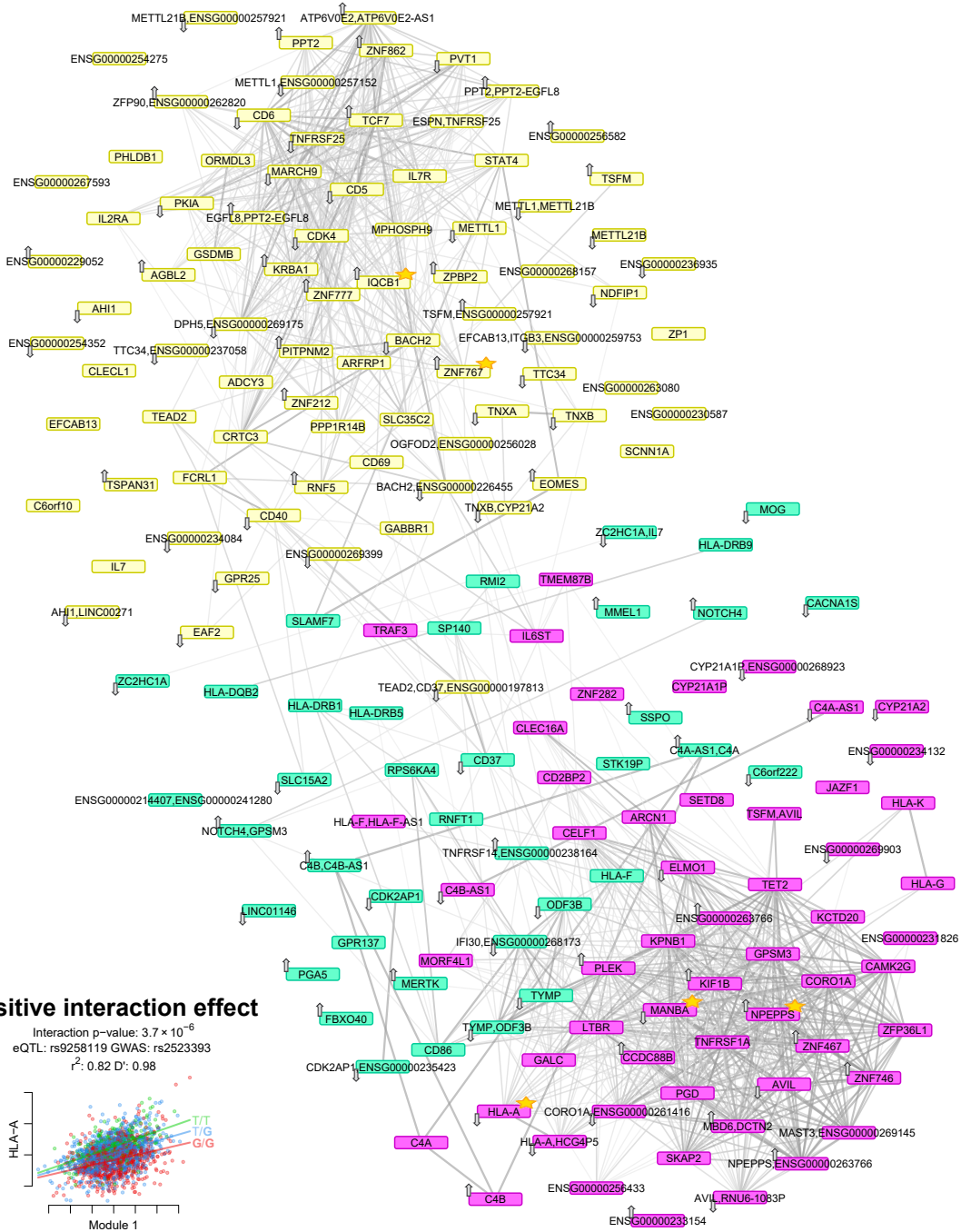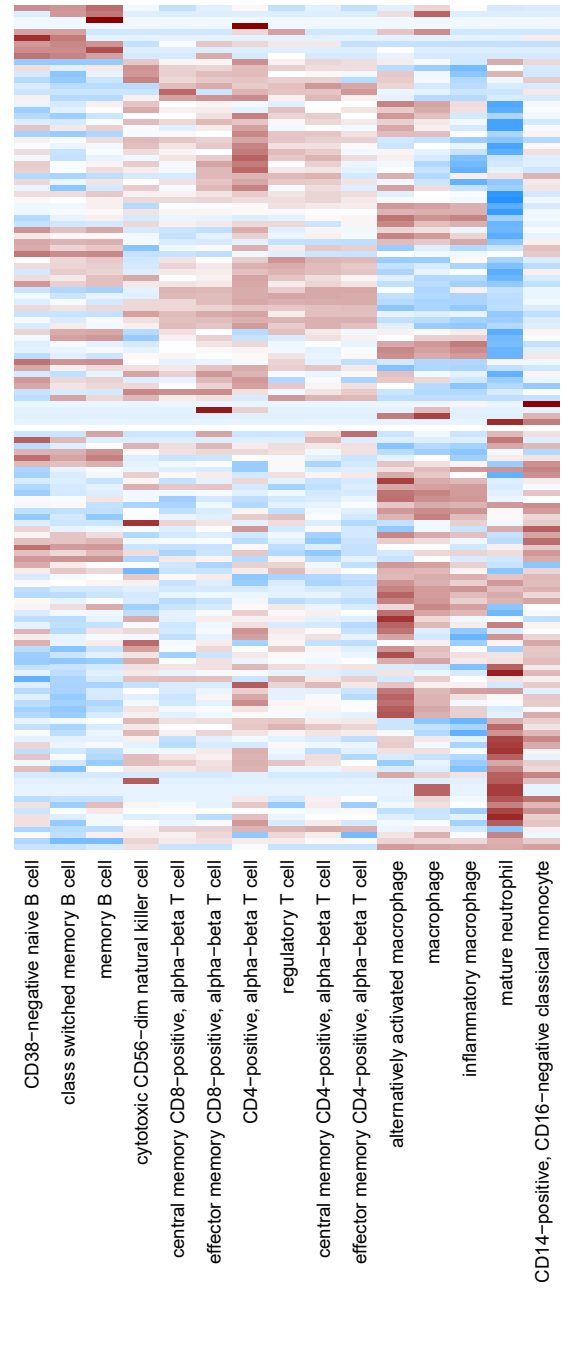# Clustering of genes with eQTL effect for Multiple sclerosis variants

