

Supplemental Information

Supplemental Experimental Methods

Reagents and antibodies

LA1 was purchased from Chembridge Corp (Cat. No. 5679982, San Diego, CA). The anti-CD11b monoclonal antibody (mAb) 44a (IgG2a) (1) and the heterodimer-specific anti-CD18 mAb IB4 (IgG2a) (2) were from ATCC. The isotype control antibodies clone X40 (IgG1) and clone X39 (IgG2a), FITC-conjugated mAbs A85-1 (rat anti-mouse IgG1), R19-15 (rat anti-mouse IgG2a) were from BD Pharmingen (San Diego, CA), and the FITC-conjugated goat anti-mouse immunoglobulin (cat# A11029) was from Invitrogen (Carlsbad, CA). The rat anti-mouse anti-CD11b mAb M1/70 (IgG2b) (3) was purchased from the monoclonal antibody core at University of California, San Francisco (UCSF). Primary antibodies used in western blot were as follows: anti-phospho IKK- α/β (cat# 2078), anti-IKK- β (cat# 8943), anti-phospho p65/NF- κ B (cat# 3036), anti-MyD88 (cat# 4283), anti-GAPDH (cat# 2118), anti-phospho AKT (cat# 4060), anti-AKT (cat# 4691), anti-phospho FoxO1/3a (cat# 9464), anti-FOXO3a (cat# 2497), anti-phospho IRF3 (cat# 4947), anti-IRF3 (cat# 4302), anti-phospho IRF7 (cat# 14767), anti-phospho c-Cbl (cat# 8869), c-Cbl (cat# 8447), anti-phospho Src (cat# 6943), and anti-Src (cat# 2108) and were purchased from Cell Signaling Technologies, Danvers, MA. Other antibodies used were anti-rabbit IgG-HRP conjugate (cat# W4011, Promega, Madison, WI), anti-mouse IgG-HRP conjugate (cat# W4021, Promega, Madison, WI), anti-NF- κ B (cat# 16502, Abcam, Cambridge, MA), and anti-IRF7 (cat# PA5-20280, Thermo Scientific, Waltham, MA). Human Fibrinogen (Plasminogen, von Willebrand Factor and Fibronectin depleted) was from Enzyme Research Laboratories (South Bend, IN), bovine serum albumin (BSA)

was from Sigma (St. Louis, MI) and the recombinant human ICAM1-Fc was from R&D Systems (Minneapolis, MN). The Highbind 384-well plates were obtained from Corning (Corning, NY). Non-fat milk was obtained from BioRad (Hercules, CA). PCR reagents, and restriction and modification enzymes were obtained from New England Biolabs Inc. (Beverly, MA). Glutathione-beads were purchased from Sigma (St. Louis, MI). All cell culture reagents were from Invitrogen Corp. (San Diego, CA). LPS (cat# tlrl-eklps), R848 (cat# tlrl-r848), polyI:C (pI:C, cat# tlrl-plc) and CpG (cat# tlrl-2216) were purchased from Invivogen (San Diego, CA). Human and mouse recombinant cytokines and ELISA kits were purchased from R&D Systems and were declared by the manufacturer to contain <0.1 ng of LPS per µg of protein.

Human samples

Data from 171 SLE cases consisting of patients of self-reported European ancestry that had serum available for IFN I analysis were obtained from multiple study centers. Clinical characteristics and demographic details for the patients in the replication cohort are summarized in Supplementary **Table S1**. Informed consent was obtained from all patients in both cohorts included in this study, and the study was approved by the institutional review boards at the respective institutions. Additional genotyped human PBMCs from normal donors carrying *ITGAM* non-risk or risk variant for cell based immunofluorescence and other assays were provided by the Genotype and Phenotype (GAP) Registry at the Tissue Donation Program at The Feinstein Institute for Medical Research (Manhasset, NY).

Genotyping

Patients were genotyped at coding change SNPs in ITGAM (rs1143678, rs1143679 and rs1143683) using custom designed Applied Biosystems Taqman primers and probes on an Applied Biosystems 7900HT PCR machine with >98% genotyping success. Genotyping scatter plots were all reviewed individually for quality, and genotype frequencies did not deviate significantly from the expected Hardy-Weinberg proportions ($p > 0.01$).

Measurement of serum IFN I activity

We used an assay, which we have used extensively to measure type I IFN in human sera (4, 5). Briefly, WISH cells (ATCC #CCL-25) were cultured with 50% sera or supernatant for 6 hours and lysed. cDNA, made from cellular mRNA, was quantified using real-time PCR using forward and reverse primers for the genes interferon-induced protein with tetratricopeptide repeats 1, myxovirus resistance 1, and dsRNA-activated protein kinase (5). The PCR product of each gene was normalized to the housekeeping gene GAPDH. Fold increase in expression levels of the IFN-induced genes of cells cultured with serum samples over cells without samples was determined. Results were standardized to a healthy reference population and type I IFN activity scores were calculated based upon the mean and standard deviation (SD) of the reference population (5). The IFN assay has previously been normalized using 100 healthy controls to establish normal values for serum IFN in healthy individuals and the calculation of the IFN scores is fully described in (6). The healthy donor data were also used to establish a cutoff value for doing binary analyses with the IFN data, with high IFN being considered two SD or greater above the

mean of the healthy donor pool. This assay has been highly informative in multiple human autoimmune diseases (7-10).

