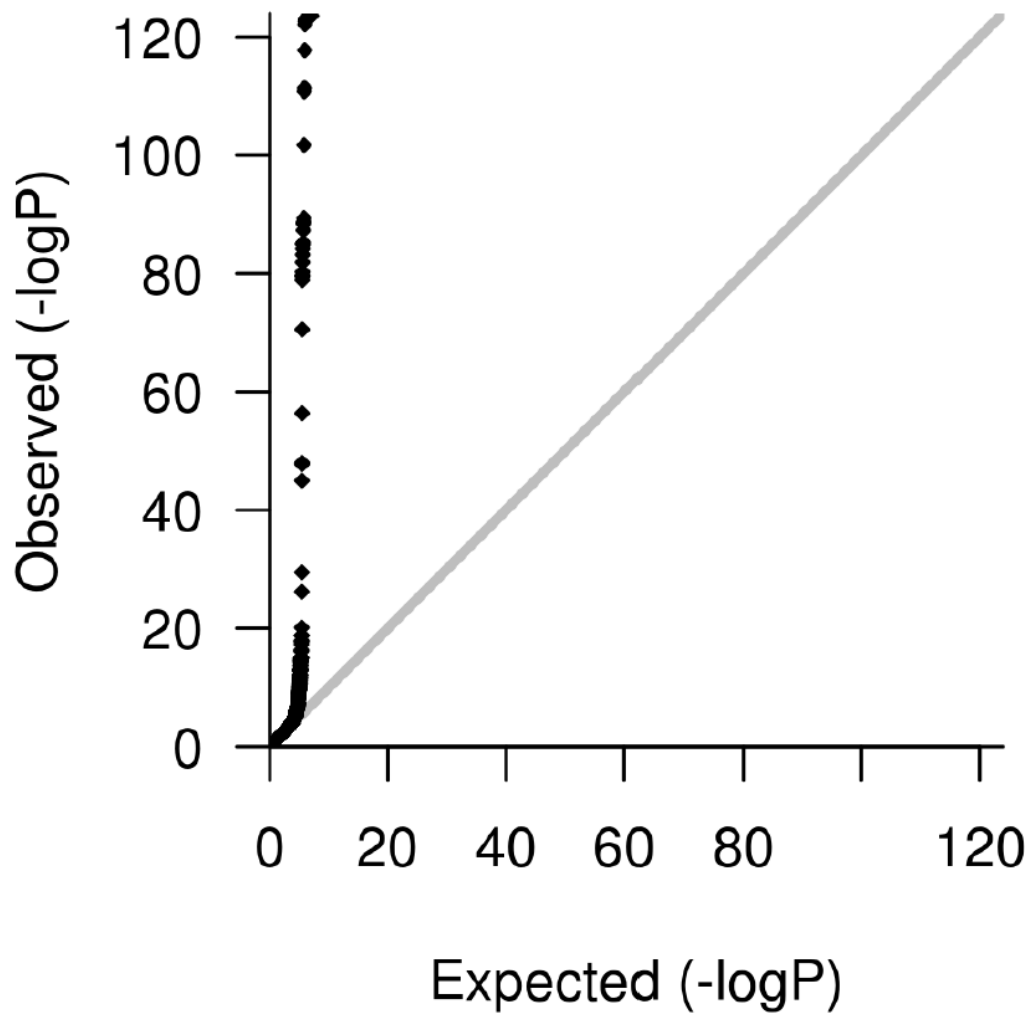


Figure S89 QQ-plot for interleukin-12p70 (IL-12p70).

QQ-plot for IL-13

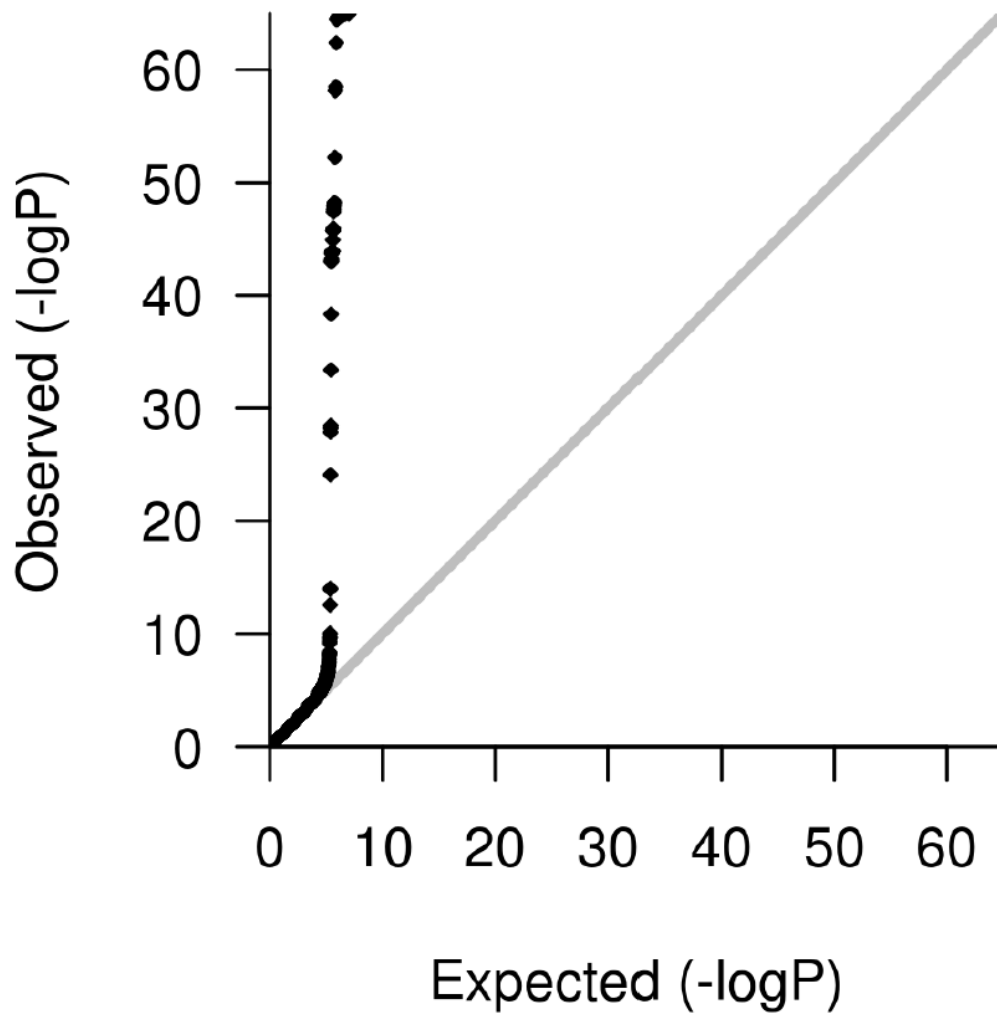


Figure S90 QQ-plot for interleukin-13 (IL-13).

QQ-plot for IL-16

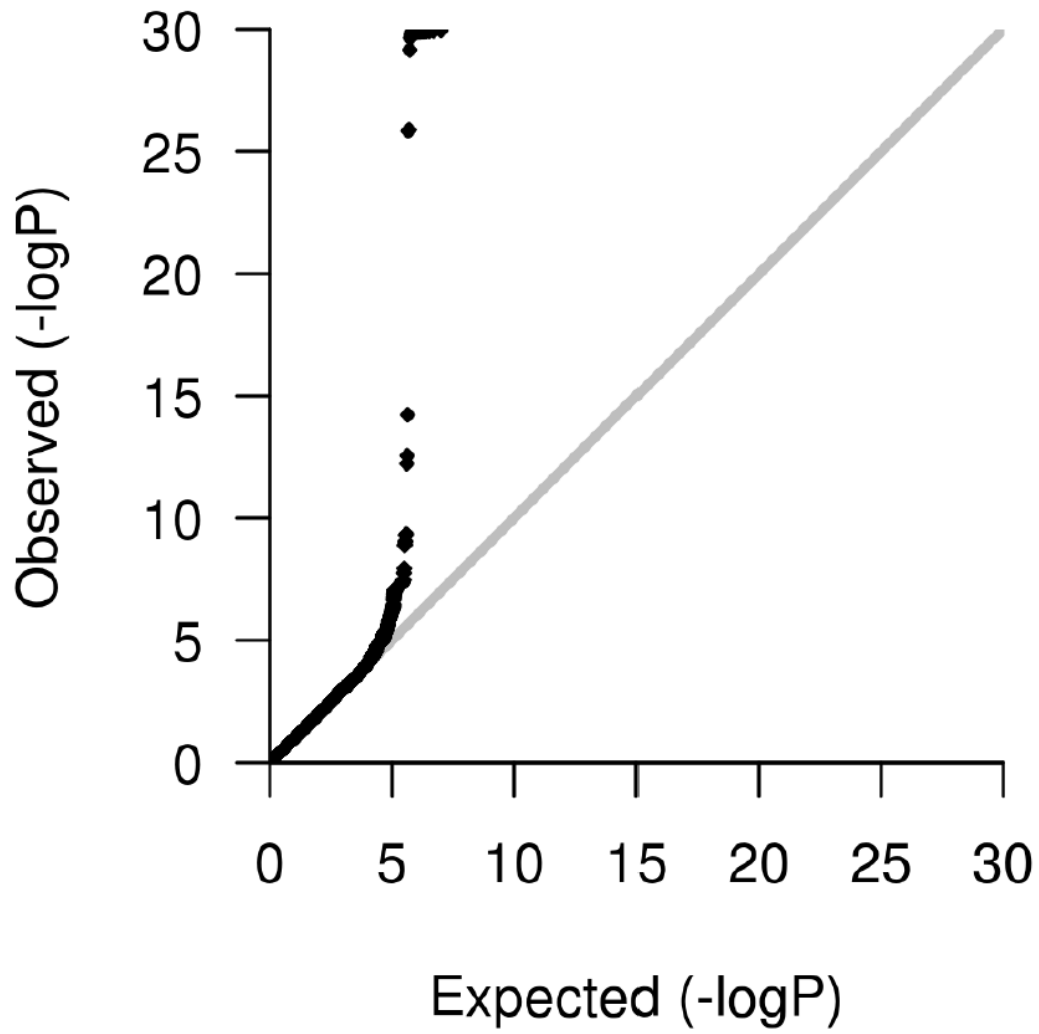


Figure S91 QQ-plot for interleukin-16 (IL-16).

QQ-plot for IL-17

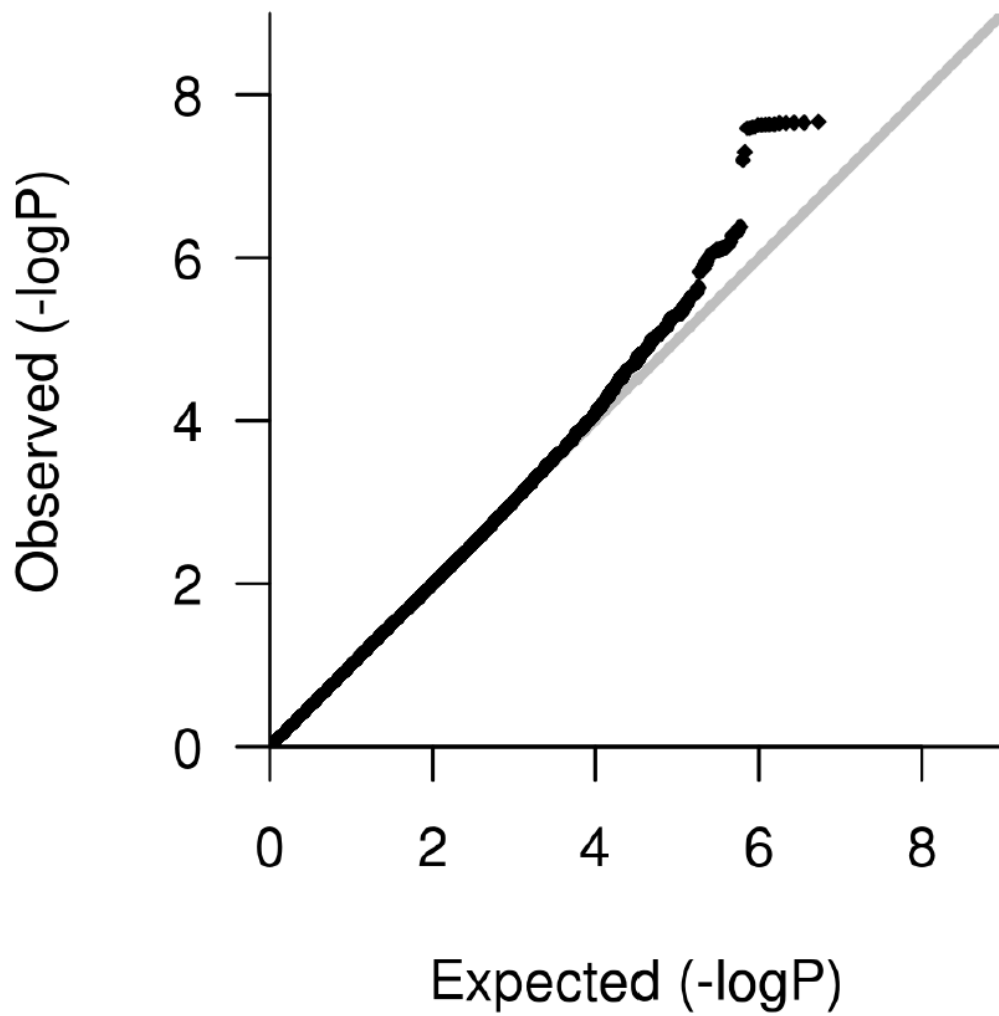


Figure S92 QQ-plot for interleukin-17 (IL-17).

QQ-plot for IL-18

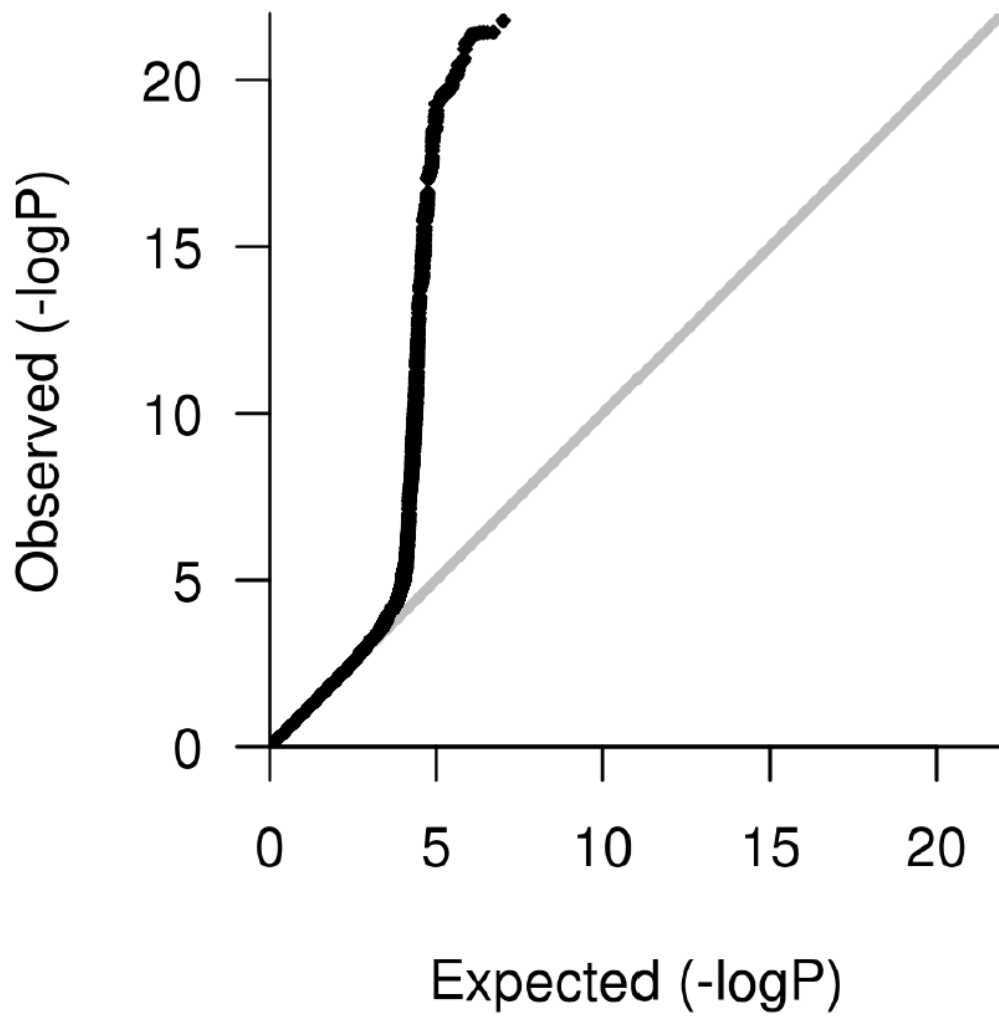


Figure S93 QQ-plot for interleukin-18 (IL-18).