Expression in Blueprint data

Function enrichment per cluster
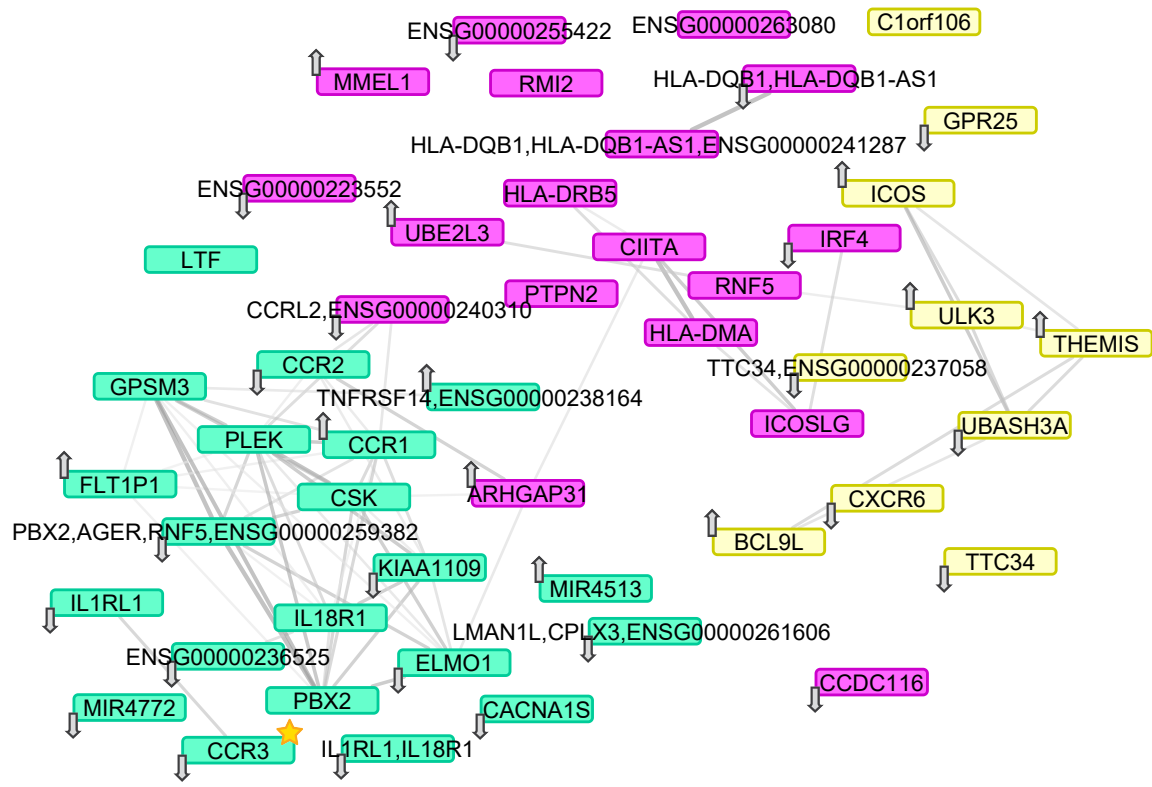
GO biological process
- regulation of lymphocyte mediated immunity
- regulation of defense response to virus by host
- regulation of immunoglobulin mediated immune response
- regulation of lymphocyte activation
- regulation of B cell mediated immunity

Reactome
- PD-1 signaling
- Generation of second messenger molecules
- TCR signaling
- Translocation of ZAP-70 to Immunological synapse
- Downstream TCR signaling

GO biological process
- positive regulation of B cell proliferation
- regulation of B cell proliferation
- adaptive immune response
- adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
- cellular response to interferon-gamma

Reactome
- Interferon gamma signaling
- Interleukin receptor SHC signaling
- Interleukin-2 signaling
- Interleukin-3, 5 and GM-CSF signaling
- Signaling by Interleukins

GO biological process
- positive regulation of innate immune response
- regulation of innate immune response
- MyD88-independent toll-like receptor signaling pathway
- Toll signaling pathway
- nerve growth factor receptor signaling pathway

Reactome
- Signaling by Interleukins
- Signalling by NGF
- Negative regulators of RIG-I/MDA5 signaling
- MyD88-independent cascade initiated on plasma membrane
- Signaling by SCF-KIT

Genes with any type of QTL effect in LD with GWAS hit colored based on clustering

Gene

⬆ Risk allele increases gene expression

⬇ Risk allele lowers gene expression

⭐ eQTL has interaction with a module

Expression

Positive interaction effect

Interaction p−value: 3.7×10^{-6}
eQTL: rs9258119 GWAS: rs2523393
r^2: 0.82 D': 0.98

HLA−A

T/T
T/G
G/G

Module 1

Heatmap columns:
CD38−negative naive B cell; class switched memory B cell; memory B cell; cytotoxic CD56−dim natural killer cell; central memory CD8−positive, alpha−beta T cell; effector memory CD8−positive, alpha−beta T cell; CD4−positive, alpha−beta T cell; regulatory T cell; central memory CD4−positive, alpha−beta T cell; effector memory CD4−positive, alpha−beta T cell; alternatively activated macrophage; macrophage; inflammatory macrophage; mature neutrophil; CD14−positive, CD16−negative classical monocyte