Association analyses

Logistic regression analysis was used to detect associations between the individual SNPs and serum IFN I activity in this study. IFN I activity was studied as a categorical trait because the trait distribution is highly skewed, such that log transformation does not result in a normal distribution and the highly skewed data did not allow for linear modeling in a quantitative trait locus analysis. We used a binning strategy that has been highly informative in previous large scale studies and multivariate analyses of the serum IFN trait in SLE (7-10), in which subjects with a value >2 s.d. above the mean of healthy controls are binned as high IFN I, and the rest are binned as low IFN I activity. Using this binning strategy prevents high outlying values from exerting an inordinate amount of influence in the model. Logistic regression analysis was carried out using PLINK v.1.07 software. Enrichment P-values were calculated using a Fisher's exact test. Graphs were also generated showing the IFN values in patients segregated by genotype, with Mann-Whitney U test used to determine statistical significance.

Mice

The C57BL/6J (B6) wild type (#000664, The Jackson Laboratory, Bar Harbor, ME), B6 CD11b^{-/-} (#003991, The Jackson Laboratory, Bar Harbor, ME) (11), female MRL/*lpr* (#000485 The Jackson Laboratory, Bar Harbor, ME) and haplotype-, age- and sex-matched control MRL/*MpJ* (#000486, The Jackson Laboratory) were maintained in

specific-pathogen-free conditions and used in accordance with the Institutional Animal Care and Use Committee (IACUC) and the respective institutional guidelines. The MRL/*Mpj* mice were used as a non-lupus prone, haplotype-matched strain to compare lupus-prone mice to normal pathology.

SLE mouse model

Female MRL/*lpr* were treated with LA-1 (2 mg/kg/day) or vehicle (1% Tween-20 in sterile saline) for 11 weeks by daily intraperitoneal injection, beginning at 8 weeks of age until euthanasia at 19 weeks of age. Haplotype-matched female MRL/*Mpj* mice were used as phenotypic controls. The assessments were blinded for histological analysis. Sample size was chosen based on previous studies using interventions in MRL/*lpr* mice to assess similar outcomes in phenotype (12). No method of randomization was used. One mouse from the LA1 treatment group was excluded from analysis due to excessive renal pathology unrelated to lupus.

Assessment of lupus nephritis and skin involvement in mice

Serum creatinine was determined by HPLC as previously described(13), except that HPLC runs were extended from 10 min to 40 min, in order to avoid a interference from a large peak at 20-25 min. Urinary albumin and creatinine concentrations were measured using a mouse albumin ELISA (Bethyl laboratories, Montgomery, TX) and a creatinine assay (R&D systems, Minneapolis, MN), respectively. Urine albumin:creatinine ratios were then calculated. Kidneys and affected skin samples were harvested after perfusion with PBS. Regions of alopecia were measured on the face and dorsum, with greatest

diameter determined to the nearest mm with calipers. One part of the removed kidney was fixed in 10% formalin and embedded in paraffin and another part was immediately snap frozen in OCT on liquid nitrogen and stored at -80°C. Paraffin embedded sections (4 µm) were stained with hematoxylin-eosin (H&E), periodic acid-Schiff (PAS), or Masson's trichrome. Stained slides were blindly evaluated by an experienced pathologist for chronic tubulointerstitial damage, glomerular sclerosis, and tubulointerstitial inflammation using a 0 (none), 1+ (<25%), 2+ (25-50%), 3+ (>50%) scoring system and collagen deposition was indicated as a percent of tissue area stained blue with Masson's trichrome. Formalin-fixed and frozen sections of the skin were prepared as for kidneys.

For immunofluorescence studies, tissue sections (4 µm) were cut and fixed in -20°C acetone before immunofluorescence staining. Sections were blocked (4% FBS, 4% BSA, 0.4% Fish gelatin in PBS) at room temperature for 1 hr and incubated with the appropriate primary antibodies - WT1 (2 µg/mL, SC-192, Santa Cruz), synaptopodin (2 µg/mL, SC-21537, Santa Cruz), activated β1 (5 µg/mL, 553715, BD Biosciences) or IgG (0.4 µg/mL, A11029, Thermofisher Scientific) in blocking buffer at 4°C overnight. Sections were incubated with the appropriate secondary antibody (Thermofisher Scientific) and mounted with DAPI medium (Vector Laboratories). Fluorescence images were acquired using a Zeiss LSM 700 confocal microscope with a PLAN-Apochromat 20x objective and an AxioCam camera and analyzed using the Zen software (Carl Zeiss Group). The number of WT1 positive cells per glomeruli was calculated manually using the confocal microscope (5 glomeruli/tissue). The fluorescence intensities for

synaptopodin, activated $\beta 1$, and IgG were calculated using the ImageJ Software (5-8 glomeruli/tissue).