QQ-plot for IP10

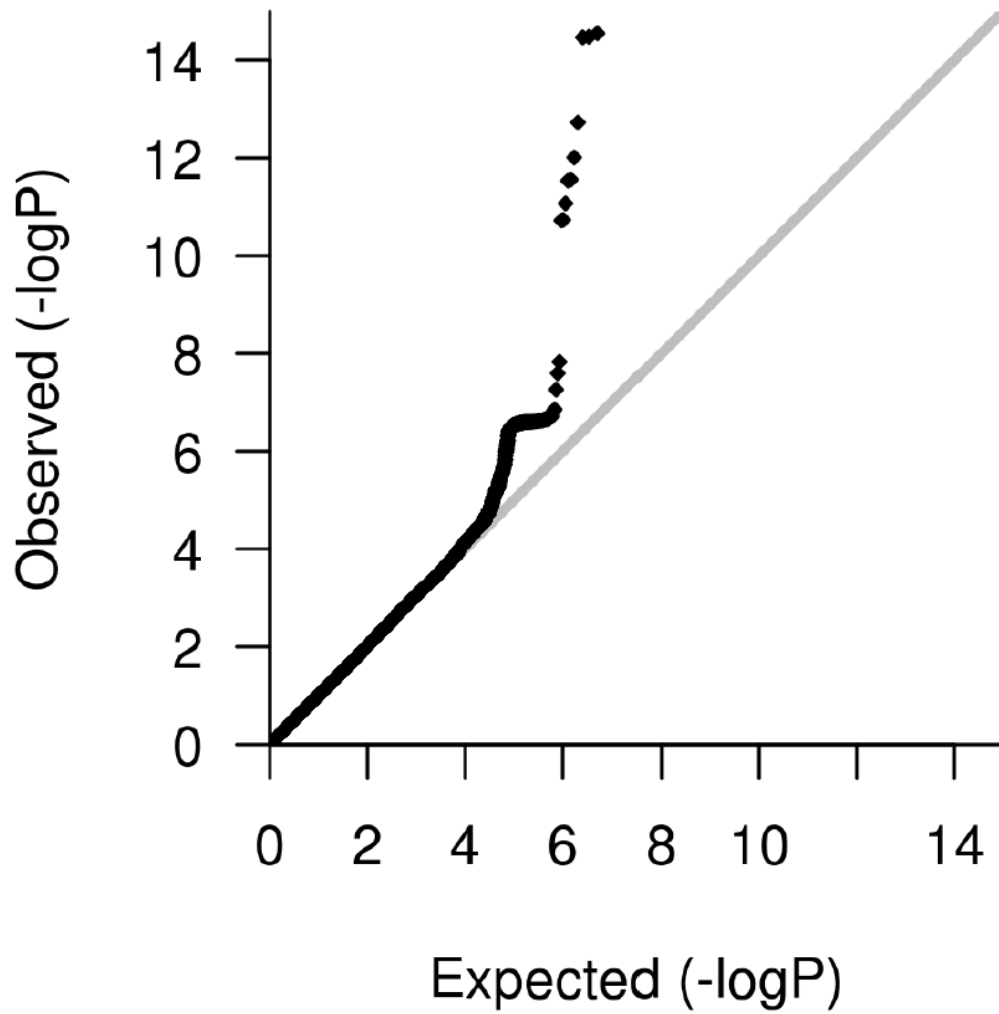


Figure S94 QQ-plot for interferon gamma-induced protein 10 (IP10; CXCL10).

QQ-plot for MCP1

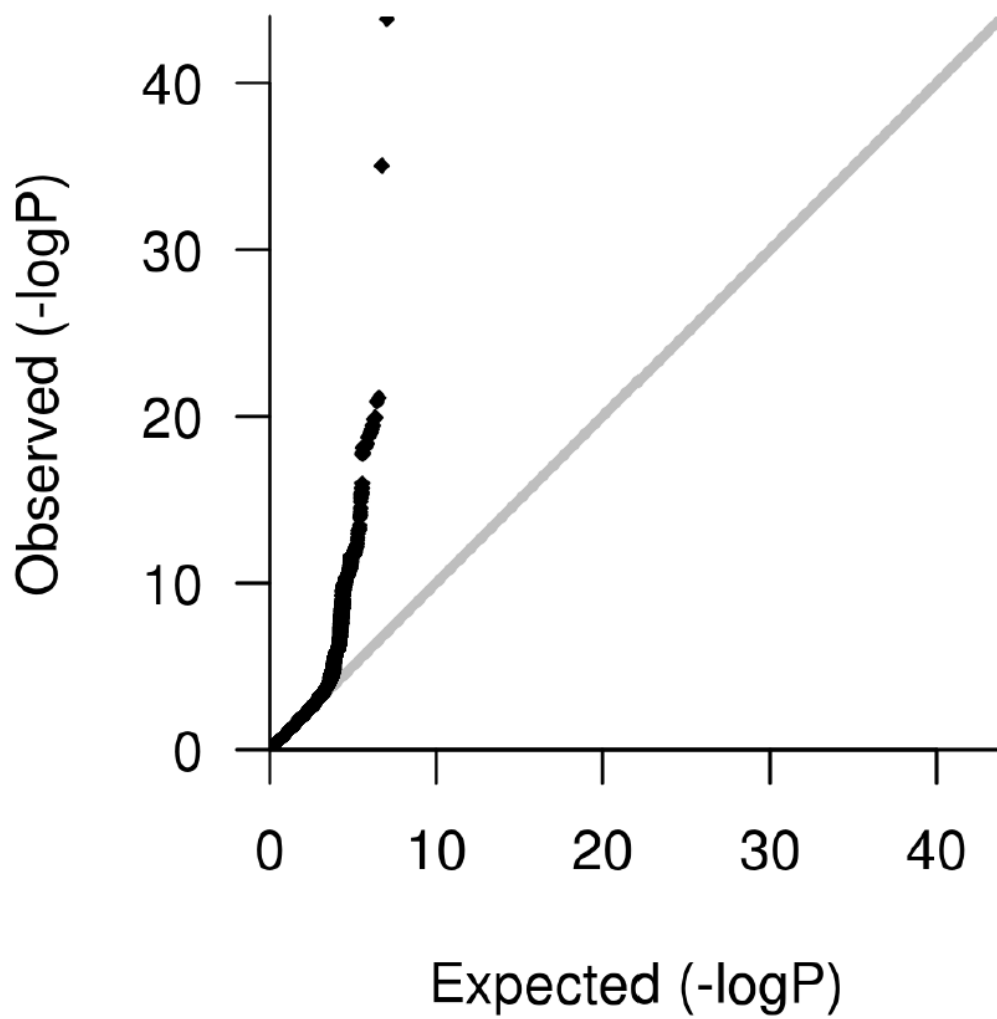


Figure S95 QQ-plot for monocyte chemotactic protein-1 (MCP1; CCL2)

QQ-plot for MCP3

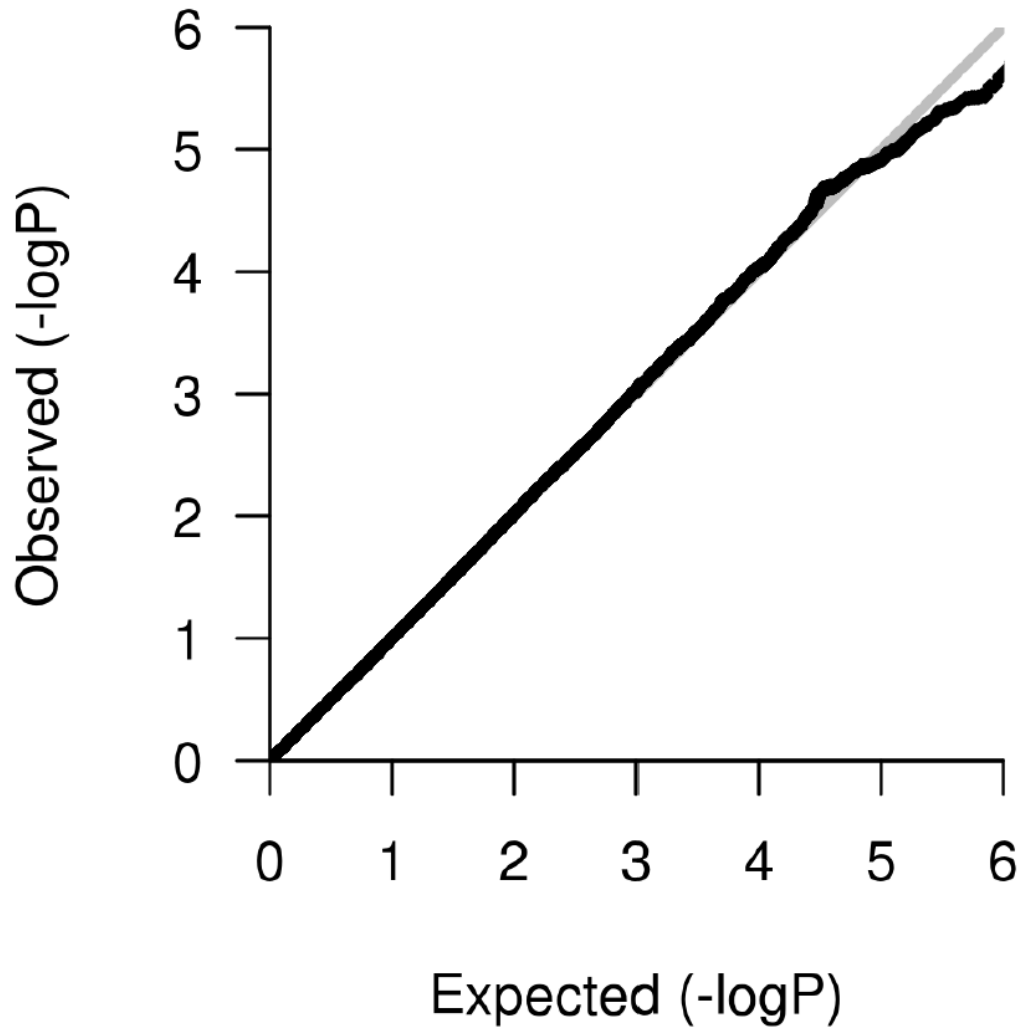


Figure S96 QQ-plot for monocyte specific chemokine 3 (MCP3; CCL7).

QQ-plot for MCSF

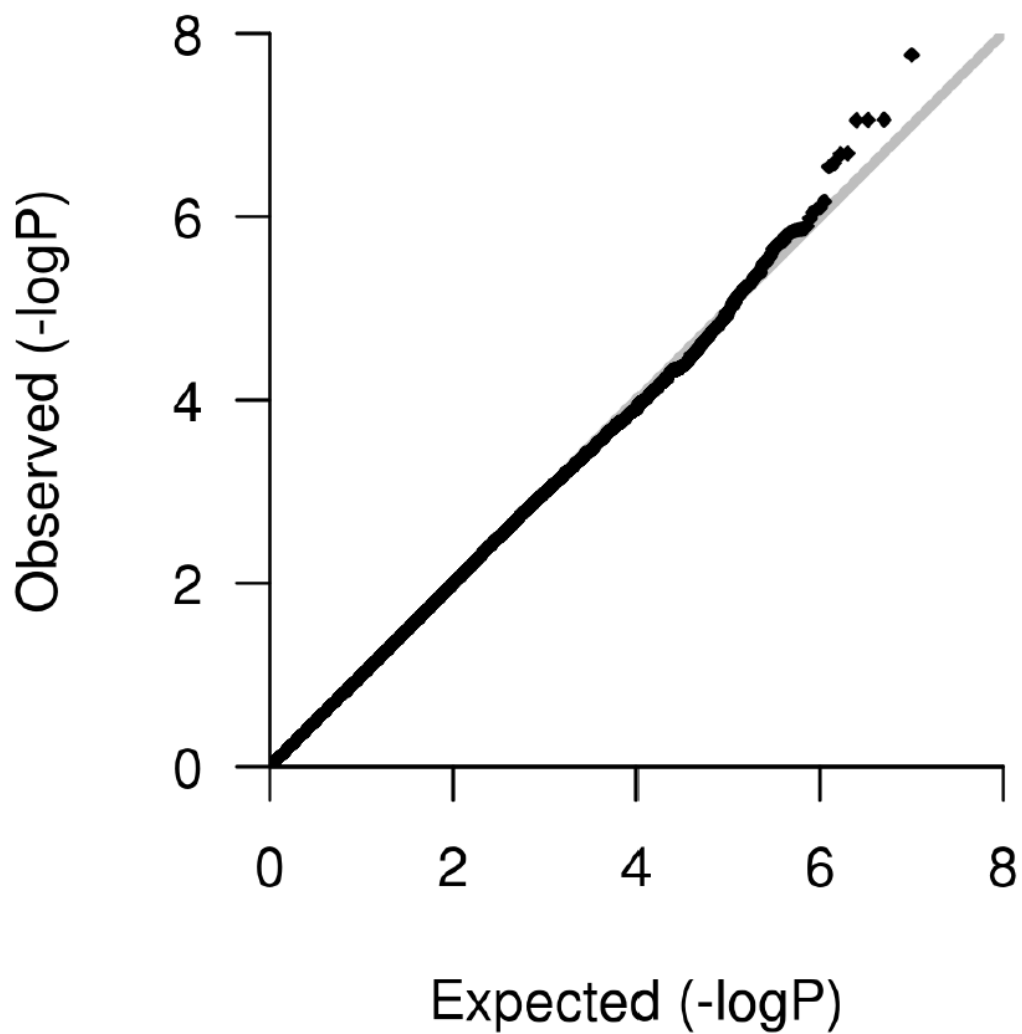


Figure S97 QQ-plot for macrophage colony-stimulating factor (MCSF).

QQ-plot for MIF

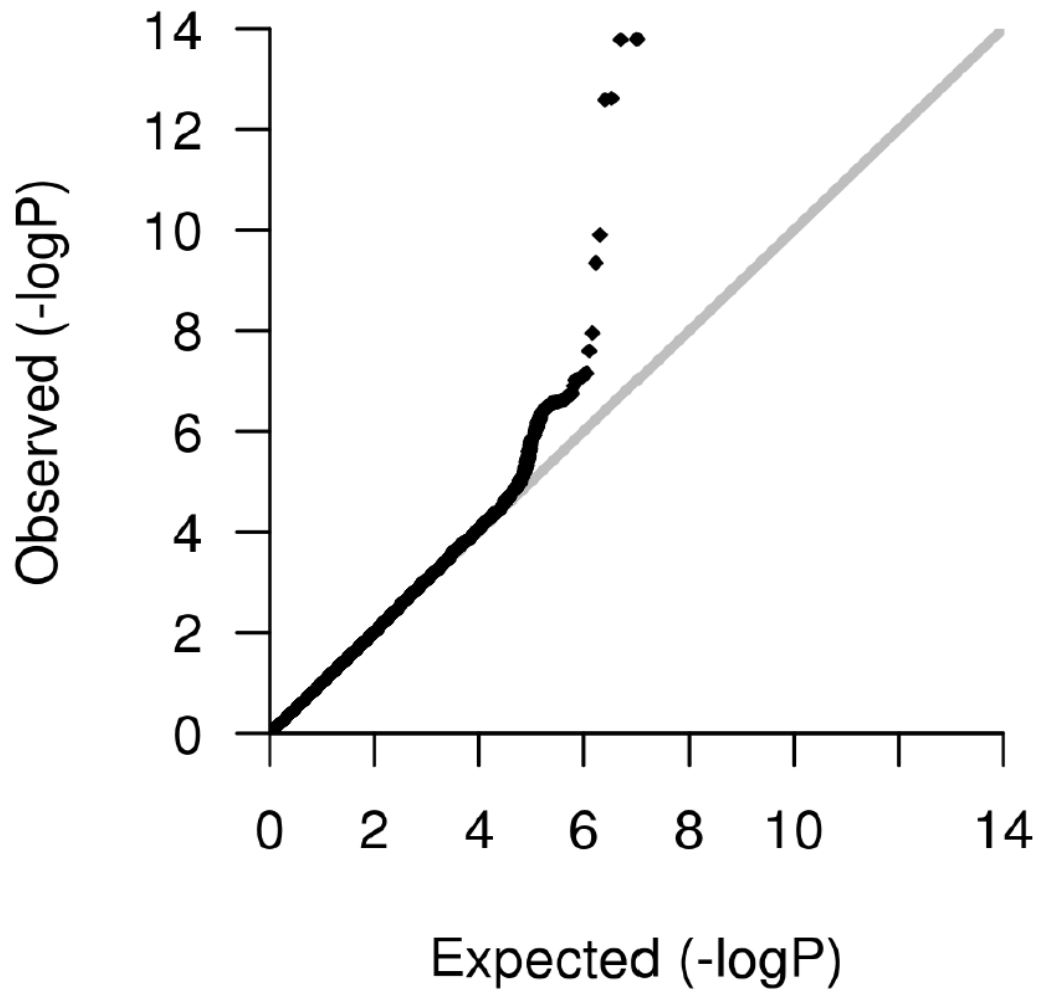


Figure S98 QQ-plot for macrophage migration inhibitory factor (glycosylation-inhibiting factor; MIF).

