

Supplementary Figures

Table S1. Full table of Global meta-analysis (GAMMA²⁵) scores predicted associations with CXorf21 based compilation of publicly available microarray data

Predicted association	Scores
IRF4	117
B cell activation	115
B cell antigen receptor	108
dendritic cell	102
VAV1	97
CD32	88
B Cells	85
CD38	73
DAP12	73
T cell activation	71
IL-4	71
MHC class II	69
T Cells	66
SH2D1A	66
chronic lymphocytic leukemia	65
CD22	64
CD86	63
CARMA1	63
CD11B	61
ZAP-70	61
RAC2	58
Monocytes	55
tyrosine phosphorylation	55
T cell development	55

linker for activation of T cells	55
SYK	54
TLR2	54
Macrophages	53
CD19	53
CD80	52
TLR7	52
AML	51
IFN-gamma	50
CR2	50
innate immunity	49
CCR7	49
LYN	49
class switch recombination	49
B-cell lymphoma	48
signal transduction	47
pleckstrin	47
p65	47
B cell development	47
B-CLL	46
OCA-B	46
cytokine production	45
cell surface receptors	45
LFA-1	45
ERK1	44
F-actin	44
NK cells	43
systemic lupus erythematosus	43

T cell proliferation	43
antigen presentation	43
type I IFN	43
B cell proliferation	43
collagen receptor	42
Toll-Like Receptors	41
CD69	41
HLA-DRA	40
Bcr-Abl	39
SH3 domain	39
Interferon	38
TLR4	38
hematopoietic stem cell	38
C-Kit	38
cell surface	37
rheumatoid arthritis	37
IL-6	37
SLP-76	37
immunological synapse	37
NF-kappaB	36
CD28	36
p38 MAPK	36
BCL6	36
signaling lymphocytic activation molecule	36
lipid rafts	36
lymphocyte activation	36
T cell antigen	36

proinflammatory cytokines	35
tyrosine kinase	35
MHC class I	35
MHC	35
CD8+ T cells	35
CD45	35
protein kinase C	35
GPVI	35
B29	35
immunoreceptor	34
cytoplasmic domain	34
Granulocytes	34
IL-2	34
JNK	34
STAT3	34
CD14	34
STAT1	34
IL-2 receptor	34
A20	34
inflammatory response	33
tyrosine phosphatase	33
CD40L	33
antigen receptor	33
PU.1	32
autoimmune diseases	32
mitogen-activated protein kinase	32
wiskott-Aldrich syndrome protein	32
cd4+ T cell	31

CXCR4	31
Chemokine Receptor	31
actin polymerization	31
B cell differentiation	31
IL-10	30
IL-1beta	30
Chemokine	30
SHP-1	30
cell motility	30
plasma cell differentiation	30
immune response	29
CD4	29
chemotaxis	29
GM-CSF	29
PKB	29
IFN-gamma production	28
IFN-ALPHA	28
heterodimer	28
Melanoma	28
CD2	28
GEF	28
CD16	27
Integrin	27
Leukemia	27
hematopoiesis	27
ERK2	27
COLORECTAL CANCER	27
IL-3	27

memory B cells	27
M-CSF	26
C-FMS	26
Phosphatidylinositol 3-Kinase	26
c-Jun	26
protein tyrosine phosphatase	26
activated macrophages	26
CD18	26
CD44	26
kinase activity	26
C-CBL	26
IL-8	25
phagocytosis	24
adapter protein	24
NK receptors	24
Src family kinases	24
RANTES	24
CDC42	24
cell migration	24
G protein-coupled receptors	24
actin cytoskeleton	24
multiple sclerosis	23
Thymocytes	23
adhesion molecules	23
Normal B cells	23
Tumor suppressor	23
oncogene	23
NF-kappaB activation	22

DNA methylation	22
eosinophils	21
homing	21
ICAM-1	21
PTEN	21
extracellular signal-regulated	20
Caspase	20
Colitis	20
NSCLC	20
receptor tyrosine kinase	19
IL-12	19
CD49D	19
cytokine secretion	18
IL-18	18
STAT5	18
dephosphorylation	17
leukocyte antigen	17
RHOA	17
cell maturation	17
CD63	17
PKC-delta	17
RANKL	16
Zymosan	16
CHRONIC MYELOID LEUKEMIA	16
Hypermethylation	16
TP53	16
activator of transcription	16
neuroinflammation	16

promyelocytic leukemia	16
JAK1	16
peritoneal macrophages	15
NADPH Oxidase	15
beta-catenin	15
SCID	15
IL-17	15
alternatively spliced	14
ubiquitination	14
MULTIPLE MYELOMA	12
Caspase-8	12
regulatory T cells	11
inhibition of apoptosis	11
MAPK signaling	10
CREB	10
transcription start site	10

TABLE S1. CXorf21 is an immune related protein. Complete table of Global meta-analysis (GAMMA²⁵) scores predicted associations with CXorf21 based compilation of publicly available microarray data and literature search

Figure S1. <http://ds.biogps.org/?dataset=GSE1133&gene=80231> BIOGPS: Expression of CXorf21 in human primary cells. This meta-analysis of 745 human primary cell samples shows changes in expression levels of CXorf21 (probe:220252_x_at) in both immune and non-immune related samples. Original source of these meta-data, Mabbot et al [29,30] combined over 100 publicly available microarray datasets derived from human primary cells.