Serum quantification of autoantibodies and total IgG

Commercial ELISAs for murine anti-dsDNA antibodies and total IgG were purchased from Alpha Diagnostic (San Antonio, TX, catalog# 5110 and 6320, respectively) and were performed according to the manufacturer's instructions in serum obtained at 19 weeks of age.

Murine bone marrow isolation

Cells were isolated from the bone marrow by flushing the femurs and tibias with HBSS with 15 mM EDTA. The cells were then spun on a 52%, 69%, 78% Percoll gradient at 1500 g for 30 minutes. Cells were collected from the 69%-78% interface and then spun down, resuspended in RBC Lysis Buffer (eBioscience) and washed before being resuspended in RPMI-1640.

Murine monocyte isolation

Isolation of mouse bone marrow or spleen monocytes was performed using the EasySep Mouse Monocyte Enrichment Kit (Cat#19761, Stemcell) according to the manufacturer's instruction.

Flow cytometry of mouse splenocytes for immunophenotyping

A single cell suspension of mouse splenocytes was prepared using a cell strainer, rinsing with FACS buffer. The cells were washed with PBS and then underwent RBC lysis using 1x multi-species RBC Lysis Buffer (Cat#00-4333-57, eBioscience). The cells were washed again in PBS and resuspended in FACS buffer (2% FBS in PBS) at 1.0×10^6 cells/mL for analysis by flow cytometry. After blocking for 15 minutes, cells were resuspended in 100uL FACS buffer and incubated with 2uL each of respective antibodies or isotype control for 30 minutes, fixed with 2% paraformaldehyde, quantified by flow cytometry using a BD FACSCanto RUO and data analyzed using FlowJo Software. Cutoff values for positive staining were determined using compensation controls for each fluorophore. All antibodies were from Biolegend (San Diego, CA): Alexa Fluor 488®-anti-mouse CD3 antibody (clone 17A2), PE-anti-mouse CD4 antibody (clone GK1.5); APC-anti-mouse CD8 antibody (clone 53-6.7); PE Cy7-anti-mouse CD11c antibody (clone N418); Alexa Fluor 488-anti-mouse CD19 antibody (clone 6D5); PE Cy7-anti-mouse CD25 antibody (clone PC61); PerCP/Cy5.5-anti-mouse CD69 antibody (clone H1.2F3); PE-anti-mouse CD80 antibody (clone 16-10A1); PerCP/Cy5.5-anti-mouse CD138 antibody (clone 281-2); Pacific Blue™-anti-mouse B220 antibody (clone RA3-6B2); APC/Cy7-anti-mouse F4/80 antibody (clone BM8); FITC anti-mouse Ly6G antibody (clone 1A8). Results are reported as number of cell subsets/million splenocytes.

Cecal ligation and puncture model

Cecal ligation and puncture (CLP) was performed as described previously (14) using B6 WT mice (8-12 weeks old). Vehicle control (1% DMSO in PBS) or LA1 (2mg/kg body weight, in PBS) was administered *intraperitoneally* 2 hrs prior to CLP and then daily

until the end of the experiment. No mice were excluded from analysis and no method of randomization was used. Sample size was chosen based on previous studies to assess similar outcomes (14). For the colony-forming units assay, blood samples from septic or mock CLP mice were collected by cardiac puncture at indicated times after surgery. Mice were subsequently perfused *in toto* with 10mL ice cold PBS and spleen, liver and kidneys were surgically removed and homogenized in 5ml of sterile PBS. Serial dilutions of blood and tissue homogenates were immediately plated on Trypticase Soy Agar II plates supplemented with 5% Sheep Blood. CFUs were counted after 12h of incubation at 37°C. The serology and cytokine measurements were performed as described (14) using plasma from blood samples obtained 24 hours post-CLP. LDH, CK, ALT and urea levels were measured using the BioAssay Systems kits (BioAssay Systems, California) according to company's protocol. Levels of IL-1 β , IL-6 and TNF α were measured using the murine ELISA kits (R&D Systems, Minneapolis) according to company's protocol.

***In vivo* viral infection assay**

H1N1 infection and viral particle quantification was performed using B6 WT mice as previously described (15). Infection was performed by intranasal application of virus solution in 20 μ l of sterile phosphate-buffered saline under light isofluorane anaesthesia. Un-infected wild-type B6 WT mice were included as controls. Sample size was chosen based on previous studies to assess similar outcomes. Body weight loss was monitored until day 14 p.i.

LPS Mouse Model

The endotoxin shock model using LPS administration in 8-12 wk old B6 WT and CD11b^{-/-} mice was performed according to literature protocols (16). Briefly, LPS (*E. coli* strain O111:B4, Invivogen) was administered by *intraperitoneal* injection (15mg/kg) in mice. Vehicle control (1% DMSO in PBS) or LA1 (2mg/kg body weight, in PBS) was administered *intraperitoneally* 30 min after the LPS injection and the animals were sacrificed after 4h and sera was collected. Mice injected with vehicle (1% DMSO in PBS) alone were used as controls (C). No mice were excluded from analysis and no method of randomization was used. Sample size was chosen based on published studies (16). IFN β level in the sera was measured using the murine ELISA kits (PBL Assay Science, Piscataway, NJ, catalog# 42400-1) according to company's protocol.