QQ-plot for MIG

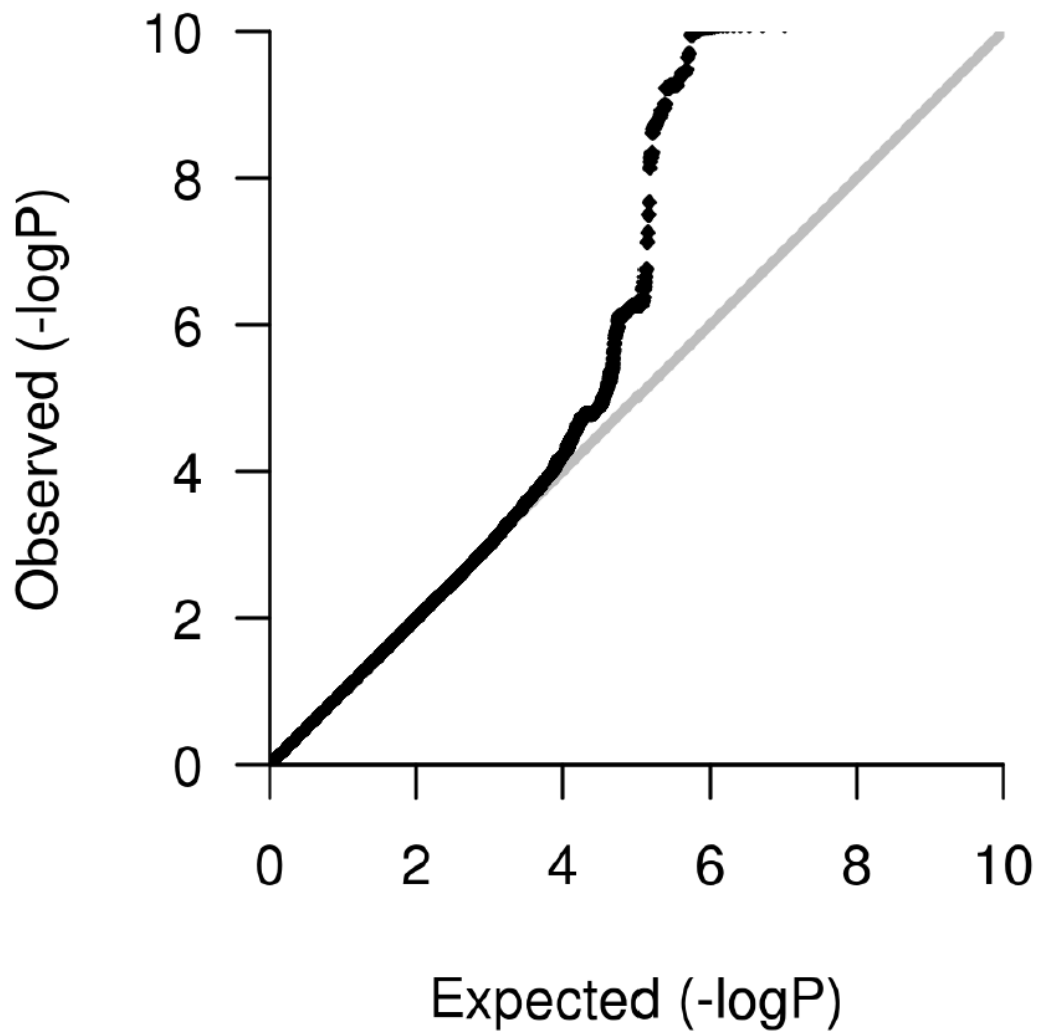


Figure S99 QQ-plot for monokine induced by interferon-gamma (MIG; CXCL9).

QQ-plot for MIP1a

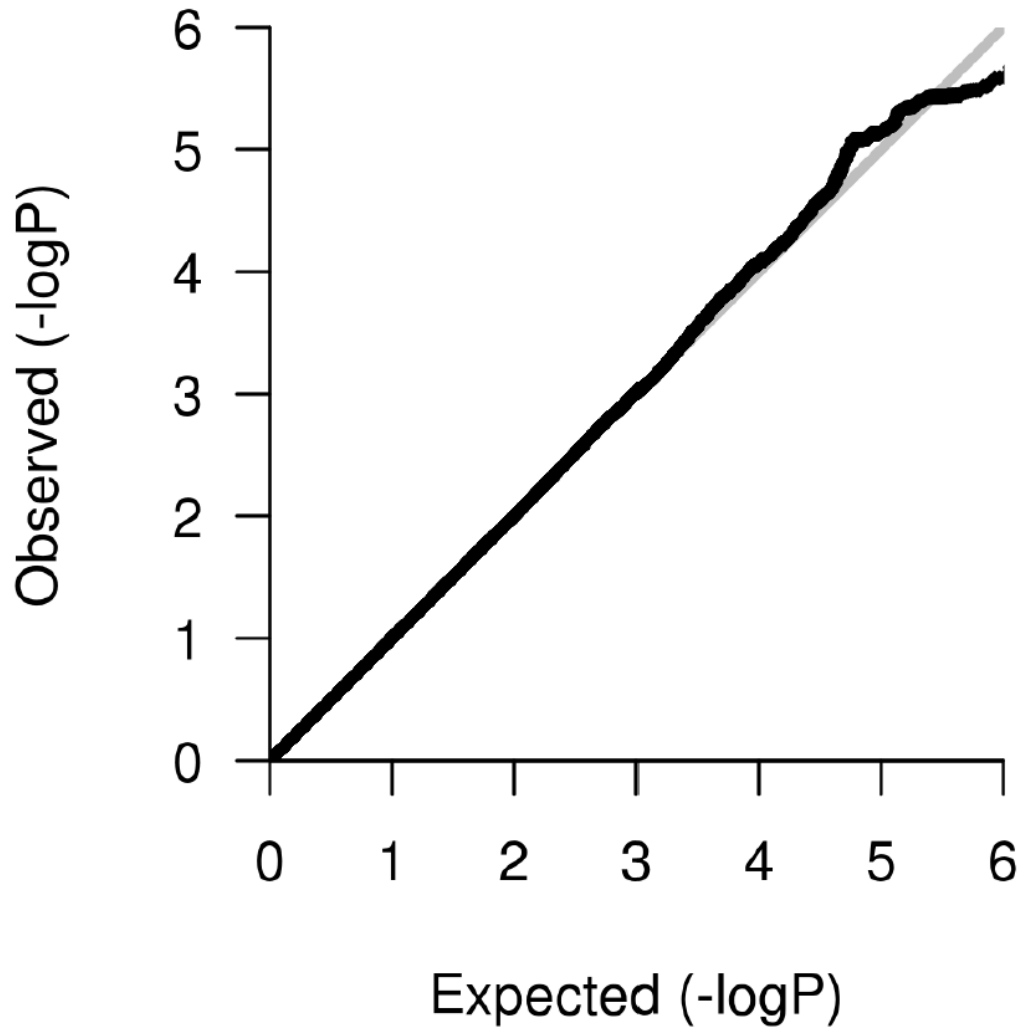


Figure S100 QQ-plot for macrophage inflammatory protein-1 α (MIP1a; CCL3).

QQ-plot for MIP1b

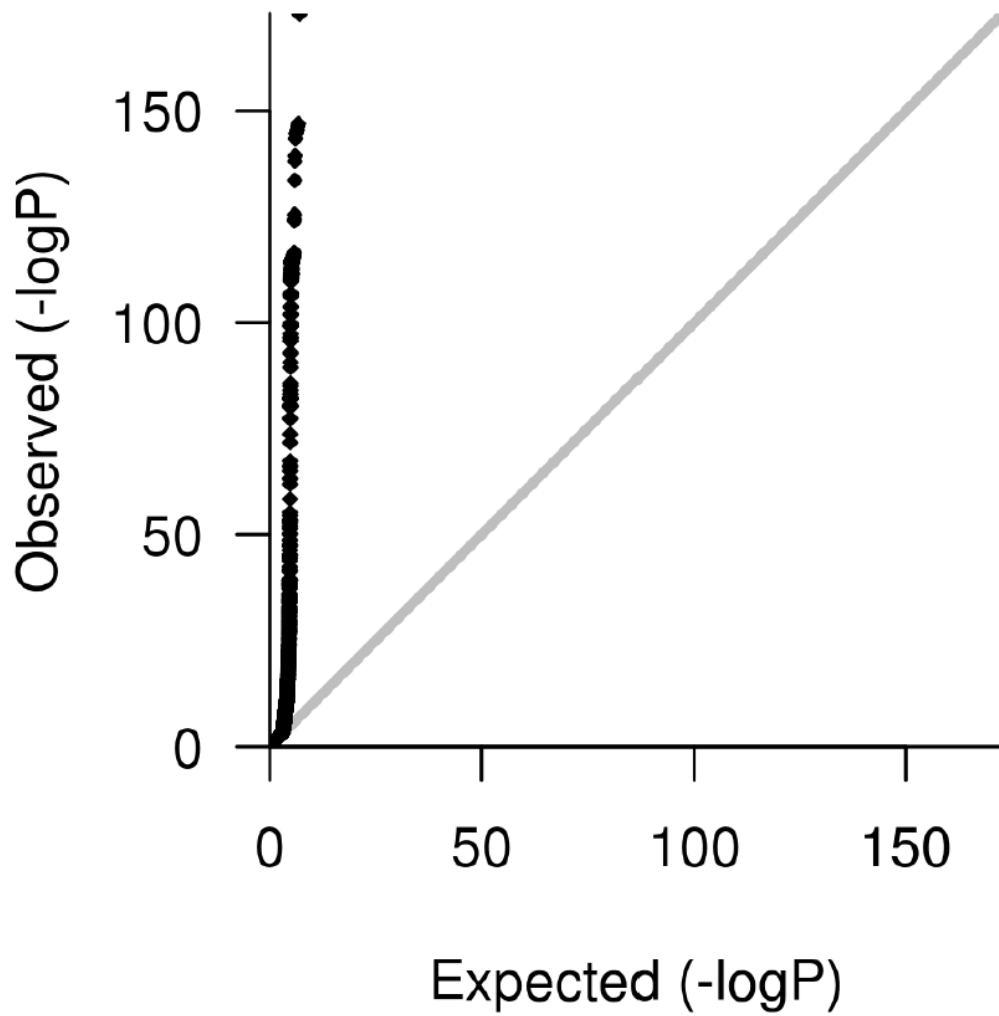


Figure S101 QQ-plot for macrophage inflammatory protein-1 β (MIP1b; CCL4).

QQ-plot for PDGFbb

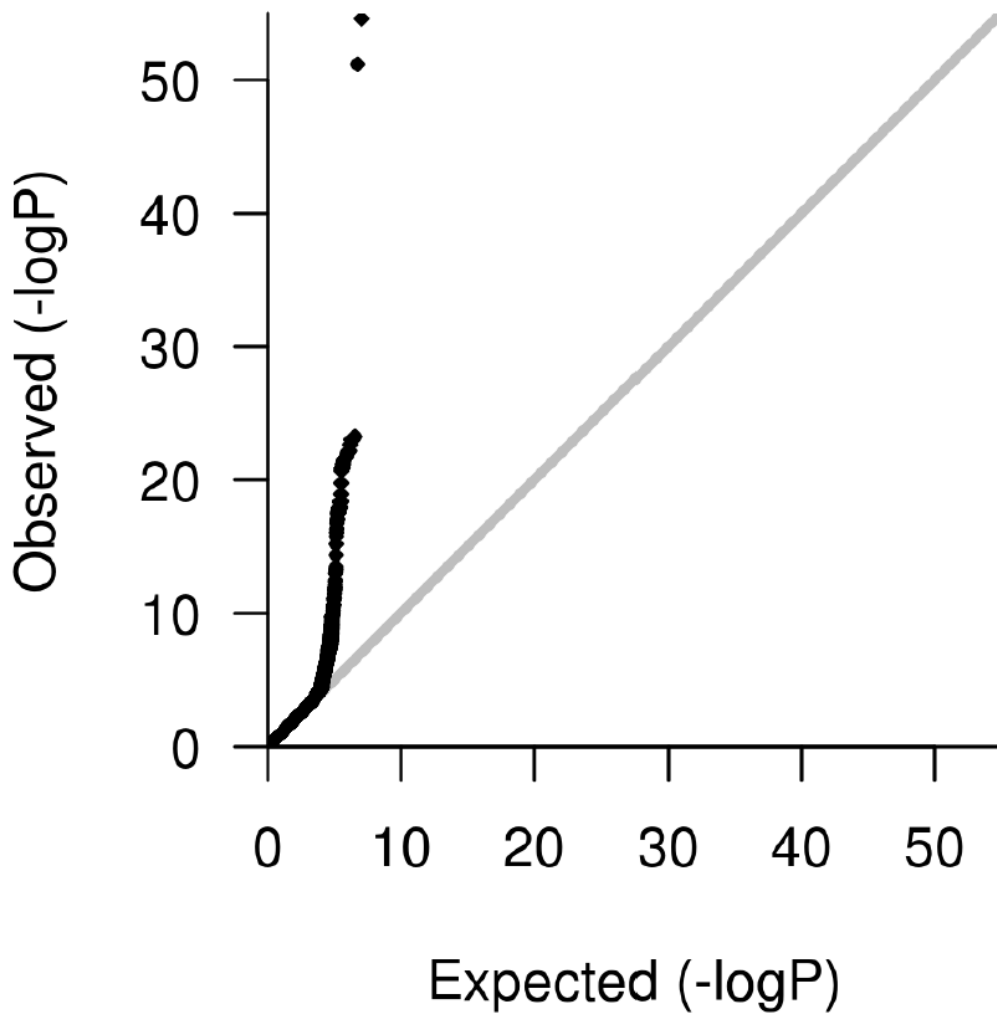


Figure S102 QQ-plot for platelet derived growth factor (PDGFbb).

QQ-plot for RANTES

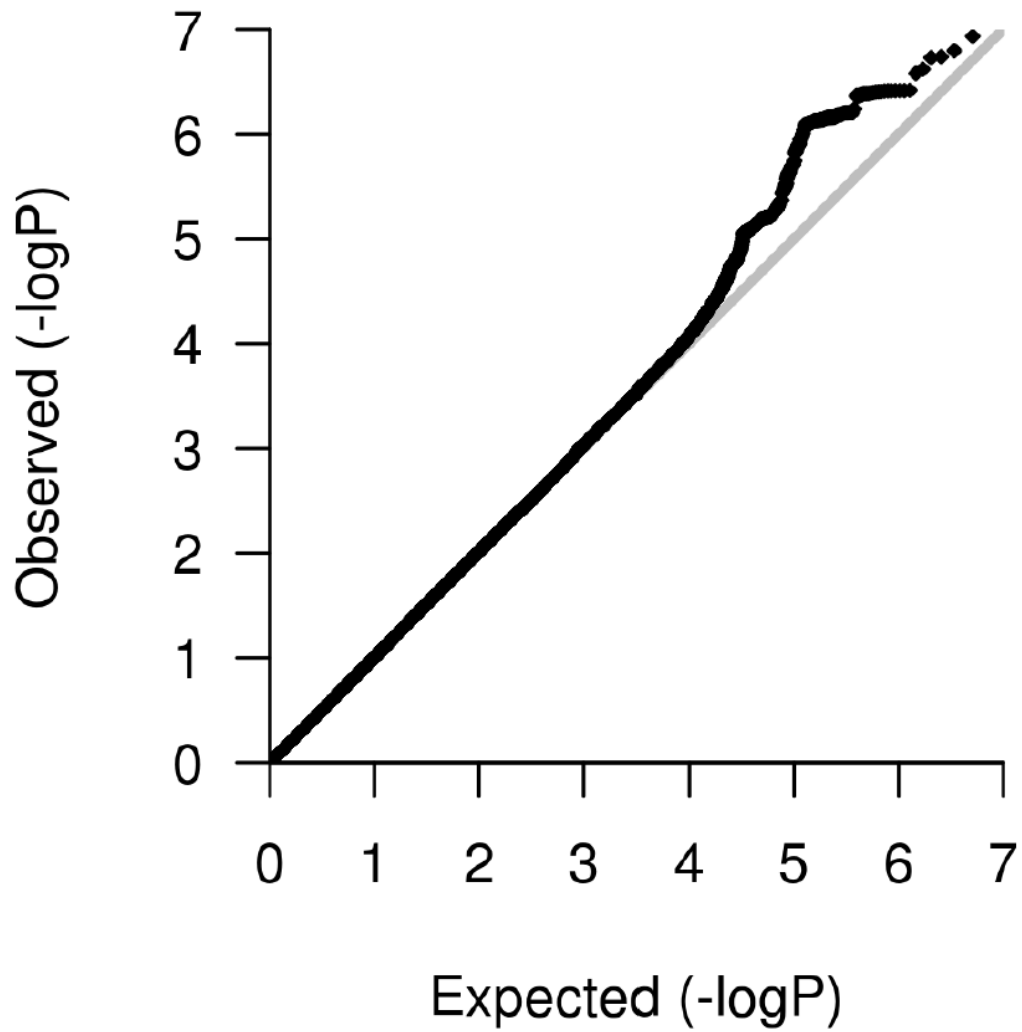


Figure S103 QQ-plot for regulated on Activation, Normal T Cell Expressed and Secreted (RANTES; CCL5).