Clustering of genes with eQTL effect for Celiac Disease variants

Expression in Blueprint data

Function enrichment per cluster

Cluster labels (left network):
C1orf106, ENSG00000255422, ENSG00000263080, MMEL1, RMI2, HLA-DQB1,HLA-DQB1-AS1, GPR25, HLA-DQB1,HLA-DQB1-AS1,ENSG00000241287, ENSG00000223552, HLA-DRB5, ICOS, UBE2L3, CIITA, IRF4, LTF, PTPN2, RNF5, RNF5, HLA-DMA, ULK3, CCRL2,ENSG00000240310, THEMIS, CCR2, TTC34,ENSG00000237058, GPSM3, TNFRSF14,ENSG00000238164, UBASH3A, PLEK, CCR1, ICOSLG, FLT1P1, CSK, ARHGAP31, CXCR6, PBX2,AGER,RNF5,ENSG00000259382, KIAA1109, BCL9L, IL1RL1, MIR4513, TTC34, ENSG00000236525, IL18R1, LMAN1L,CPLX3,ENSG00000261606, MIR4772, ELMO1, CCDC116, CCR3, PBX2, IL1RL1,IL18R1, CACNA1S

GO biological process
- positive regulation of T cell activation
- positive regulation of lymphocyte activation
- positive regulation of leukocyte activation
- B cell apoptosis
- positive regulation of cell activation

Reactome
- Downstream TCR signaling
- Interferon gamma signaling
- TCR signaling
- Cytokine Signaling in Immune system
- Interferon Signaling

GO biological process
- regulation of interleukin-1 beta production
- phosphatidylinositol 3-kinase cascade
- T cell differentiation in thymus
- positive regulation of viral genome replication
- regulation of interleukin-1 production

Reactome
- PERK regulated gene expression
- Activation of Genes by ATF4
- RNA Polymerase II Transcription Pre-Initiation And Promoter Opening
- RNA Polymerase II Transcription Initiation And Promoter Clearance
- HIV-1 Transcription Initiation

GO biological process
- regulation of lymphocyte activation
- regulation of leukocyte activation
- cytosolic calcium ion homeostasis
- elevation of cytosolic calcium ion concentration
- B cell proliferation

Reactome
- Generation of second messenger molecules
- Interleukin-2 signaling
- Interleukin receptor SHC signaling
- Adaptive Immune System
- Regulation of KIT signaling

Heatmap column labels:
CD38-negative naive B cell; class switched memory B cell; memory B cell; cytotoxic CD56-dim natural killer cell; central memory CD8-positive, alpha-beta T cell; effector memory CD8-positive, alpha-beta T cell; CD4-positive, alpha-beta T cell; regulatory T cell; central memory CD4-positive, alpha-beta T cell; effector memory CD4-positive, alpha-beta T cell; alternatively activated macrophage; macrophage; inflammatory macrophage; mature neutrophil; CD14-positive, CD16-negative classical monocyte