Vascular re-endothelialization in rats

The wild type Fischer 344 rats were purchased from Harlan Laboratories (Indianapolis, IN). Vascular healing was evaluated after balloon induced arterial injury. All operative procedures were under isoflurane anesthesia (Baxter, IL, USA). The endothelium of the right iliac artery of male Fisher rats (280-320 grams) was removed using a 2F Fogarty catheter (Baxter Corp., Irvine, CA, USA) adapted to a custom angiographic kit (Boston Scientific, Scimed) (17). Rats received daily peritoneal injections of LA1 or vehicle. Seven days post-surgery, 0.5 mL of 5% Evans blue was injected into the tail vein of treated and control animals 30 min before euthanasia, and perfusion-fixation with 4% phosphate-buffered paraformaldehyde were performed. The injured arterial segment was dissected and mounted on a microscopic glass slide. The blue-stained area, denuded area was measured with the Image Pro Plus software (Media Cybernetics). Alternatively,

injured segments were immersed in 1 ml of N,N-dimethyl formamide (Sigma, St. Louis, Mo.) for 48 h to extract the Evans blue dye. The absorbance of Evans blue dye solution was measured in a spectrophotometer at 630 nm. The re-endothelialization was further confirmed using immunohistochemistry (18) with a rabbit anti-human Von-Willebrand factor antibody (DAKO, 1:400) after paraffin-embedding and cross sectioning of all injured vessels. Morphometric analysis was performed in a blinded fashion using NIH ImageJ.

Cell lines

The cell lines HEK 293T, K562 and RAW murine macrophage were all obtained from the American Type Culture Collection (ATCC) and were maintained accordingly. K562 cells stably transfected with integrin CD11b/CD18 (K562 CD11b/CD18) using the pcDNA3 plasmids encoding CD18 wild type and either CD11b wild type (WT), mutant CD11bE320A (E320A), CD11bI316G (I316G) or CD11bR77H (R77H) were prepared as described previously (19, 20). The pcDNA3 CD11bR77H plasmid was a gift from S. Fagerholm (University of Helsinki, Helsinki, Finland) (20). Cell lines were tested and determined to be mycoplasma free.

Cell adhesion assays

Cell-based adhesion assays with immobilized Fg as ligand were performed as previously described (19). A stock solution of LA1 was prepared in DMSO at a concentration of 10 mM. The final concentration of DMSO in the assay wells was approximately 2%. Assays

were performed in 3 to 6 replicate wells. Data shown are from one of at least three independent experiments.

Isolation of human monocytes and differentiation into primary macrophages

Human peripheral blood mononuclear cells (PBMCs) were isolated from fresh blood collected from healthy volunteers under an IRB-approved protocol and using RosetteSep (human monocyte Enrichment Cocktail, Cat# 15068 Stemcell Technologies, Vancouver, Canada) followed by Ficoll-Hypaque density gradient centrifugation according to published protocols(21). The cells were washed, resuspended in RPMI1640 with GlutaMAX (Cat# 61870-036, GIBCO) and autologous human serum (5%) (complete medium), and seeded into T75 (75 cm²) tissue culture flask (Cat#156800, Thermo). Non-adherent cells were removed by gentle pipette aspiration after 2 h of incubation at 37°C in a humidified atmosphere containing 5% CO₂. Subsequently, an equal volume of fresh complete medium was added to each flask and the cells were placed back in the incubator for approx. 24h. Subsequently, adherent cells were washed twice with PBS, detached from the flask by scraping with a rubber policeman, stained with trypan blue dye and counted using a hemocytometer. The cells ($\geq 85\%$ monocytes as determined by flow cytometric analysis after staining with anti-CD14 mAbs) were seeded in 6-well tissue culture dished (Cat #353847, Corning) at a density of 2×10^6 cells/well and were cultured for 5-7 additional days at 37°C in 5% CO₂ to promote their full differentiation into monocyte-derived macrophages (22, 23).

Isolation of murine primary neutrophils and macrophages

Thioglycollate-elicited neutrophils and macrophages were isolated from B6 WT mice or B6 CD11b^{-/-} mice, as described previously (19). Neutrophils were collected 4h after thioglycollate injection followed by 1h adherence purification before collecting non-adherent cells. The macrophages were collected four days post thioglycollate injection and adherence purified for 1h, followed by a wash with PBS to remove non-adherent cells. For the bone marrow derived macrophages (BMM), 2 x 10⁶ cells/well of harvested cells were plated in 6-well plates in RPMI containing 10% FBS and were cultured for 5-7 days. Macrophages were generated from bone marrow derived monocytes cells as described in the literature (24).