QQ-plot for SCF

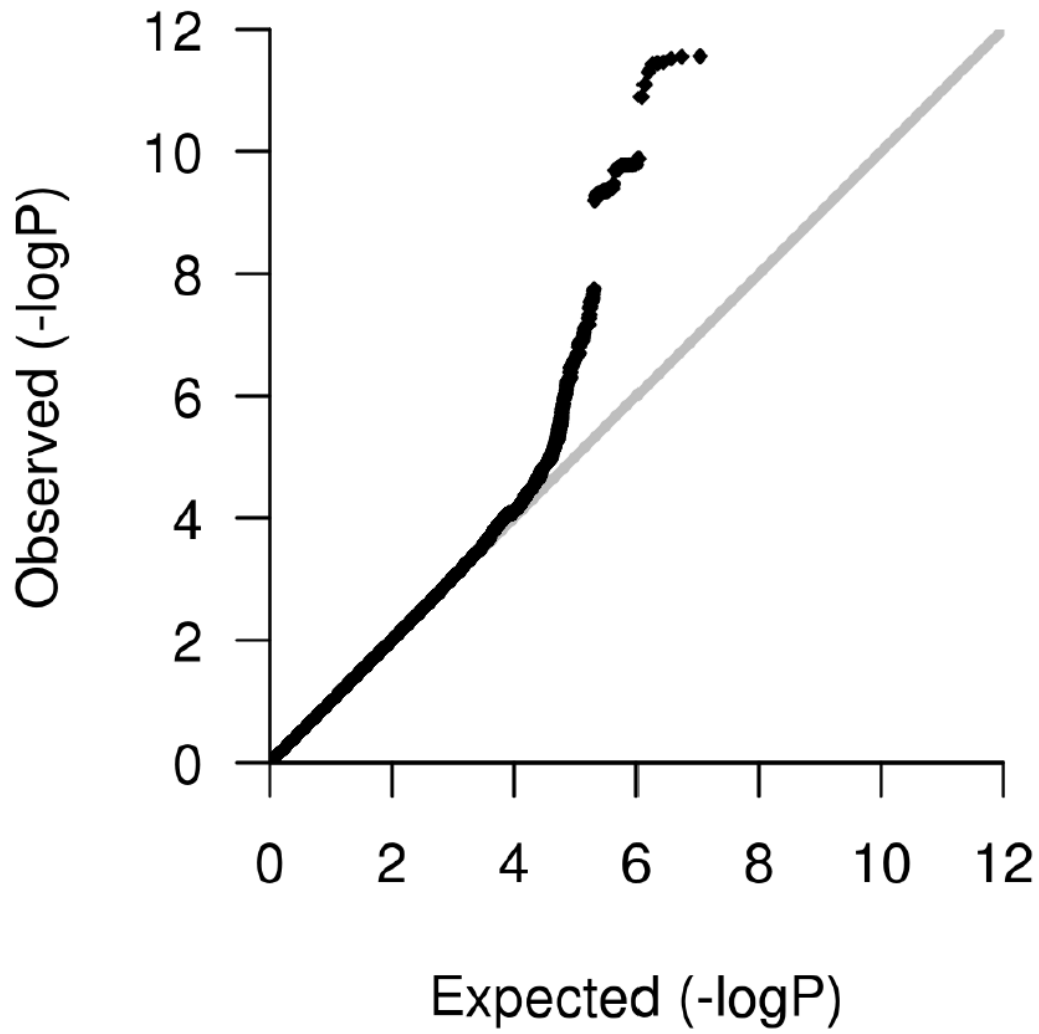


Figure S104 QQ-plot for stem cell factor (SCF).

QQ-plot for SCGFb

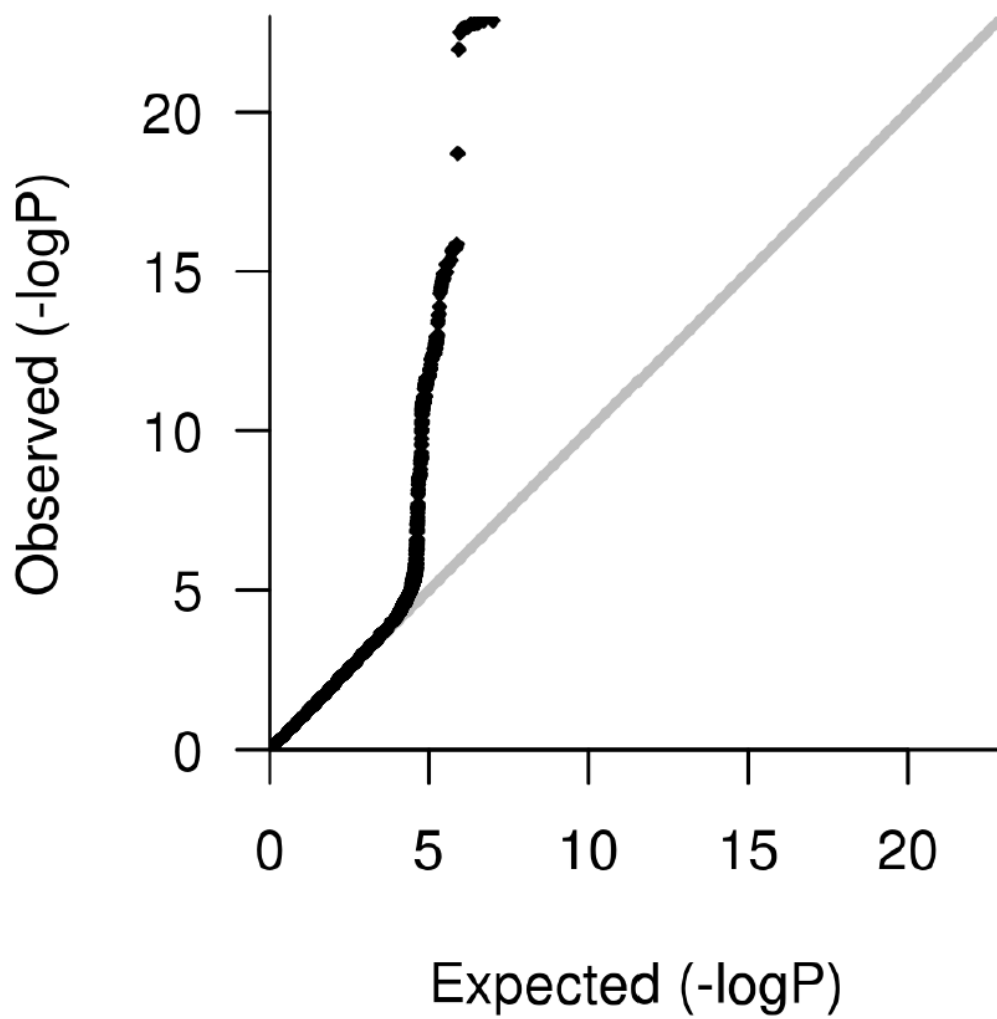


Figure S105 QQ-plot for stem cell growth factor beta (SCGFb).

QQ-plot for SDF1a

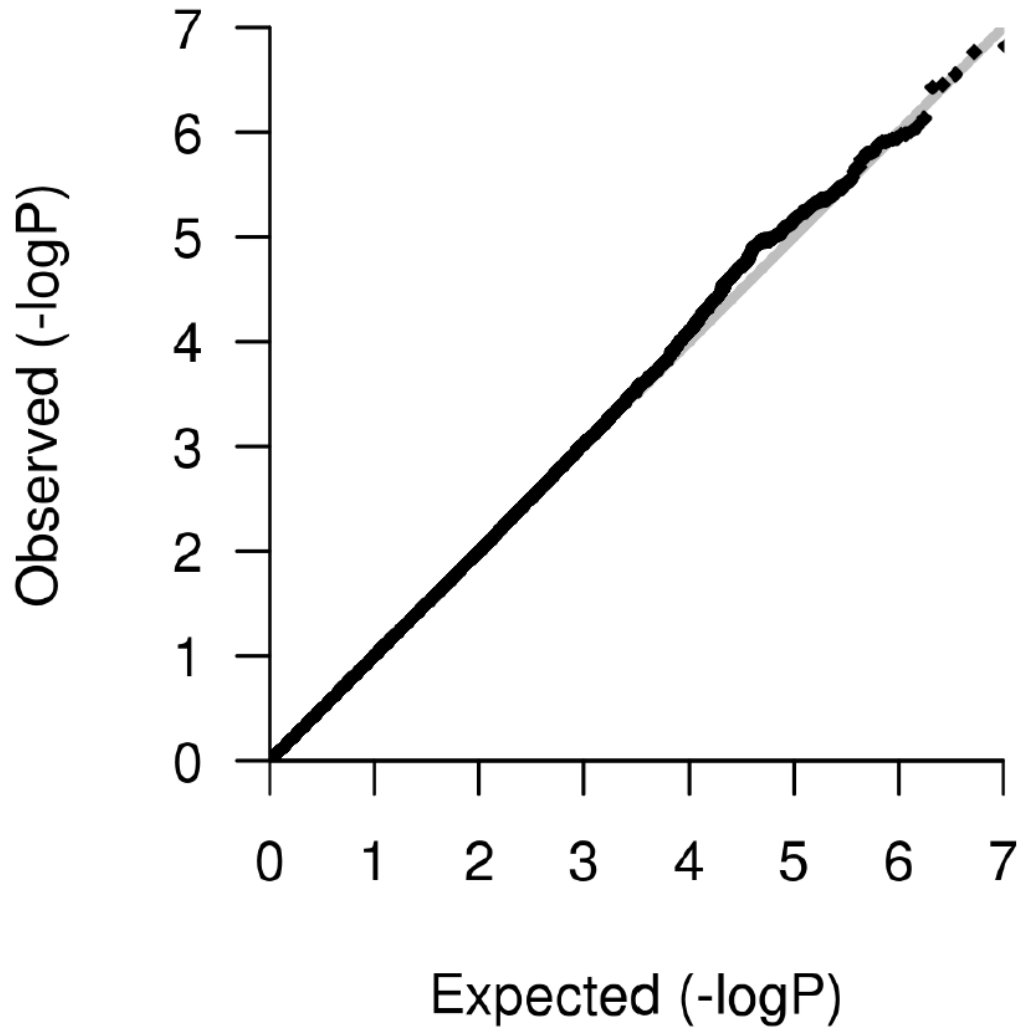


Figure S106 QQ-plot for stromal cell-derived factor-1 alpha (SDF1a; CXCL12).

QQ-plot for TNFa

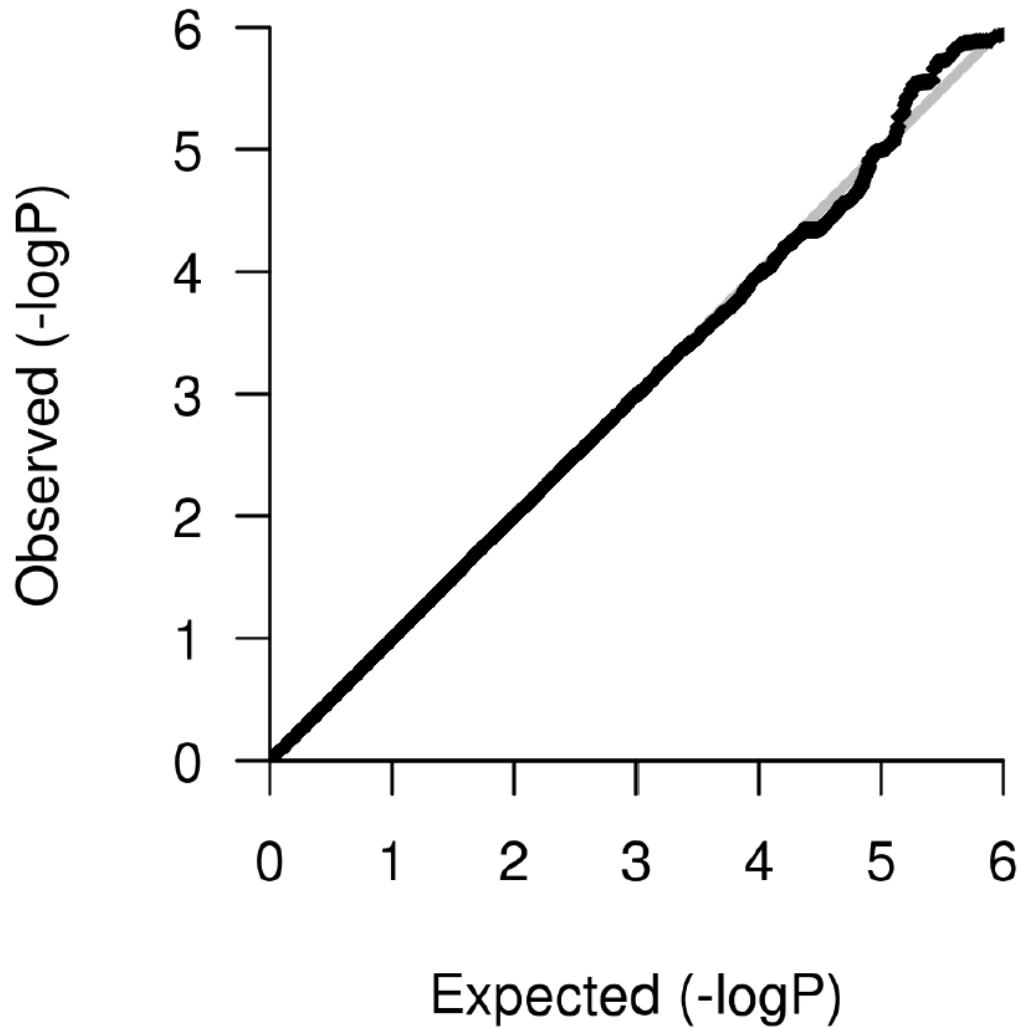


Figure S107 QQ-plot for tumor necrosis factor-alpha (TNFa).

QQ-plot for TNFb

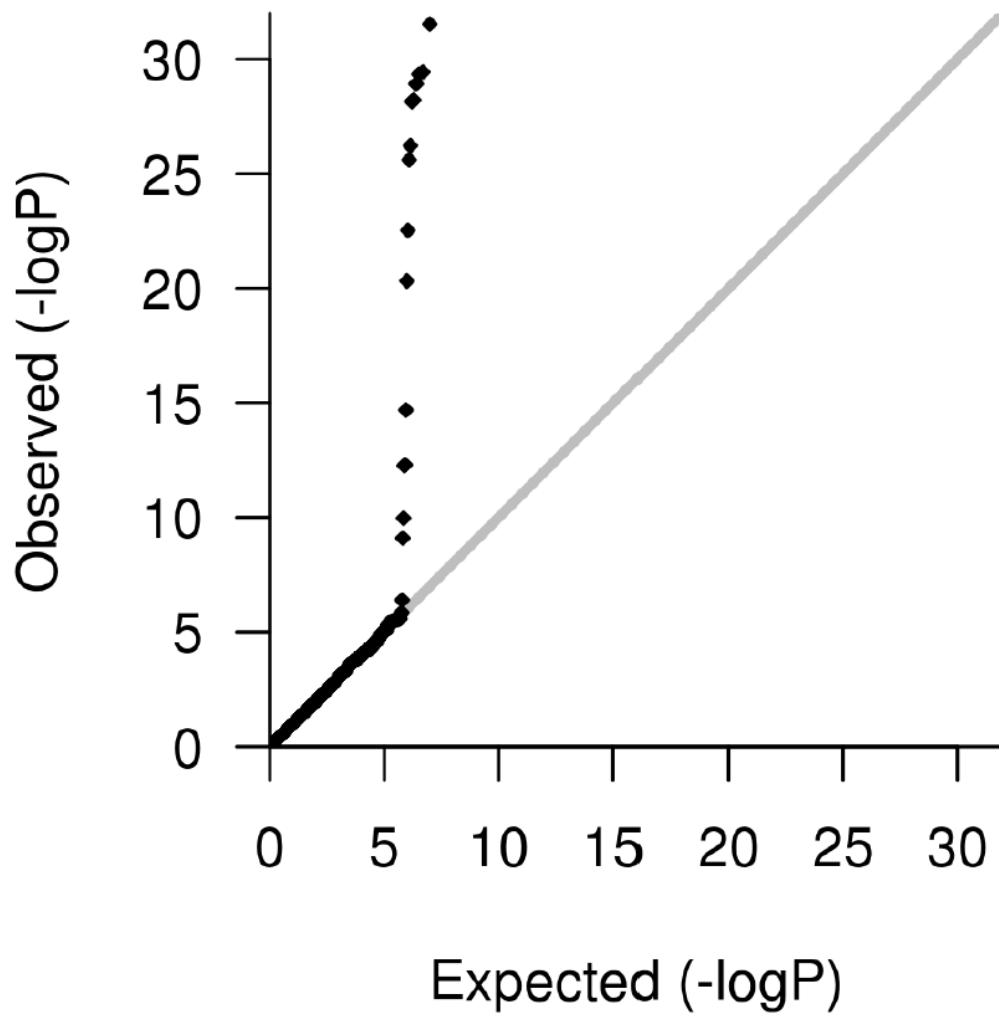


Figure S108 QQ-plot for tumor necrosis factor-beta (TNFb).

QQ-plot for TRAIL

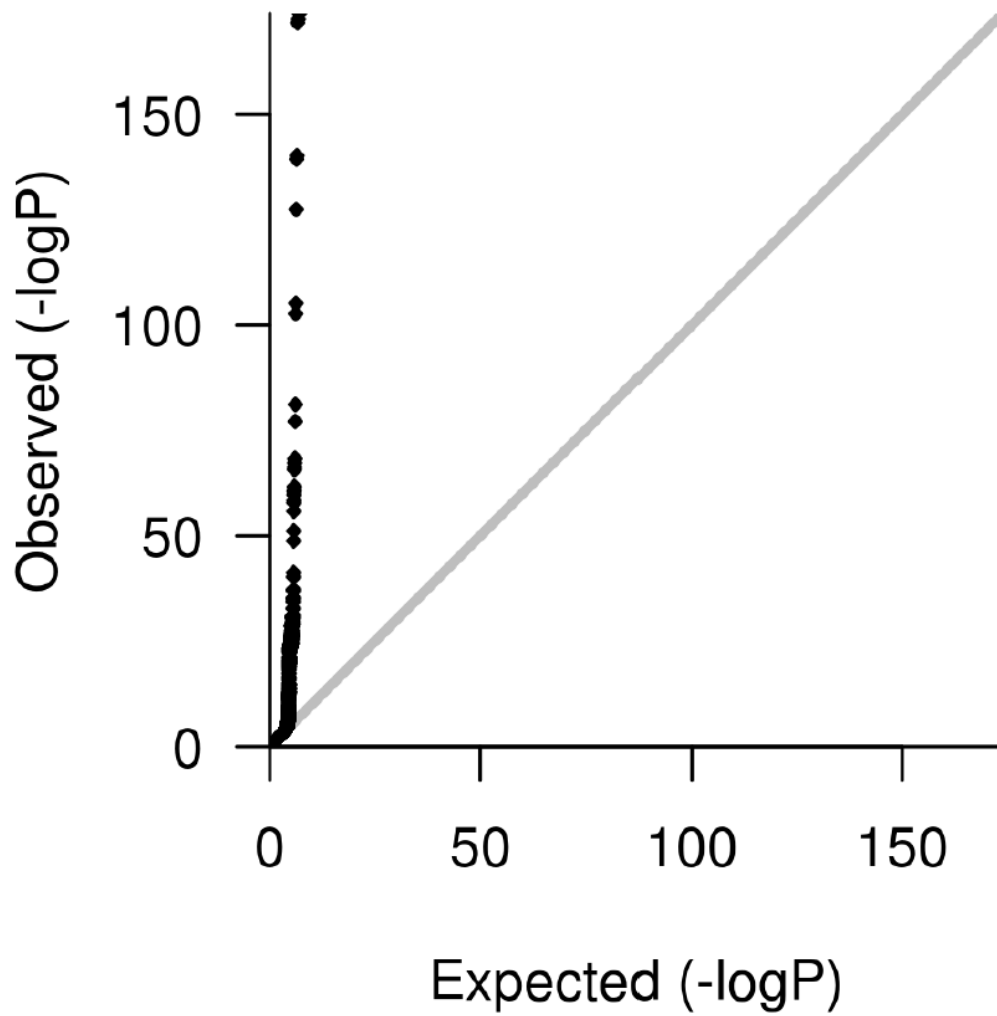


Figure S109 QQ-plot for TNF-related apoptosis inducing ligand (TRAIL).