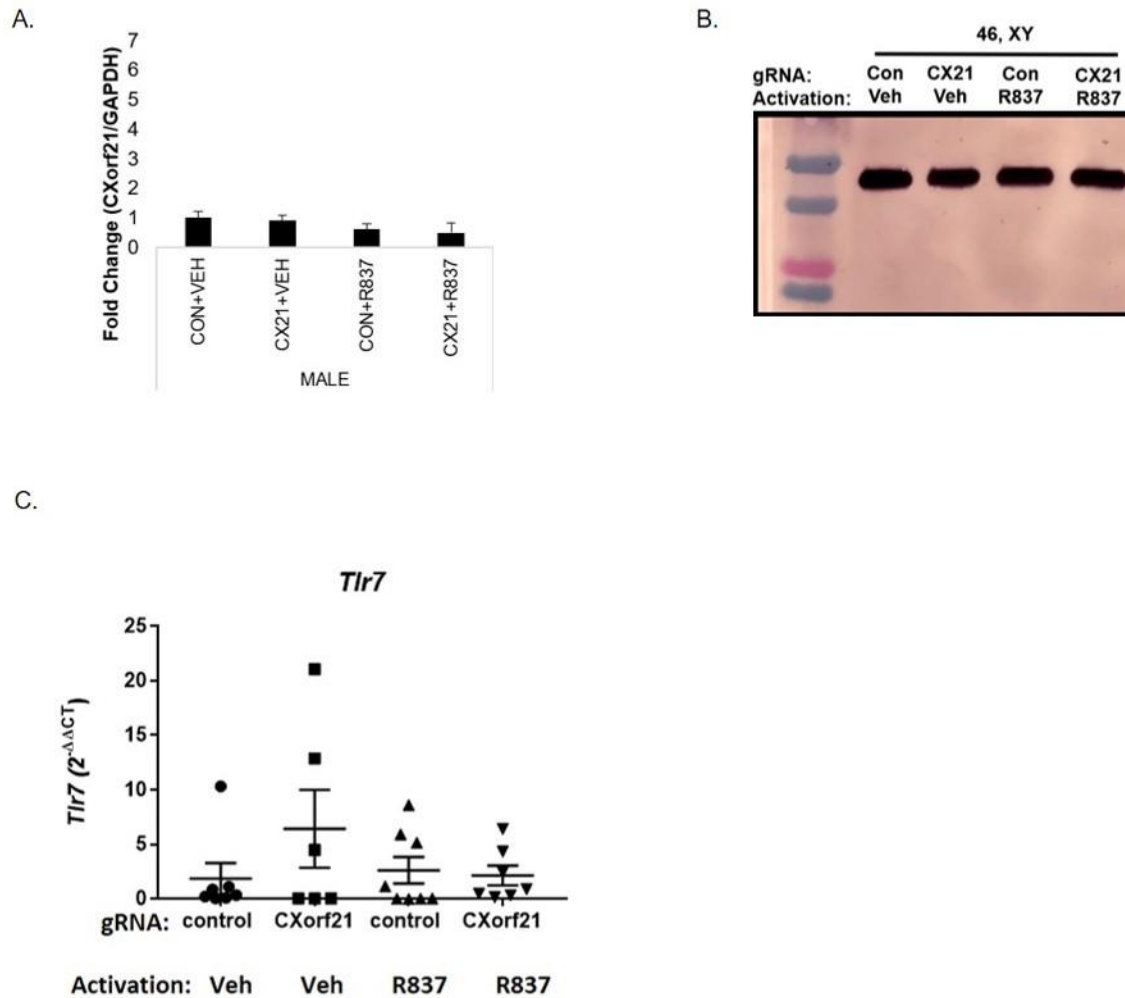


Figure S2. CRISPR-Cas9 knockdown of CXorf21 has no effect on CXorf21 and Tlr7 expression in male monocytes. (A.) RT-qPCR of CXorf21 mRNA expression from primary monocytes from either healthy 46,XY males with control (Con) or CXorf21-specific gRNA (CX21). Ligand stimulation were performed for 24 hours with vehicle (Veh) or R837 (1μM). Fold changes for male samples show relative expression to male Con-Veh. Data represents monocytes 6 male in replicates of 3. Error bars represent SEM. Data was not significant. B. Total protein extract from 46,XY male primary monocytes subjected to SDS-PAGE. Western blotting using human anti-CXorf21 antibody (34kD) identifying bands at the appropriate molecular weight. Human anti-alpha actin (42kD) is shown as a loading control. (l-r) lane 1 and 2 is healthy 46,XY male monocytes treated with vehicle following transfection with control (Con) or CXorf21-specific gRNA (CX21), R837. Lane 3 and 4 samples were treated with R837 following transfection. C. RT-qPCR of TLR7 mRNA expression from male primary monocytes transfected with control (Con) or CXorf21-specific gRNA (CX21). Error bars represent SEM. One-way ANOVA Kruskal-Wallis nonparametric test with a Dunn's multiple comparisons. *p*-values *<0.05.