Microarray analysis

Human macrophages (2 X 10⁶) were cultured in 6-well tissue culture plates and were treated with LPS (50ng/mL) in the absence or presence of LA1 (20μM) for 4h as previously described (19). Cells were washed with ice cold PBS and the lysed in TRIzol (Thermo Fisher Scientific, Waltham, MA) for total RNA isolation. RNA sample quality was analyzed using a 2100 Bioanalyzer (Agilent). Whole genome transcriptional profiling was performed at the University of Chicago Genomics Core using Illumina HT-12 human gene expression arrays. The raw data from microarray analyses was uploaded on GeneSpring™ software v13. Quality control steps were performed and data was Quantile normalized and log₂ transformed to mean of all samples. Significance test was performed using the unpaired Student's t-test and p-values were multiple testing corrected using the Benjamini-Hochberg method. Only significant genes (p-value ≤ 0.05 and fold change ≥ 2) were considered for pathway analysis. We deposited all

microarray data in the Gene Expression Omnibus database in the series GSE76802. We generated hierarchical clustering graphs on normalized gene expression fold change with respect to the mean expression value using Plotly.

Pathway analysis

Significantly different genes between two conditions were loaded on GeneGO™ web portal from Thomson Reuters. Significantly enriched pathways (p-values < 0.05) were generated and analyzed on the portal.

mRNA quantification in human macrophages using nCounter

Human macrophages were stimulated with LPS (50ng/mL) for various amount of time (0, 0.5, 2, 4, 8 and 24h) in the absence or presence of LA1 (20μM) as described previously (19). Total RNA was extracted using TRIZOL reagent and QIAGEN's total RNA isolation kit according to manufacturer's instructions. RNA sample quality was analyzed using a 2100 Bioanalyzer (Agilent). Expression levels of selected genes were measured using an inflammation panel set and the nCounter Digital Analyzer (Nanostring Technologies, Seattle, WA) as previously described (25) and following the manufacturer's instructions at the University of Miami Genomics Core. Data analysis was performed as described (25) after normalization using internal Nanostring controls (spike-normalization following manufacturer's instructions).

Quantification of IFN I-inducible genes and FOXO3 in murine cells

RNA isolation and real-time PCR for quantification of IFN I–inducible genes were performed as described previously. Briefly, RNA was isolated from spleens and bone marrow using TriPure Isolation Reagent (Roche) according to the manufacturer’s instructions. cDNA was synthesized using MMLV RT (Invitrogen) and 1 µg of RNA using a MyCycler Thermocycler (Bio-Rad). Five IFN I–responsive genes and 1 housekeeping gene (β -actin) were quantified by real-time PCR using SYBR Green PCR Supermix (BIO RAD, USA) according to the manufacturer’s instructions. The primer sequences for the *Mx1*, *Irf7*, *Ip-10*, *Isg15*, and *Ifng* genes have been described by our group previously and are as follows:

<i>mIRF7_F</i>	TGC TGT TTG GAG ACT GGC TAT
<i>mIRF7_R</i>	TCC AAG CTC CCG GCT AAG T
<i>mMCP1_F</i>	AGG TCC CTG TCA TGC TTC TG
<i>mMCP1_R</i>	TCT GGA CCC ATT CCT TCT TG
<i>mISG15_F</i>	CAG AAG CAG ACT CCT TAA TTC
<i>mISG15_R</i>	AGA CCT CAT ATA TGT TGC TGT G
<i>mIFNg_F</i>	ATG GCT AGR CTC TGT GCT TTC CT
<i>mIFNg_R</i>	AGG GCT CTC CAG AYT TCT GCT CTG

For quantification of murine FOXO3 mRNA levels, RNA from splenic monocytes was isolated using Direct-Zol RNA MiniPrep Plus (Cat#R2072, Zymo Research). cDNA was synthesized with 500 ng of RNA using BioRad 5x iScript Reverse Transcription Supermix (Cat#170-8841, Bio-Rad) using a Veriti 96-Well Thermal Cycler (Applied Biosystems). *Foxo3* and the house-keeping gene β -actin were quantified by real-time

PCR using the SsoAdvanced Universal SYBR Green SuperMix (Cat#1725274, Bio-Rad). The primer sequences for *Foxo3* and *β-actin* are listed below, and real-time PCR was carried out using the C1000 Touch Thermo Cyclor (Bio-Rad). The transcripts were normalized using *β-actin* gene. The data was presented as fold change based on the formula $2^{-\Delta\Delta Ct}$.

<i>mFoxo3_F</i>	AAC AGA CCA GCC ACC TTC TCT T
<i>mFoxo3_R</i>	TGA AGC AAG CAG GTC TTG GA
<i>mβ-Actin_F</i>	CCA ACC GCG AGA AGA TGA
<i>mβ-Actin_R</i>	CCA GAG GCG TAC AGG GAT AG

Quantification of IFN I pathway genes in human PBMCs

Total RNA was isolated from human PBMCs using QIAzol Reagent (Life Technologies) and Qiagen RNA isolation kit according to the manufacturer's instructions. cDNA was synthesized using High Capacity cDNA Archive Kit (Life Technologies) and the resulting cDNA samples were subject to real-time quantitative reverse-transcription polymerase chain reaction (qRT-PCR) analysis with CFX96™ Real-Time System (Bio-Rad). qRT-PCR was run in a 20-μL reaction using TaqMan Gene Expression Master Mix (Applied Biosystems) according to the manufacturer's instructions. Briefly, qRT-PCR was performed (40 cycles of 95 °C for 15 s and 60 °C for 1 min) and the resulting cycle threshold (Ct) values of individual genes were normalized to Ct values for human GAPDH (ΔCt), and then were used to calculate fold change in relative gene expression ($2^{-\Delta\Delta Ct}$). All samples were run in at least duplicates. The predesigned TaqMan gene

expression assays for human *IFNBI* (Hs01077958_s1), *IRF7* (Hs01014809_g1), and *GAPDH* (Hs02758991_g1) were purchased from Thermo Fisher Scientific.