QQ-plot for VEGF

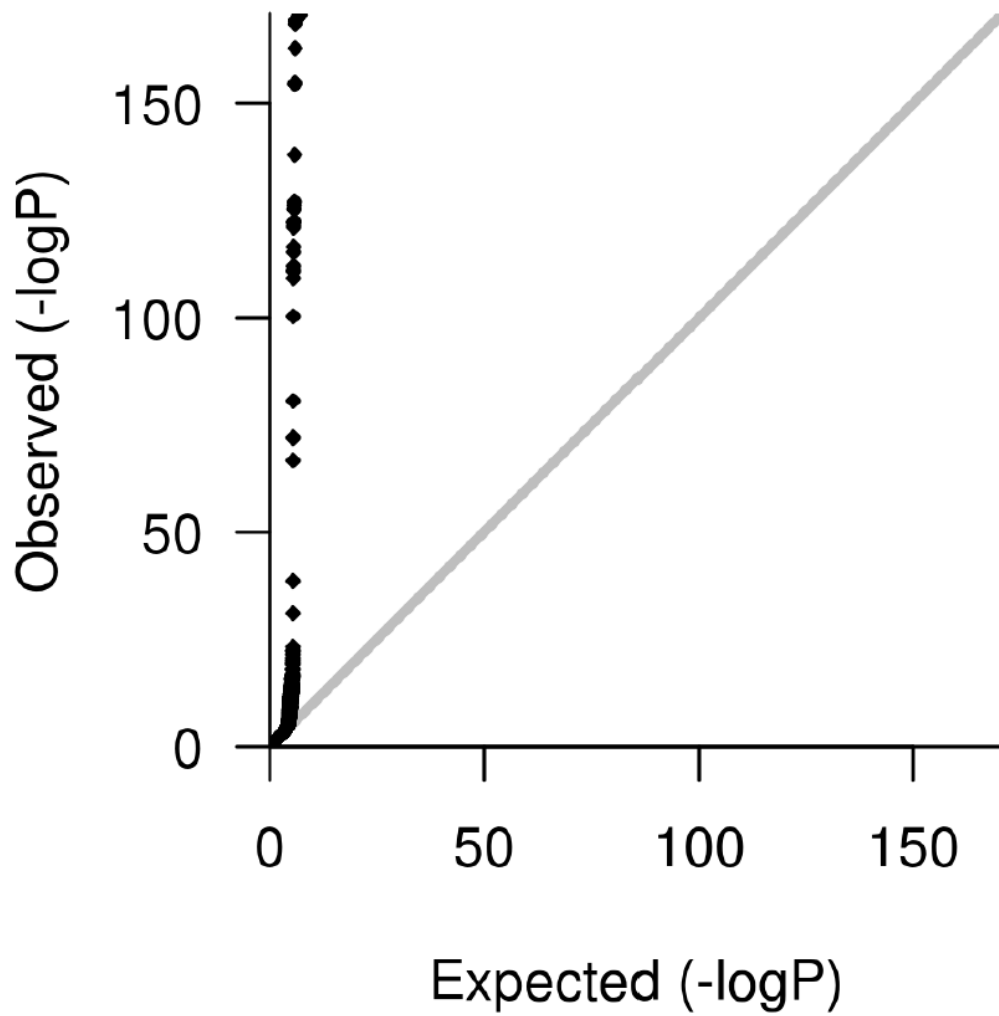


Figure S110 QQ-plot for vascular endothelial growth factor (VEGF).

CTACK - rs201003839

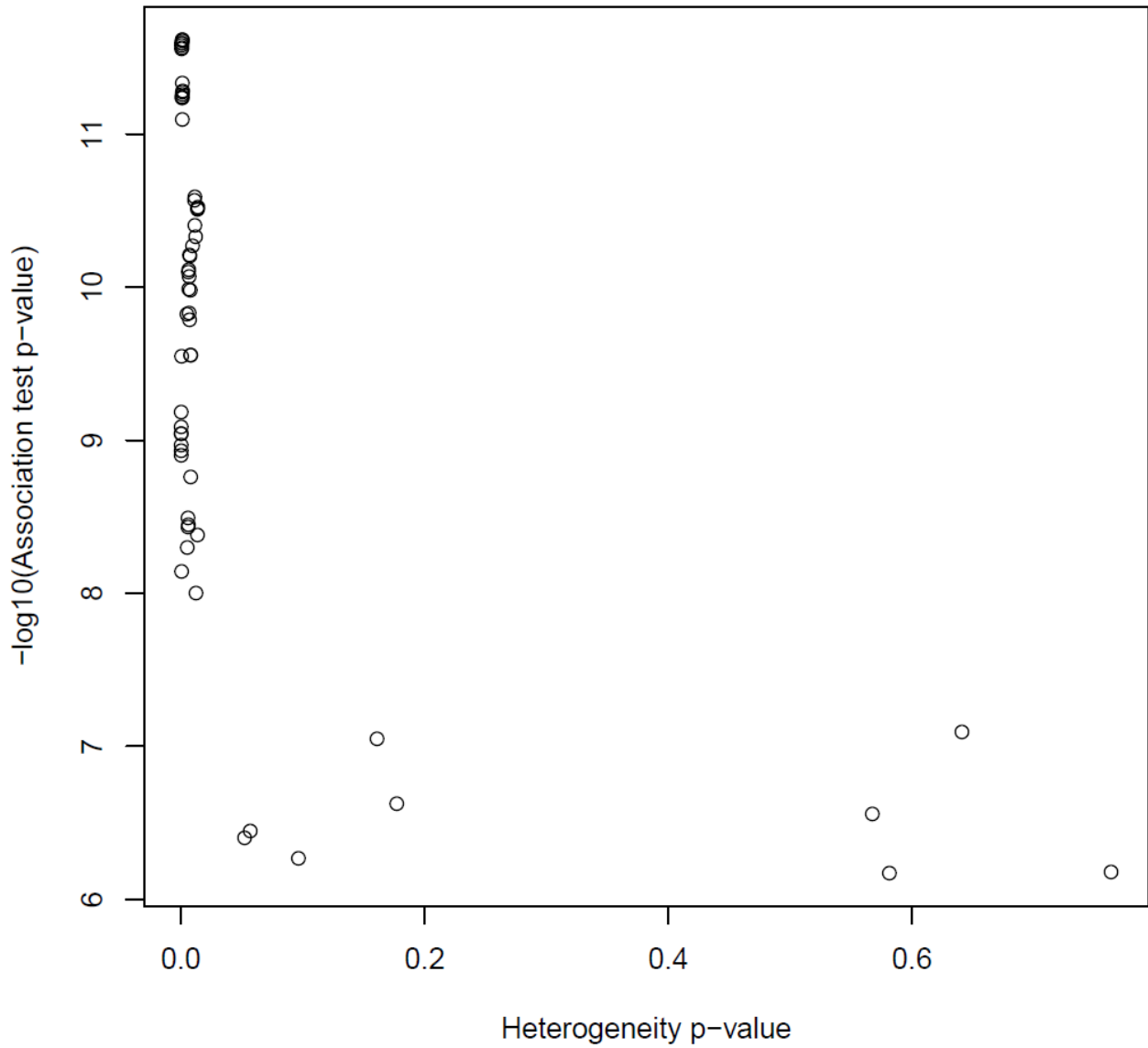


Figure S111 Heterogeneity plot for cutaneous T-cell attracting (CTACK; CCL27). Meta-analysis p-value is depicted on y-axis and heterogeneity p-value on x-axis.

CTACK - rs2070074

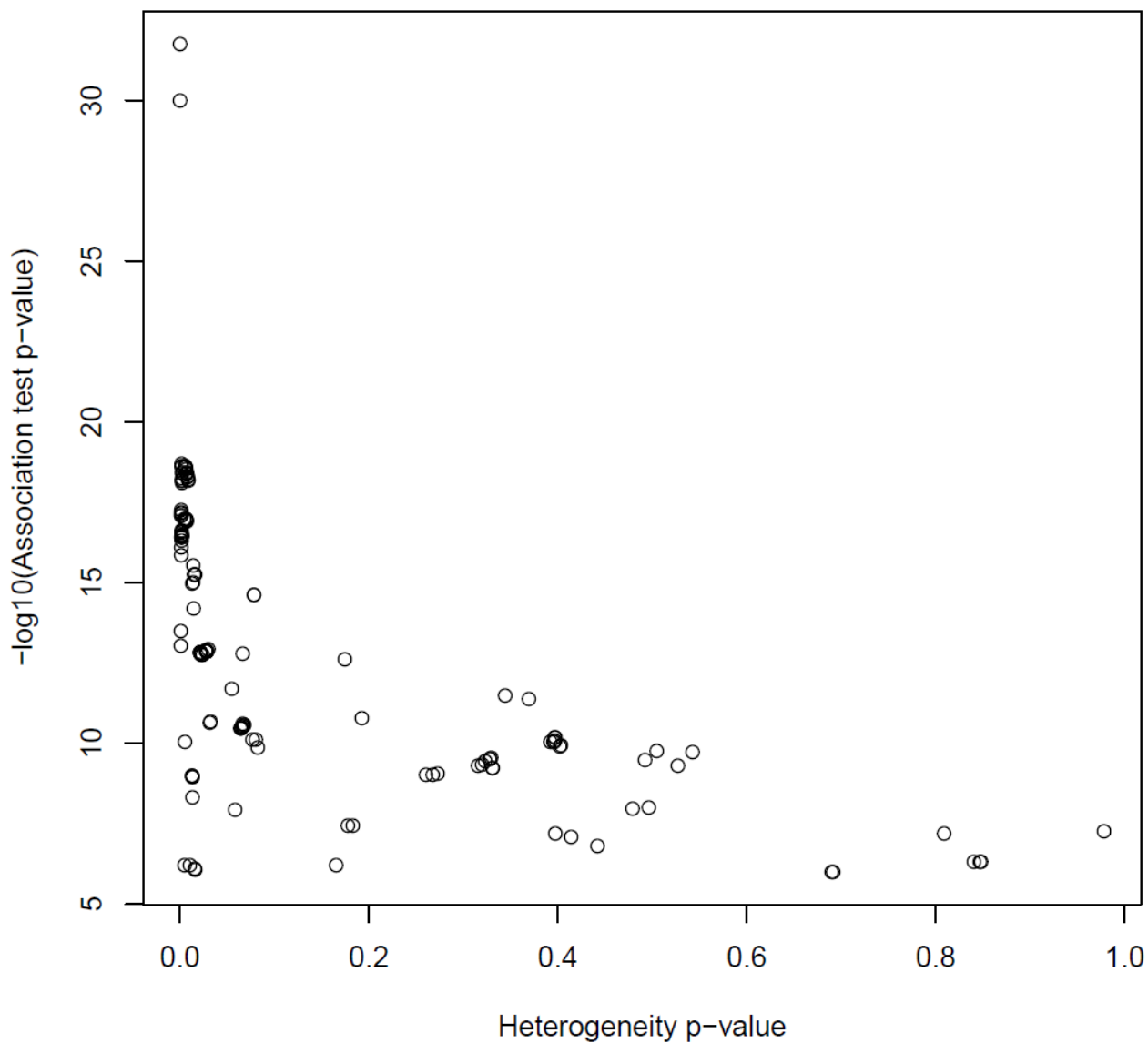


Figure S112 Heterogeneity plot for cutaneous T-cell attracting (CTACK; CCL27). Meta-analysis p-value is depicted on y-axis and heterogeneity p-value on x-axis. In 9p13.3, where the rs2070074 resides, exist SNPs without heterogeneity (Cochrane Q-test heterogeneity p-value > 0.1) and with significant association test p-value (less than 1.2×10^{-9}).

GROa - rs508977

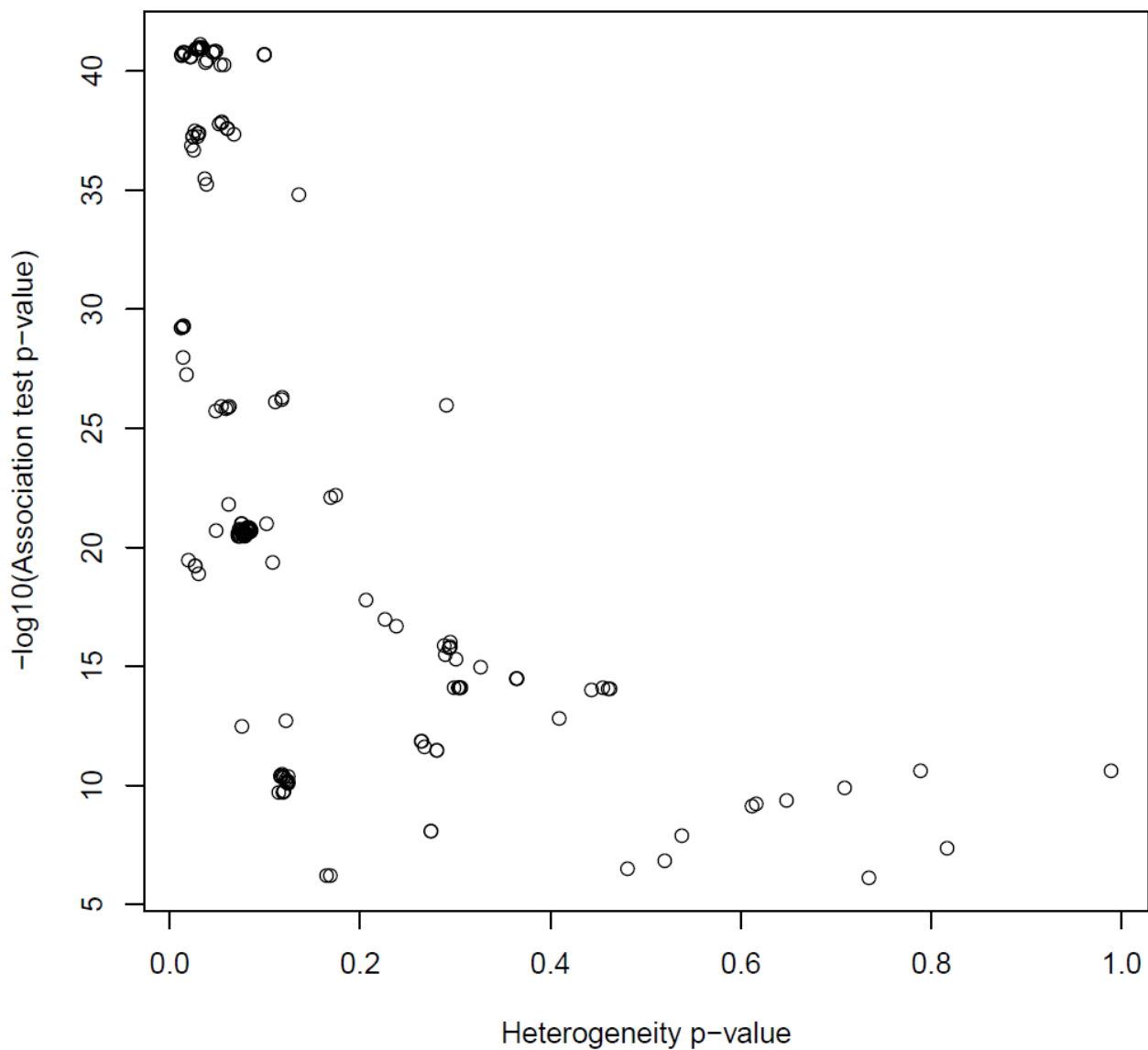


Figure S113 Heterogeneity plot for growth regulated oncogene- α (GROa; CXCL1) from 4q13.3. The lead SNP rs508977 has heterogeneity across the involved cohort but the locus contains SNPs with significant association test p-value and no heterogeneity.