Legend:
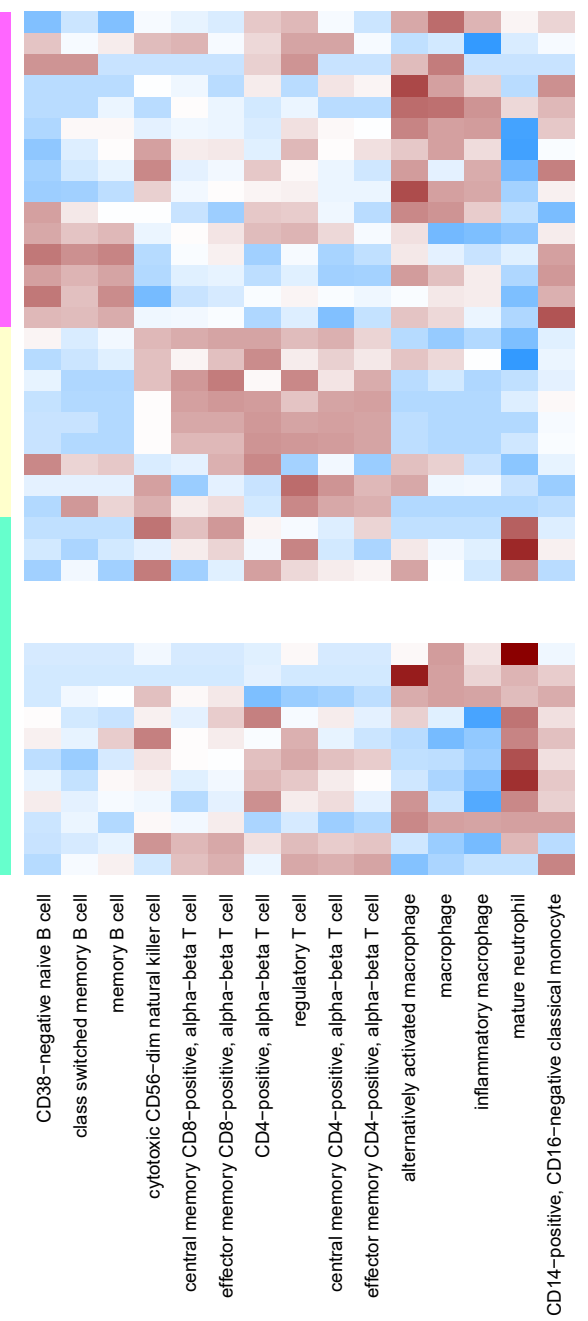- Gene — Genes with any type of QTL effect in LD with GWAS hit colored based on clustering
- Risk allele increases gene expression