Luminex analysis of serum cytokine samples

The concentrations of mouse serum cytokines were determined using the cytokine mouse 20-plex panel for Luminex platform (Invitrogen/ThermoFisher Scientific) according to the manufacturer's protocols. The concentrations of cytokines were calculated according to the standards for each assay.

ELISA assays

Primary human and mouse macrophages were cultured in the presence of vehicle (1% DMSO), LA1 (20 μ M), LPS (50ng/mL), or LPS (50ng/mL) and LA1 (20 μ M) for various time points (4h, 8h, 12h) and the cell culture supernatant was collected. Human cell culture supernatants were assayed using a sandwich ELISA kits for human IL6 (R&D Systems, Minneapolis, MN, catalog# D6050), IL-1 β (R&D Systems, Minneapolis, MN, catalog# DLB50), TNF- α (R&D Systems, Minneapolis, MN, catalog# DTA00C) and MCP-1 (R&D Systems, Minneapolis, MN, catalog# DCP00) according to manufacturer's instructions. Mouse cell culture supernatants were assayed using commercially available sandwich ELISA kits for mouse IL6 (R&D Systems, Minneapolis, MN, catalog# M6000B), IL-1 β (R&D Systems, Minneapolis, MN, catalog# MLB00C), and TNF- α (R&D Systems, Minneapolis, MN, catalog# MTA00B) according to manufacturer provided instructions. For measuring IFN β levels, mouse macrophages (WT and CD11b^{-/-}) were cultured in the presence of vehicle (1% DMSO), LA1 (20 μ M), LPS (100ng/mL),

or LPS (100ng/mL) and LA1 (20 μ M) for 12h and the cell culture supernatant were assayed using commercially available sandwich ELISA kits for mouse IFN β (PBL Assay Science, Piscataway, NJ, catalog# 42400-1) according to manufacturer provided instructions.

Western blot

RAW macrophages were cultured in the presence of vehicle (1% DMSO), LA1 (20 μ M), LPS (50ng/mL), or LPS (50ng/mL) and LA1 (20 μ M), or pI:C (25 μ g/mL), or pI:C (25 μ g/mL) and LA1 (20 μ M), for various durations (0, 30, 60, 120 and 240 min). Human and mouse primary macrophages were similarly treated. The cells were washed with ice cold PBS and were subsequently lysed in Laemmli buffer (120mM Tris-HCl pH 6.8, 4% w/v SDS, 20% glycerol, 1% β -mercaptoethanol) along with protease inhibitor cocktail (Roche Applied Science, Indianapolis, IN Cat# 11836153001) and phosphatase inhibitor cocktail (Thermo Scientific, Rockford, IL, Cat# 88667) for 30 minutes at 4°C. Nucleic acid was sheared by passing through 28.5 gauge syringe 5 to 10 times. Lysate was cleared by centrifugation at 16,000 xg for 10 min at 4°C. Protein concentration was determined using the BCA Protein Assay (Pierce, Rockford, IL). Equal amount of proteins were separated on a 4-12% gradient NuPAGE Bis-Tris Gel (Invitrogen) and blotted to a PVDF membrane (Millipore). Membrane was blocked with 10% BSA for 1 hr at RT, followed by incubation with various primary antibodies overnight at 4°C. Subsequently, membrane was washed and incubated with either HRP conjugated goat anti-mouse or anti-rabbit for 1 hour at RT and detected using chemiluminescent substrate (Cat# 34080, Thermo Scientific, Waltham MA). Membranes were stripped with Restore

stripping buffer (cat#21059 Thermo Scientific, Pierce, Rockford, IL), and reprobed with anti-GAPDH antibody (cat# 2118, Cell Signaling) and developed as mentioned above. Data presented is representative of at least three independent experiments.

For quantification of FOXO3 protein in murine bone marrow monocytes from lupus mice, the isolated cells were lysed with 50mM Tris-HCl pH 7.4, 300 mM NaCl, 0.5% w/v Triton X-100, 5mM EDTA, protease inhibitor cocktail (Roche Applied Science, Indianapolis, IN) for 30 minutes at 4° C. Lysate was cleared by centrifugation at 16,000 xg for 10 min at 4° C. Protein concentration was determined using the BCA Protein Assay (Pierce, Rockford, IL). Equal amounts of protein were separated on a 4-12% gradient NuPAGE Bis-Tris Gel (Invitrogen) and blotted to a PVDF membrane. Membrane was blocked with 10% BSA for 30 min at RT, followed by incubation with either anti-total FOXO3a (75D8) (Cell Signaling) or anti-phospho FOXO3a (S253) (Cell Signaling) overnight at 4°C. Subsequently, membrane was washed and developed as mentioned above. Data presented is representative of at least three independent experiments.