IL-18 – rs385076

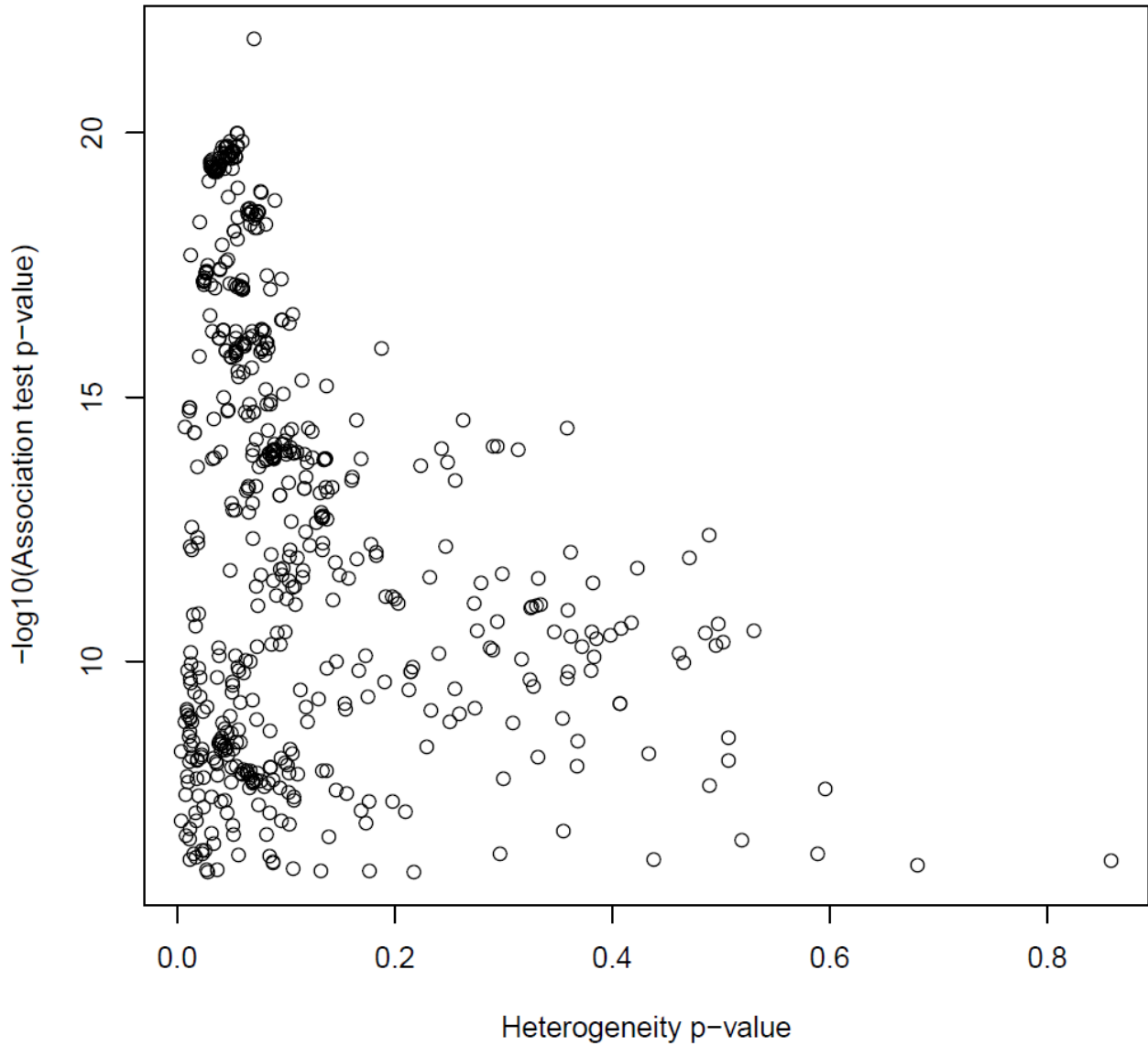


Figure S114 Heterogeneity plot for interleukin-18 (IL-18) in 2p22.3. The lead SNP rs385076 has low degree of heterogeneity in meta-analysis (heterogeneity p-value 0.07). However, the locus contains significant SNPs without heterogeneity.

MCP1 - rs12075

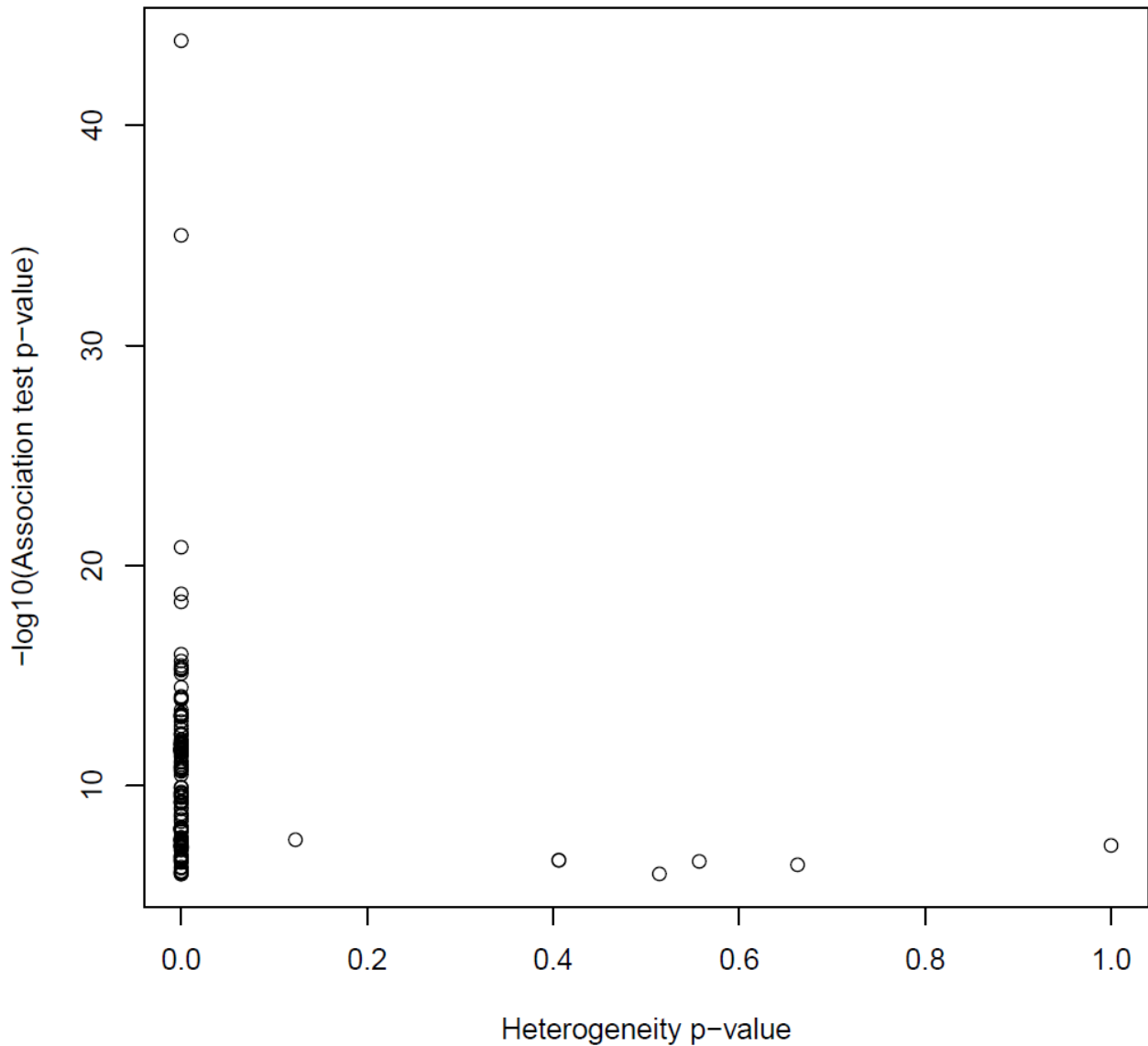


Figure S115 Heterogeneity plot monocyte chemotactic protein-1 (MCP1; CCL2). The heterogeneity is likely explained by differences in sample processing. The cytokine quantification was performed from EDTA plasma in FINRISK1997, from heparin plasma in FINRISK2002 and from serum in YFS.

MIP1b - rs113877493

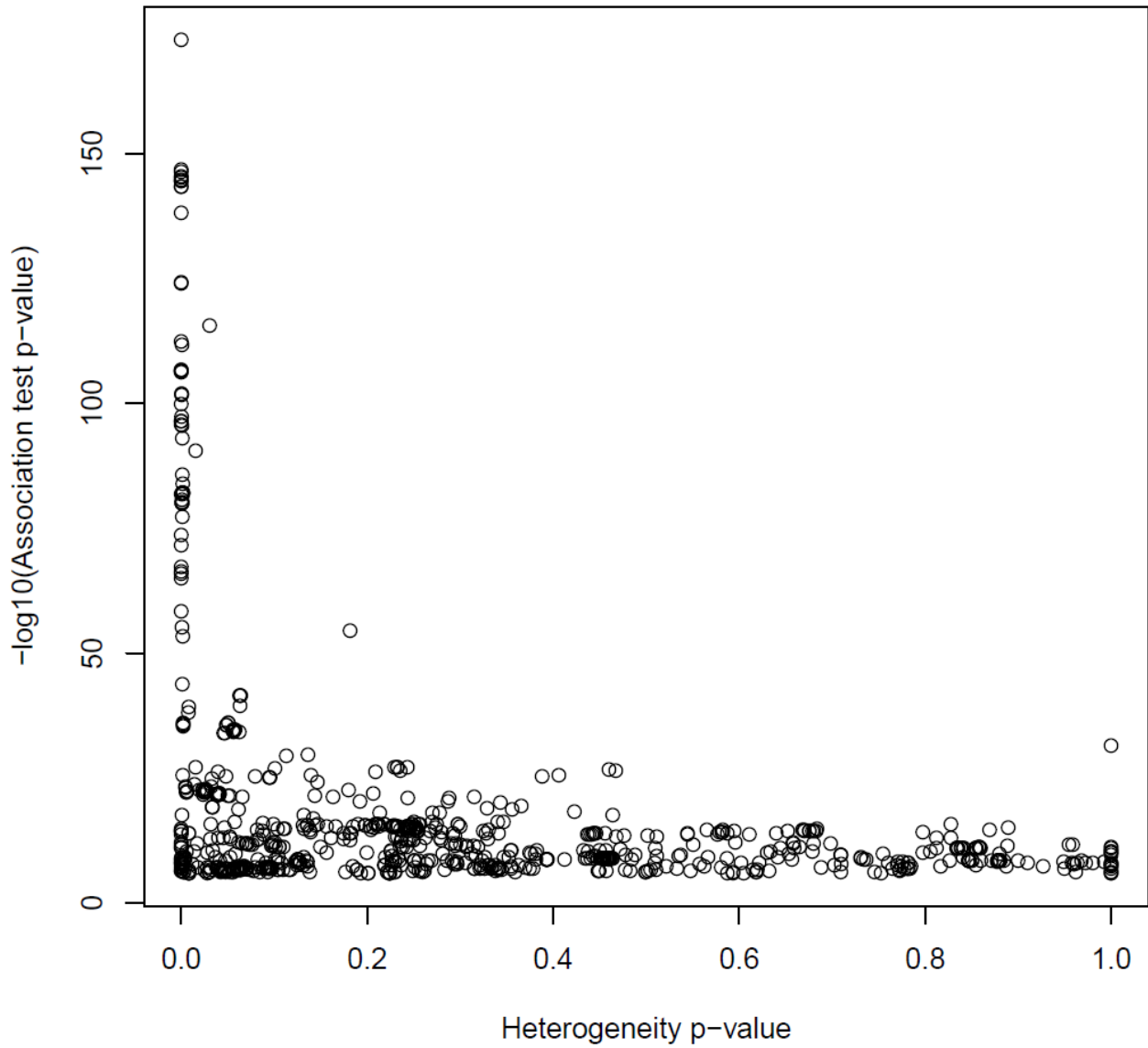


Figure S116 Heterogeneity plot for macrophage inflammatory protein-1 β (MIP1b; CCL4).

PDGFbb - rs13412535

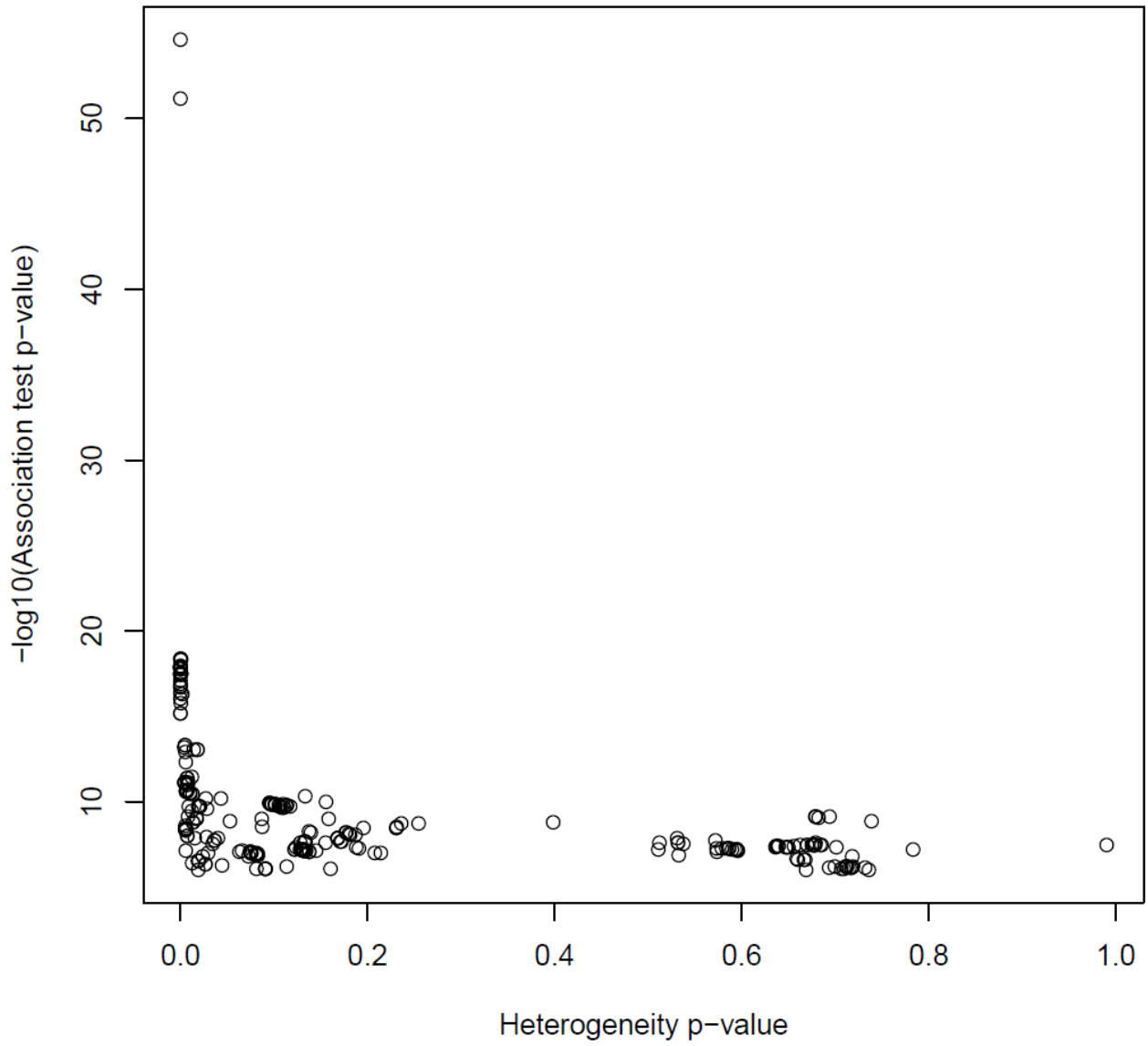


Figure S117 Heterogeneity plot for platelet derived growth factor BB (PDGFbb).

PDGFbb - rs4965869

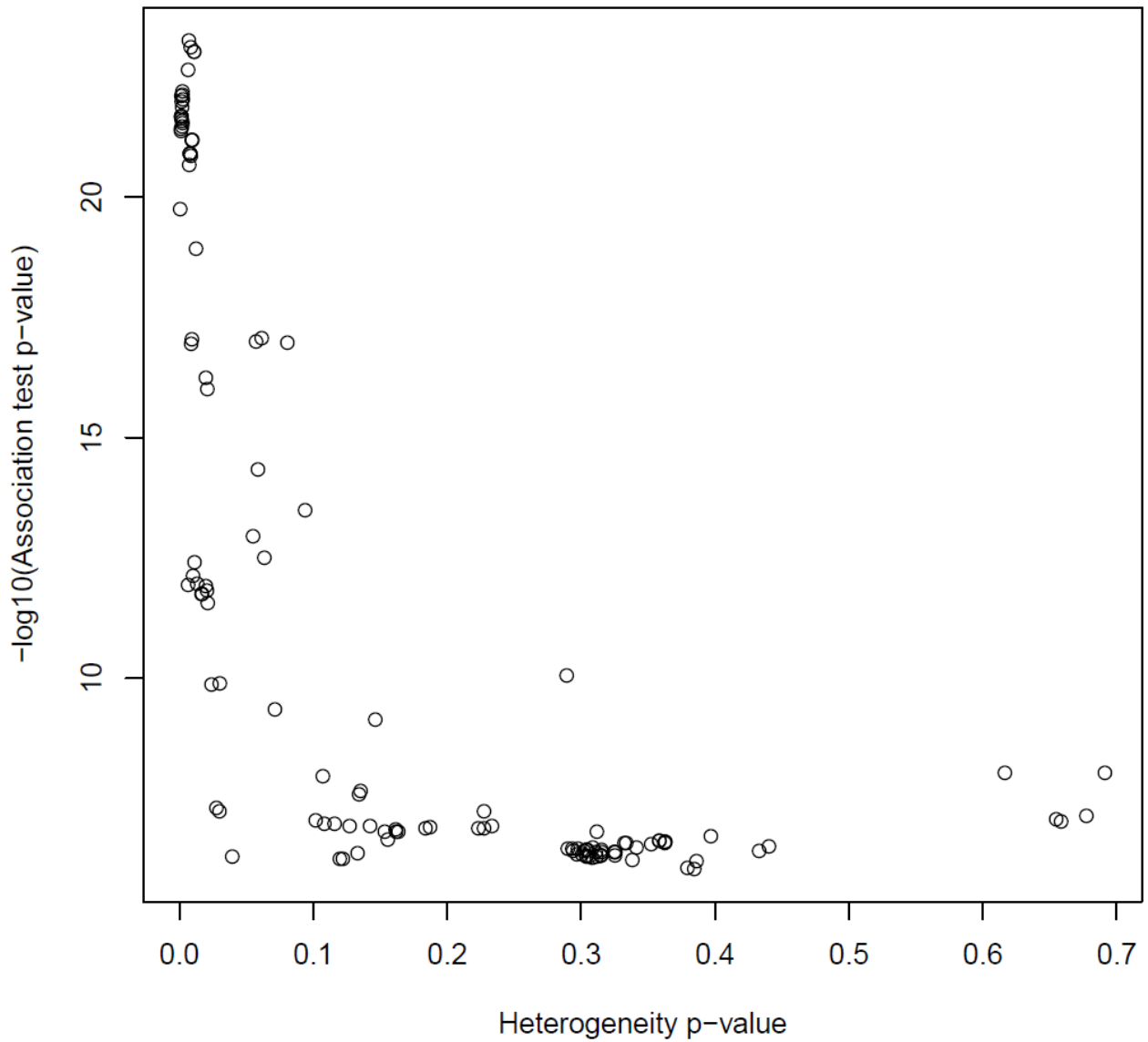


Figure S118 Heterogeneity plot for platelet derived growth factor BB (PDGFbb) from 15q26.3.