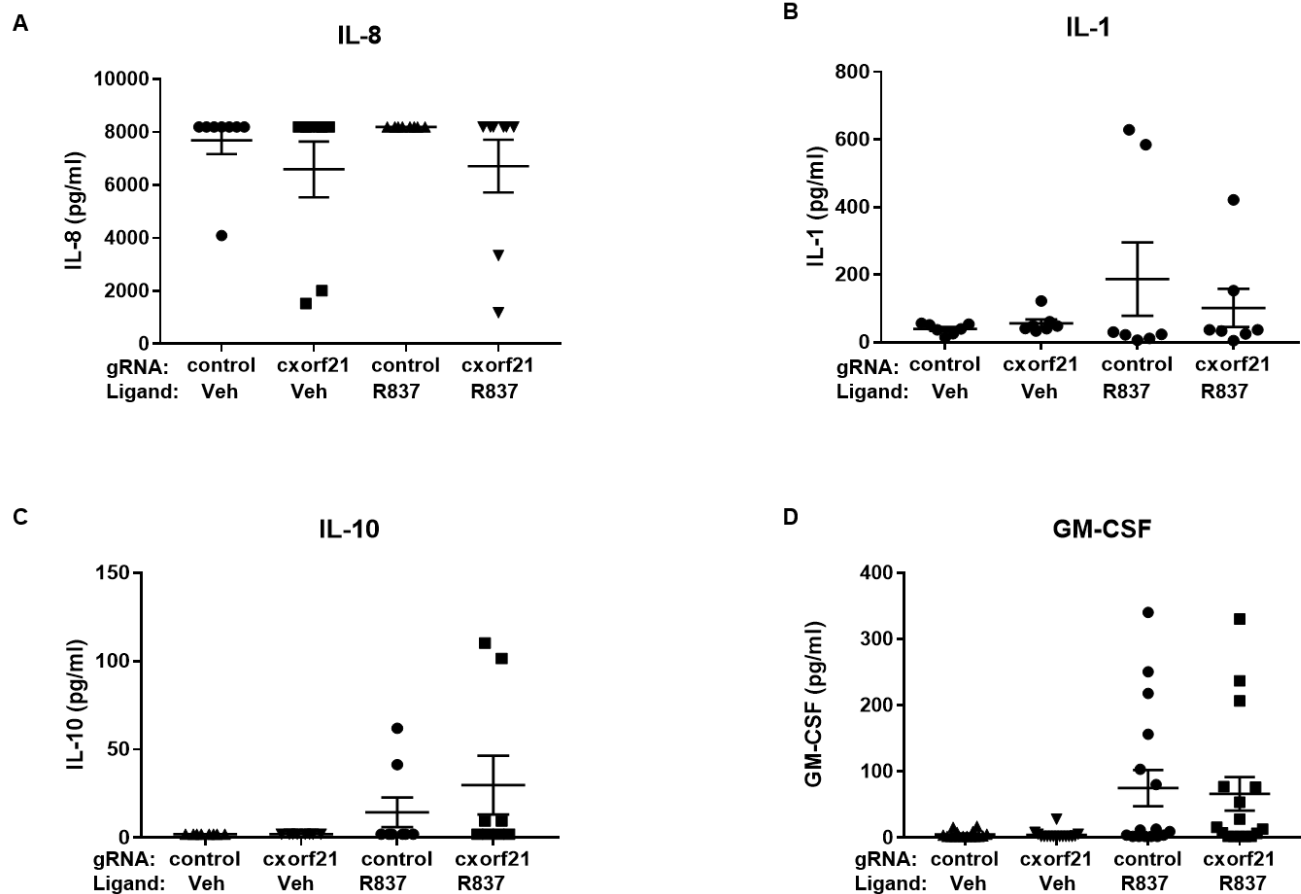


Figure S3. Regulation of inflammatory cytokines following *CXorf21* knockdown in primary monocytes. (A.) IL-8, (B.) IL-1, (C.) IL-10 and (D.) GM-CSF plots show cytokine production in 46, XX female primary monocytes transfected with control (Con) or *CXorf21*-specific gRNA (CX21). Ligand stimulation were performed for 24 hours with vehicle (Veh) or R837 (1 μ M) and cytokine in media detected via ProcartaPlex™ Platinum Human Multiplex Assays. Error bars represent SEM.