Assessment of endothelium-dependent vasorelaxation

After euthanasia, thoracic aortas were excised, cleaned, and cut into 2-mm length rings. Endothelium was left intact, and aortic rings were mounted in a myograph system (Danish Myo Technology A/S). Vessels were pre-contracted with PSS containing 100 mM potassium chloride (KPSS) and then returned to PSS. Cumulative concentrations of PE (10^{-9} M to 10^{-6} M) were then added to the bath to establish a concentration-response

curve. A PE concentration corresponding to 80% maximum was added, and contraction was allowed to reach a stable plateau. To examine endothelium-dependent relaxation, Acetylcholine (Ach, 10^{-9} M to 10^{-6} M) was added cumulatively to the bath and a curve was generated. Finally, a normal vascular smooth muscle response was confirmed by removing PE and Ach.

Expression and purification of recombinant CD11bA

The recombinant human CD11bA (CD11bA) spanning residues Gly111-Gly321 was obtained as previously described (19). Briefly, the CD11bA domain in pGEX-2T was expressed as glutathione S-transferase (GST) fusion protein in *Escherichia coli* and purified by affinity chromatography (Glutathione-beads, Sigma) following manufacturer's instructions. The GST-tag was removed using TEV protease to release CD11bA, which was further purified using Fast Protein Liquid Chromatography (FPLC, AKTA purifier) with a Source S column and eluted with a NaCl gradient (0-0.5M) in 20 mM Tris-HCl, pH 8.0. The purity of CD11bA was confirmed by 1D SDS-polyacrylamide gel electrophoresis analysis. Purified CD11bA was dialyzed against 20 mM Tris-HCl, pH 7.5, 150 mM NaCl and subsequently used in ITC assays.

Isothermal titration calorimetry (ITC)

ITC experiments were performed using published protocols (26) using a MicroCal ITC₂₀₀ microcalorimeter (GE healthcare) with a reaction cell volume of 200 μ l and syringe volume of 40 μ L. Briefly, the heat flow resulting from the binding of LA1 to CD11bA in the absence or presence of various metal ions (Mn^{2+} , Ca^{2+} and Mg^{2+}) was measured at

25 °C (298 K) with high sensitivity. LA1 (5 μ M) in reaction buffer (0.2% DMSO in Tris buffered saline (TBS)) was placed in the calorimeter reaction cell and stirred at 1000 rpm. CD11bA (70 μ M) was placed in the calorimeter syringe in the same reaction buffer and in the absence or presence of various metal ions (1mM each). The protein was injected in a step-wise fashion into the reaction cell with an injection volume of 2.5 μ L, with duration of 4s. Interval between injections was 60s. In another set of experiments, CD11bA (20 μ M) was placed in the calorimeter reaction cell in the absence or presence of LA1 (5 μ M). The solution in the cell was titrated with concentrated metal ions (Mn²⁺, Ca²⁺ and Mg²⁺) filled in the calorimeter syringe. The reaction buffer, injection volume, duration and interval between the injections were as above. The heat flows from control experiments (injection of protein into reaction cell containing only the reaction buffer) were also measured and were subtracted from the heats measured for each of the binding reactions. Data were analyzed and fitted using the Microcal Origin software provided with the instrument. The experimental data were fitted to a model for simple binding of LA1 to a single class of sites (n=1) on the protein CD11bA. The enthalpy of binding, ΔH (kcal/degree/mol), was determined from the heat release measurement, which is independent of the binding model.

Computational modeling and molecular dynamics simulations

We employed a multistep computational strategy to investigate the interactions of LA1 with CD11bA. In the first step, published X-ray structures of CD11bA (27, 28) were used to build LA1 docked computational models, as previously described (19). Structures were equilibrated using all-atom 30 ns molecular dynamics (MD) simulations in an aqueous

solution using the GROMACS program (29, 30) and the OPLS-AA (Optimized Potentials for Liquid Simulations) force field (31). In the simulations, the starting structures were placed in a large cubic box ($60.0 \times 60.0 \times 60.0 \text{ \AA}^3$) to avoid artificial interactions with their images in the neighboring boxes created by the application of periodic boundary conditions. The box was filled with TIP3P water molecules. Some water molecules were replaced with sodium and chloride ions to neutralize these systems and to simulate an experimentally used ion concentration of 150mM. The starting structures were subsequently energy-minimized with a steepest descent method for 3000 steps. The results of these minimizations produced the starting structure for the MD simulations. The MD simulations were then carried out with a constant number of particles (N), pressure (P) and temperature (T), *i.e.*; NPT ensemble. The SETTLE algorithm was used to constrain the bond length and angle of the water molecules (32), while the LINCS algorithm was used to constrain the bond length of the protein (33). The long-range electrostatic interactions were calculated by the Particle-Mesh Ewald (PME) method (34). A constant pressure of 1 bar was applied with a coupling constant of 1.0 ps peptide, water molecules and ions were coupled separately to a bath at 300 K with a coupling constant of 0.1 ps. The equation of motion was integrated at each 2 fs time steps using leap-frog algorithm (35). The tools available in the GROMACS program package and the YASARA software (v.13.2.2) were utilized for analyzing trajectories and simulated structures (36). The most representative structure provided by these simulations was subsequently used to study CD11bA-LA1 interactions. The most representative structures were derived from cluster analysis, where the trajectories were analyzed by grouping structurally similar frames (root-mean-square deviation cutoff = 0.30 nm) (37), and the