The locus contains significant associations without heterogeneity.

SCGFb - rs116924815

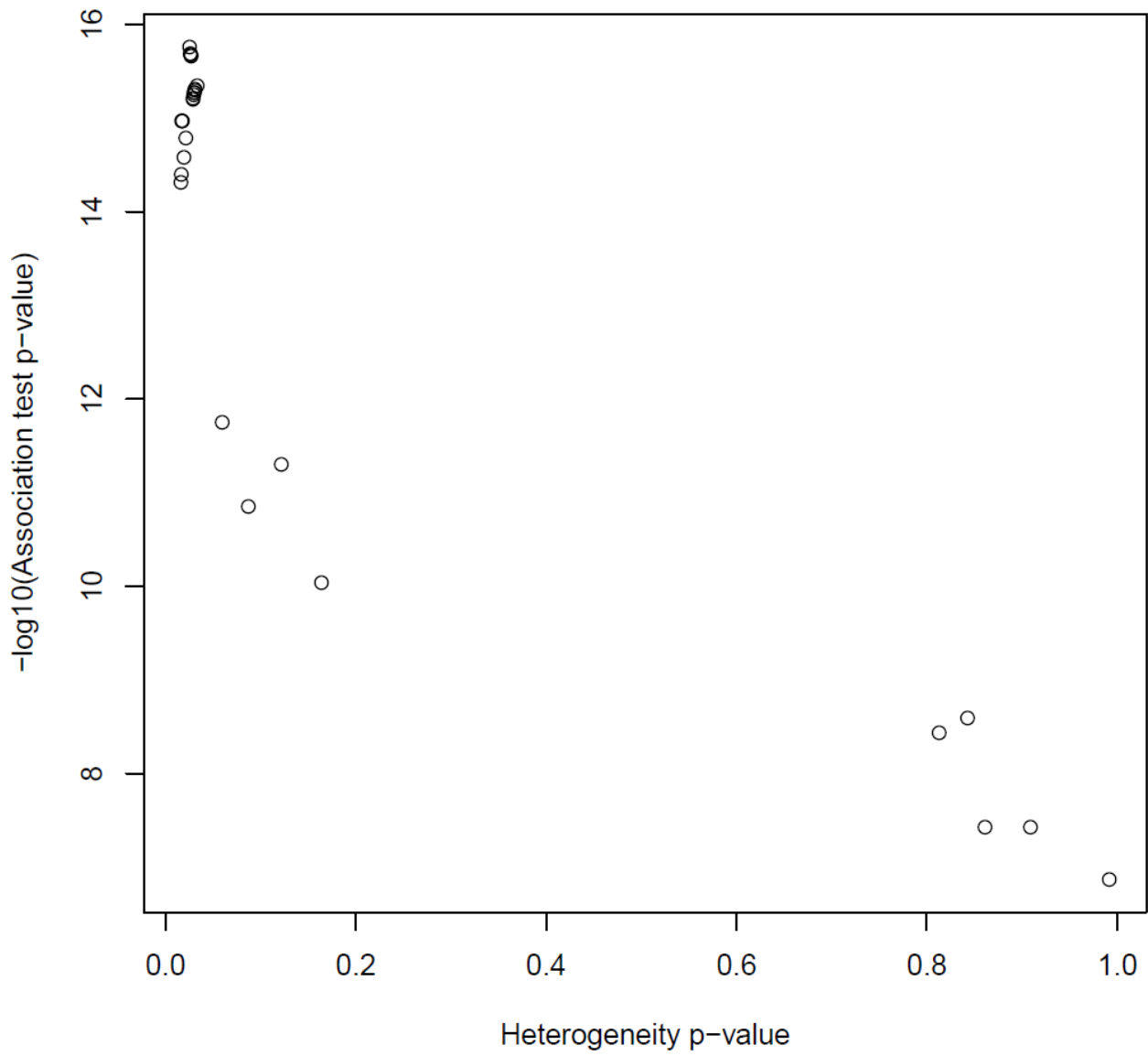


Figure S119 Heterogeneity plot for stem cell growth factor beta (SCGFb) from 19q13.33.

SCGFb - rs187503377

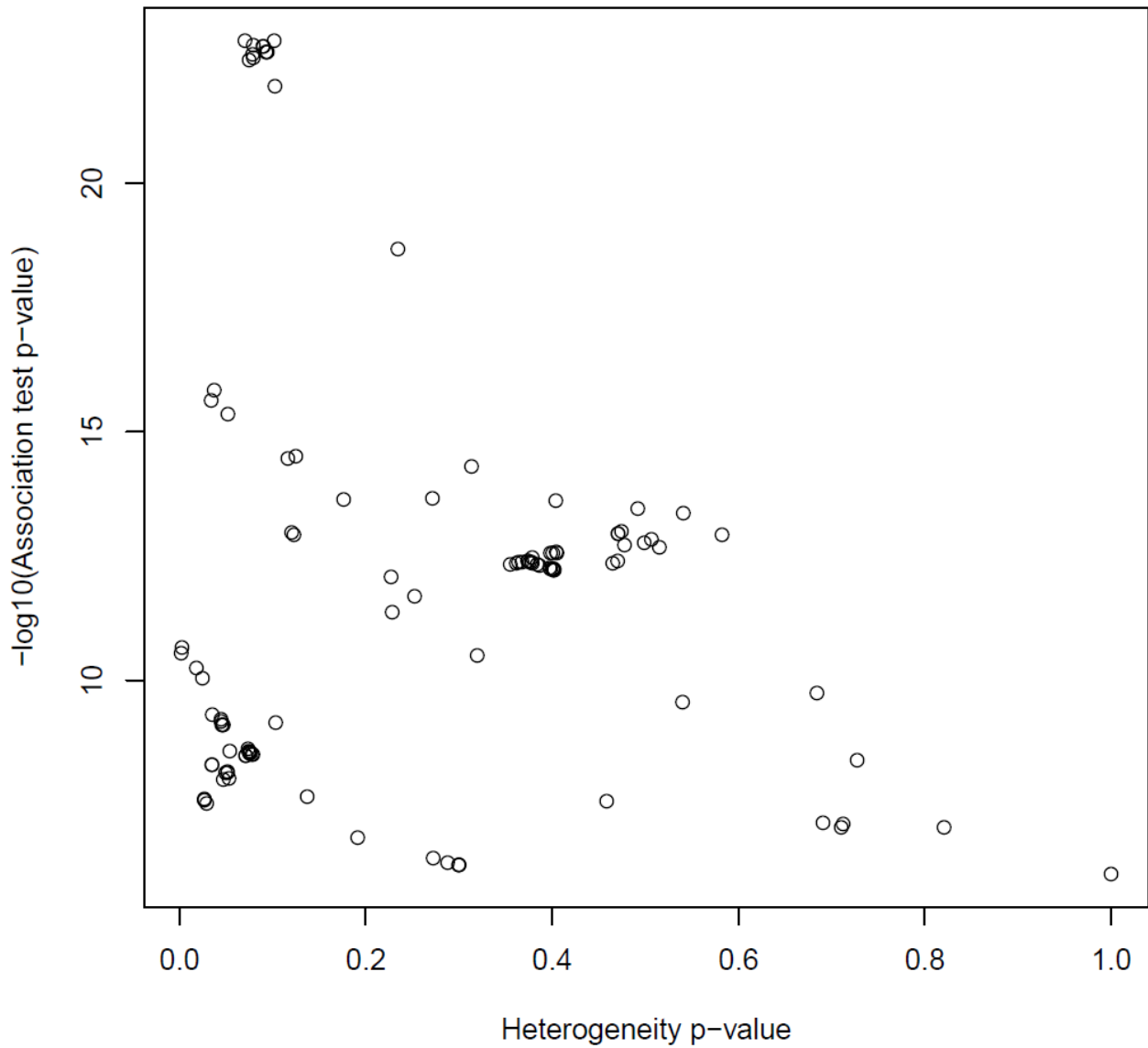


Figure S120 Heterogeneity plot for stem cell growth factor beta (SCGFb). The association between SCGFb and lead SNP rs187503377 is heterogenic across cohorts. However, the locus contains multiple significant SNPs without heterogeneity.

SCGFb - rs4656185

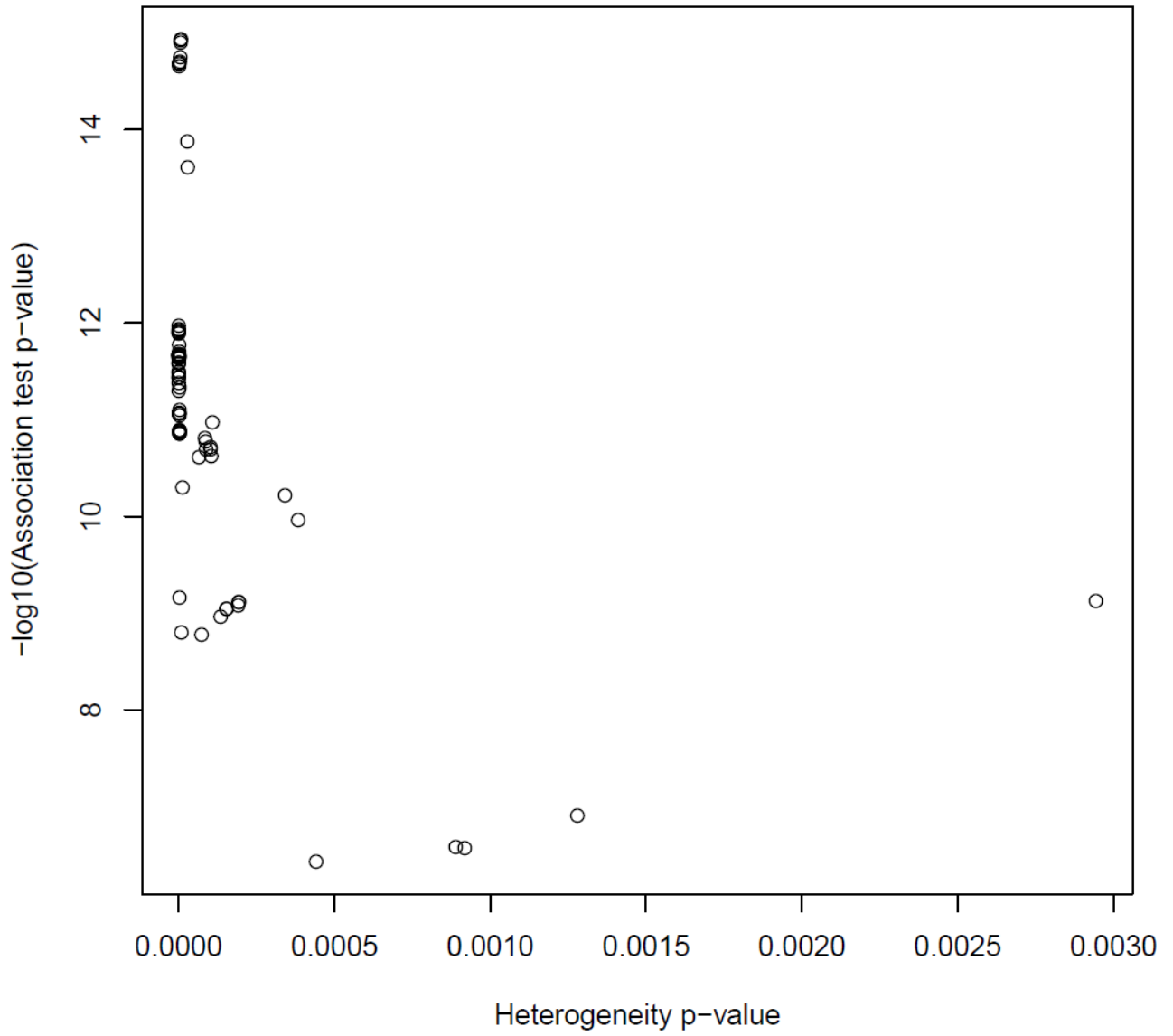


Figure S121 Heterogeneity plot for stem cell growth factor beta (SCGFb) from 1q24.2

TRAIL - rs192989810

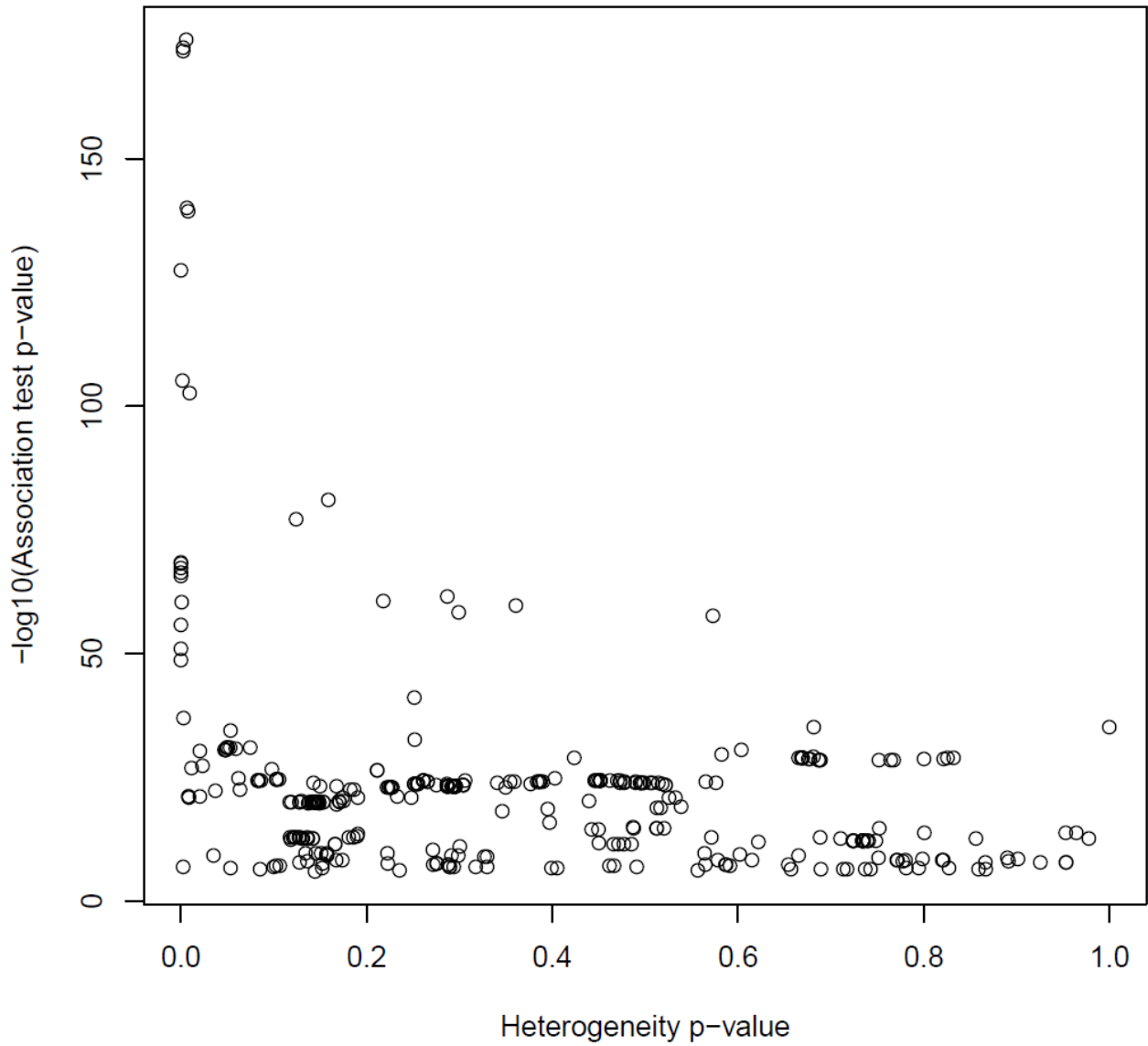


Figure S122 Heterogeneity plot for TNF-related apoptosis inducing ligand (TRAIL).