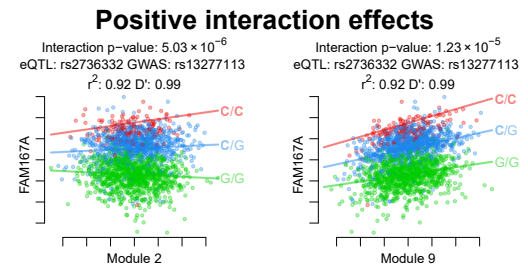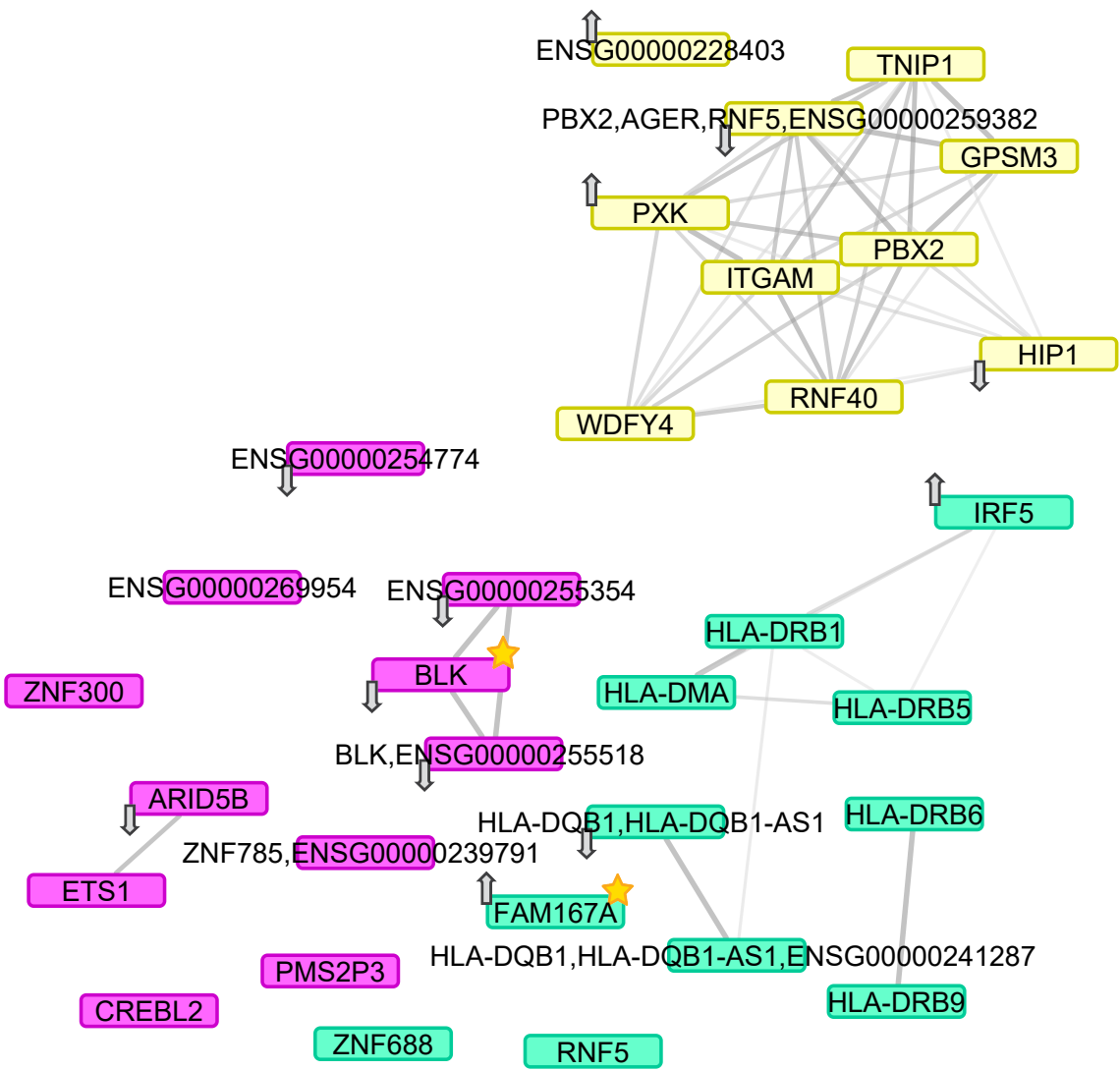- Risk allele lowers gene expression
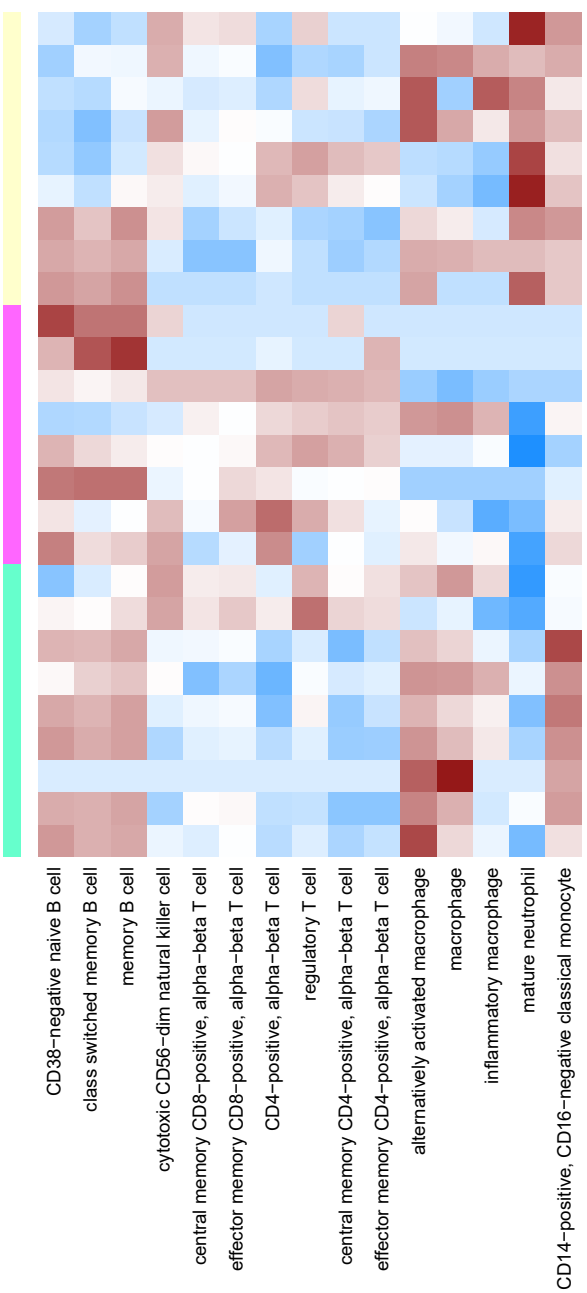- eQTL has interaction with a module
- Expression