VEGF - rs6921438

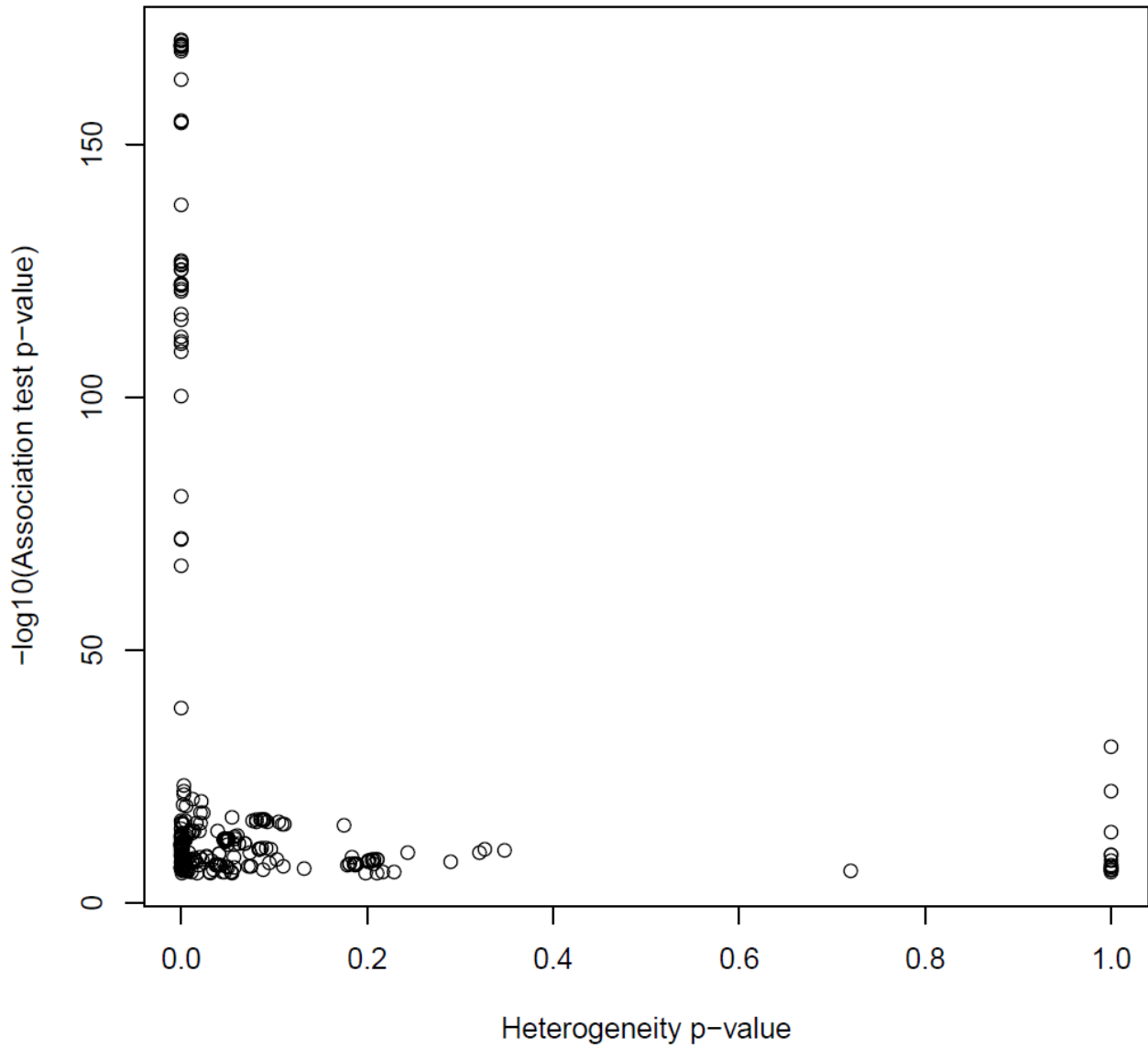


Figure S123 Heterogeneity plot for vascular endothelial growth factor. The SNP is located in 6p21.1.

VEGF - rs7030781

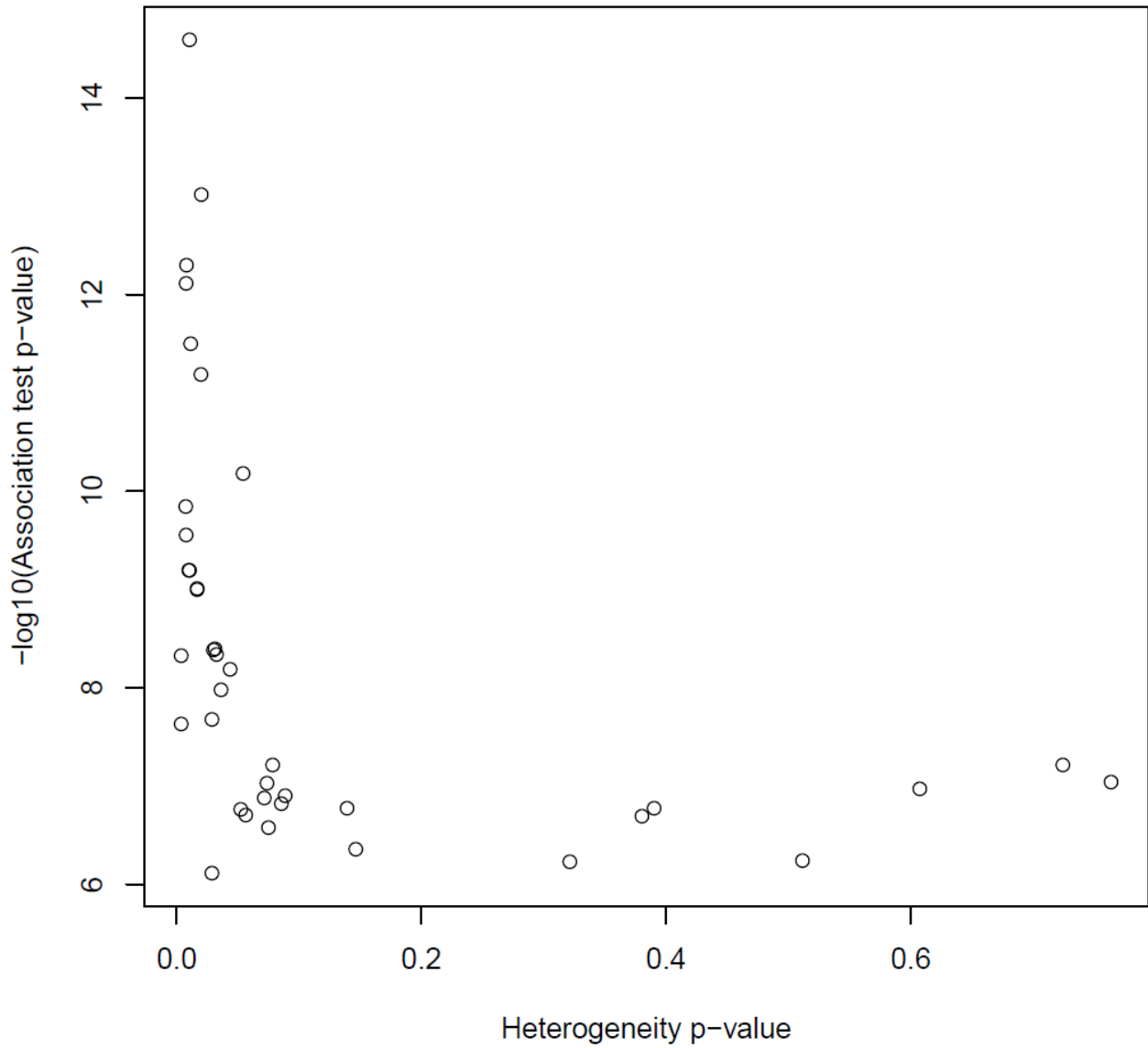


Figure S124 Heterogeneity plot for vascular endothelial growth factor (VEGF). No significant SNPs (association test p-value $< 1.2 \times 10^{-9}$) without heterogeneity can be found from this locus (9p24.2).

Table S2 Results from random effects meta-analysis for SNPs with heterogeneity p-value < 0.1 in Table 1

Cytokine	rs-id	Beta	SE	P-value
CTACK	rs201003839	0.181	0.0740	0.0147
CTACK	rs2070074	-0.430	0.1342	0.0013
Eotaxin	rs2228467	0.389	0.0566	6.72E-12
GROa	rs508977	0.376	0.0447	4.57E-17
IL-18	rs385076	0.246	0.0196	5.55E-36
MCP1	rs12075	0.267	0.2168	0.2172
MIP1b	rs113877493	-0.625	0.0809	1.05E-14
PDGFbb	rs13412535	0.369	0.1067	5.38E-04
PDGFbb	rs4965869	0.196	0.0359	4.97E-08
SCGFb	rs116924815	0.616	0.1277	1.40E-06
SCGFb	rs187503377	0.990	0.1741	1.29E-08
SCGFb	rs4656185	0.197	0.1088	0.0707
TRAIL	rs192989810	2.129	NA ^a	NA
VEGF	rs6921438	-0.534	0.1811	0.0032
VEGF	rs7030781	-0.141	0.0329	1.70E-05

^a = Could not be calculated.

Table S3 The non-heterogenic lead SNPs from the associated loci.

Cytokine	Rs-id	Gene	Locus	Position	A1	A2	MAF	Info	Beta (SD)	SE (SD)	P-value	HetPVal
MCP1	rs11453649	ACKR1	1q23.2	57697602	A	AT	0.01	0.94	0.10	0.02	2.66E-07	0.56
SCGFb	rs184243701	F5	1q24.2	158862992	T	C	0.26	0.94	-0.67	0.14	1.46E-06	0.21
IL-18	rs1090846	NLRC4	2p22.3	31816341	T	C	0.31	0.99	0.17	0.03	1.10E-11	0.36
PDGFbb	rs1035311	SERPINE2	2q36.1	225173500	T	C	0.42	0.99	0.10	0.02	1.87E-10	0.11
Eotaxin	rs10433605	ACKR2	3p22.1	42868074	T	C	0.26	0.99	0.14	0.02	1.23E-15	0.58
GROa	rs10015342	CXCL1	4q13.3	74713799	A	T	0.19	0.97	-0.19	0.03	1.86E-10	0.12
VEGF	rs1740077	VEGFA	6p21.1	43949907	T	C	0.44	1.00	0.10	0.02	1.82E-08	0.19
VEGF	rs10812481	VLDLR	9p24.2	2694596	T	C	0.22	0.93	-0.11	0.02	1.67E-07	0.39
CTACK	rs10972164	IL11RA	9p13.3	34604136	A	G	0.23	0.99	-0.18	0.03	1.16E-10	0.40
SCGFb	rs10507170	STAB2	12q23.3	104245046	A	G	0.07	0.97	-0.24	0.05	1.48E-07	0.19
PDGFbb	rs8024621	PCSK6	15q26.3	101972931	A	G	0.09	0.99	-0.15	0.03	7.00E-08	0.68
MIP1b	rs1005552	CCL4L1	17q12	34949598	T	C	0.41	1.00	0.13	0.02	1.42E-15	0.25
TRAIL	rs1020839	MEP1B	18q12.1	28989674	T	C	0.12	0.99	-0.19	0.02	1.28E-14	0.95
SCGFb	rs55716780	CLEC11A	19q13.33	51314791	T	C	0.18	0.78	0.18	0.03	1.35E-07	0.99
CTACK	rs135570	PPARA	22q13.31	46532781	A	G	0.43	1.00	-0.12	0.02	2.36E-07	0.18

Positions refers to Human Genome Build 37. A2 is the effect allele. HetPVal reports the effect size heterogeneity statistics between the cohorts.

Table S4 Raw mean cytokine concentrations in the Cardiovascular Risk in Young Finns Study by lead SNP allele

Trait	Rsid	Mean (SD)			Number of subjects		
		A1	A12	A2	A1	A12	A2
MCP1	rs12075	29.8 (36.9)	33.2 (10.2)	44 (15.7)	559	1177	707
SCGFb	rs4656185	10905.2 (4478.4)	12366.6 (5167.7)	14068.5 (5329.7)	1256	981	206
IL-18	rs385076	61.2 (32.7)	70.1 (36.8)	78.4 (40.6)	312	1033	1098
PDGFbb	rs13412535	8331.4 (2743.9)	9836.3 (3288.5)	12224.7 (4496.6)	1627	742	74
Eotaxin	rs2228467	137.2 (199.6)	159.1 (249.4)	192 (66.7)	2085	347	11
MIP1b	rs113010081	87.3 (79.3)	99 (28.8)	163.1 (67.7)	1840	560	43
IL-17	rs1530455	303.3 (152)	285.6 (118.2)	276.4 (105.3)	289	1136	1018
TRAIL	esv2656942	152.9 (122.5)	126.1 (77.6)	95.2 (30)	2260	178	5
HGF	rs3748034	543.9 (206.5)	569.6 (212.8)	582.8 (202.9)	1892	512	39
GROa	rs508977	82.1 (41.9)	100.1 (50.5)	129.3 (63.2)	1398	906	139
IP10	rs141053179	719.5 (542.9)	1193 (555.4)	NA (NA)	2405	38	0
IL-18	rs17229943	71.4 (38.4)	79.7 (38)	102.7 (46.2)	2085	346	12
VEGF	rs6921438	115.2 (49.4)	79.7 (41.3)	45.5 (23.8)	672	1247	524
HGF	rs5745687	553.7 (208.3)	505.4 (202.1)	543 (32)	2244	196	3
VEGF	rs7030781	89.1 (49.2)	82.6 (49.9)	68.2 (32.5)	832	1185	426
CTACK	rs2070074	874.9 (245)	753.7 (207)	592.2 (210.7)	1922	482	39
IL2ra	rs12722497	83.1 (59.1)	108.5 (41.9)	142.7 (44.5)	2152	283	8
VEGF	rs10761731	77 (42.6)	85.2 (50.1)	87.4 (50.7)	976	1120	347
IL-18	rs71478720	76.7 (42.4)	68.7 (32.7)	59.5 (25.4)	1395	917	131
SCGFb	rs187503377	11661.8 (4890.6)	14689.9 (5447.7)	NA (NA)	2358	85	0
IL-16	rs4778636	88 (63.9)	53.8 (47.2)	NA (NA)	2220	218	5
PDGFbb	rs4965869	8488.7 (2921.7)	9250.6 (3158.5)	10375.6 (3677.4)	1377	896	170
MIP1b	rs113877493	98.5 (83.5)	77.1 (23.8)	55.7 (11.8)	1713	660	70
TRAIL	rs192989810	140.8 (80.6)	551.5 (410.8)	NA (NA)	2386	57	0
SCGFb	rs116924815	11659 (4917)	13696 (5003)	14810 (NA)	2309	131	3
MIF	rs2330634	211.3 (182.3)	182.8 (119.7)	168.1 (140.3)	326	1146	971
CTACK	rs201003839	767.6 (217.1)	819.5 (228.5)	877.7 (254)	178	934	1331

Table S5 Genomic inflation factors from meta-analyses calculated by METAL software for each involved sample

Trait	Genomic lambda		
	YFS	FR97	FR02
bNGF	0.999	NA	1.012
CTACK	1.004	NA	0.992
Eotaxin	0.998	1.012	1.006
FGFBasic	0.999	1.007	0.997
GCSF	0.994	1.006	0.989
GROa	0.994	NA	0.986
HGF	0.986	1.018	1
IFNg	0.999	1.01	1.024
IL-10	1.004	1.003	1.007
IL-12p70	1.009	1.009	1.009
IL-13	1.006	NA	1.001
IL-16	0.997	NA	0.993
IL-17	0.997	1.011	1.011
IL-18	0.991	NA	1.007
IL-1b	0.998	NA	1.015
IL1ra	0.998	NA	1.008
IL-2	0.998	NA	1.003
IL2ra	0.993	NA	1.006
IL-4	1.001	1.017	1.009
IL-5	0.992	NA	1.004
IL-6	0.995	1.018	0.99
IL-7	1	NA	0.984
IL-8	0.996	NA	0.987
IL-9	1.008	NA	1.001
IP10	1.001	NA	1.005
MCP1	1.007	1.017	1.01
MCP3	1.004	NA	1.001
MCSF	0.99	NA	0.994
MIF	1.004	NA	0.999
MIG	0.993	NA	0.994
MIP1a	1.004	NA	1.001
MIP1b	0.999	1.008	1.003
PDGFbb	1.009	1.013	1.007
RANTES	0.993	NA	1.011
SCF	1	1.011	0.993
SCGFb	1.002	NA	0.999
SDF1a	0.994	1.017	0.995
TNFa	1.006	NA	1.001
TNFb	1.004	NA	0.998
TRAIL	0.999	1.005	0.999
VEGF	1.017	1.014	1.004

NA denotes that cytokine measurements were not available from the study.

Table S7 Variance explained by identified SNPs

Cytokine	Proportion of total variance explained
MIP1b	0.343
VEGF	0.149
TRAIL	0.141
GROa	0.096
IL-13	0.089
IL-12p70	0.076
PDGFbb	0.070
SCGFb	0.068
IL-18	0.068
IL2ra	0.066
CTACK	0.053
IL-7	0.052
IL-10	0.045
MIF	0.040
Eotaxin	0.038
IL-16	0.037
MCP1	0.036
IP10	0.034
MIG	0.022
HGF	0.012
MCP1	0.009
SCF	0.006
IL-17	0.005