Clustering of genes with eQTL effect for Systemic Lupus Erythematosus variants

ENSG00000228403
TNIP1
PBX2,AGER,RNF5,ENSG00000259382
GPSM3
PXK
PBX2
ITGAM
HIP1
RNF40
WDFY4
ENSG00000254774
IRF5
ENSG00000269954
ENSG00000255354
HLA-DRB1
BLK
HLA-DMA
HLA-DRB5
ZNF300
BLK,ENSG00000255518
ARID5B
HLA-DQB1,HLA-DQB1-AS1
HLA-DRB6
ZNF785,ENSG00000239791
ETS1
FAM167A
PMS2P3
HLA-DQB1,HLA-DQB1-AS1,ENSG00000241287
CREBL2
HLA-DRB9
ZNF688
RNF5

Positive interaction effects

Interaction p−value: 5.03×10^{-6}
eQTL: rs2736332 GWAS: rs13277113
r^2: 0.92 D': 0.99

FAM167A
C/C
C/G
G/G
Module 2

Interaction p−value: 1.23×10^{-5}
eQTL: rs2736332 GWAS: rs13277113
r^2: 0.92 D': 0.99

FAM167A
C/C
C/G
G/G
Module 9

Expression in Blueprint data

CD38−negative naive B cell
class switched memory B cell
memory B cell
cytotoxic CD56−dim natural killer cell
central memory CD8−positive, alpha−beta T cell
effector memory CD8−positive, alpha−beta T cell
CD4−positive, alpha−beta T cell
regulatory T cell
central memory CD4−positive, alpha−beta T cell
effector memory CD4−positive, alpha−beta T cell
alternatively activated macrophage
macrophage
inflammatory macrophage
mature neutrophil
CD14−positive, CD16−negative classical monocyte

Function enrichment per cluster

GO biological process
• myeloid leukocyte activation
• phagocytosis
• endocytosis
• membrane invagination
• regulation of MAP kinase activity

Reactome
• Signal regulatory protein (SIRP) family interactions
• Interferon gamma signaling
• Interleukin-3, 5 and GM-CSF signaling
• Regulation of signaling by CBL
• Interleukin-2 signaling

GO biological process
• regulation of immunoglobulin mediated immune response
• regulation of B cell mediated immunity
• positive regulation of bone resorption
• positive regulation of bone remodeling
• regulation of DNA recombination

Reactome
• Cross-presentation of soluble exogenous antigens (endosomes)
• Regulation of Apoptosis
• N-Glycan antennae elongation
• Ubiquitin-dependent degradation of Cyclin D1
• Ubiquitin-dependent degradation of Cyclin D

GO biological process
• regulation of T-helper 1 type immune response
• positive regulation of T-helper cell differentiation
• positive regulation of T cell activation
• regulation of lymphocyte differentiation
• positive regulation of T cell differentiation

Reactome
• Costimulation by the CD28 family
• PD-1 signaling
• Translocation of ZAP-70 to Immunological synapse
• Phosphorylation of CD3 and TCR zeta chains
• Regulation of Insulin-like Growth Factor (IGF) Activity by Insulin-like Growth Factor Binding Proteins (IGFBPs)

Gene — Genes with any type of QTL effect in LD with GWAS hit colored based on clustering

⬆ Risk allele increases gene expression

⬇ Risk allele lowers gene expression

★ eQTL has interaction with a module

Expression