frame with the largest number of neighbors was denoted as a middle structure that represented that particular cluster. In the next step, a LA1 molecule was docked inside the cavity of CD11bA using the Autodock Vina 1.1.2 software (38). In these docking experiments the protein was kept rigid, but the LA1 molecule had the flexibility to adopt different conformations. In the next step, the most promising poses provided by the docking procedure were subjected to 30 ns all-atom MD simulations in an aqueous solution. These simulations were also performed using GROMACS (29, 30) and GROMOS96 53A6 (39). The secondary structure analyses were performed by employing the defined secondary structures of proteins (DSSP) protocol (40). The RMSD of all trajectories indicated that they were well equilibrated within the 30 ns time frame.

Flow chamber assay

The flow chamber assay was performed as described (41). A polystyrene Petri dish was prepared by coating with a 5 mm diameter, 20 μ L spot of 20 μ g/mL purified h-ICAM-1/Fc or 20 μ g/mL Fibrinogen in coating buffer (PBS, 10 mM NaHCO₃, pH 9.0) for 1 hr at 37°C, followed by blocking with 2% BSA in coating buffer for 1 hr at 37°C. HEK 293T cells were transiently transfected with CD11b WT and CD18 WT plasmids (WT), CD11bE320A and CD18 WT (E320A), or CD11bI316G and CD18 WT (I316G) as previously described (42). The transfected HEK 293T cells were washed twice with wash buffer (20 mM HEPES, 150 mM NaCl, pH 7.4, 5 mM EDTA/0.5% BSA) and, subsequently, once with HEPES buffered saline (HBS) containing 1 mM Ca²⁺ and 1mM Mg²⁺ (HBS⁺⁺). The cells were resuspended at the concentration of 5x10⁶/mL in HBS⁺⁺ (Ca²⁺ and Mg²⁺-free HBS, 0.5% BSA) and kept on ice. Cells were incubated with LA1

(25 μM) or vehicle (2% DMSO) for 30 min at 37°C prior to infusion in the flow chamber using a Harvard apparatus programmable syringe pump. Upon infusion, the cells were allowed to settle down for 5 min, and accumulate for 30 sec at a shear stress of 0.3 dyn/cm^2 and 10 sec at 0.4 dyn/cm^2 . Subsequently, shear stress was increased every 10 sec from 1 dyn/cm^2 up to 32 dyn/cm^2 , in 2-fold increments. The number of cells remaining abundant at the end of each 10-sec interval was determined by manual counting. Rolling velocity at each shear stress was calculated from the average distance traveled by rolling cells in 3 sec. Rolling adherent cells were defined as cells moving with a velocity of more than 1 $\mu\text{m}/\text{s}$.

Immunofluorescence

Sub-cellular localization of FOXO3 and NF κ B in primary macrophages and in RAW cells was quantified as described (43). Briefly, cells (1×10^4 to 5×10^4) were plated on poly-L-lysine-coated MatTek glass-bottom dishes (MatTek Corporation, Ashland, MA) and were treated with vehicle (1% DMSO) (C), LA1 (20 μM), LPS (50 ng/mL), or LPS (50 ng/mL) and LA1 (20 μM) for 4h. The cells were fixed (4% paraformaldehyde in PBS), blocked (5% normal goat serum in PBS), permeabilized (with 0.1% Triton X-100), and stained with either anti-FOXO3a (cat# 2497, Cell Signaling) or anti-p65 (NF κ B) (cat# 16502, Abcam) antibodies. Subsequently, the cells were washed and stained with AlexaFluor568-conjugated secondary antibody (Cat# A11011, Life technologies). Nuclear staining was performed using DAPI dye. Images were captured on a Zeiss LSM 700 Confocal Microscope and analyzed in a blinded fashion with NIH ImageJ software.

Apoptosis assays

Apoptosis was evaluated by TUNEL using TACS 2TdT-Fluor Apoptosis detection kit (cat# 4812-30-K, TREVIGEN) as per manufacturer's assay protocol where nicked DNA was used as positive control and nuclear staining was performed using DAPI. Apoptosis was also evaluated as a measure of Lactate dehydrogenase (LDH) release by the cells using LDH cytotoxicity assay kit (cat# 601170, Cayman chemical, MI) according to the manufacturer's protocol.

Statistical analysis

To calculate statistical significance, a two-tailed student's *t*-test was used, unless otherwise specified. The differences in the cytokines concentrations were statistically analyzed using the Mann-Whitney test, and plotted with GraphPad Prism software package. For multiple comparisons, one-way ANOVA with Tukey's test was used. A value of $P < 0.05$ was considered statistically significant. For endothelium-dependent vasorelaxation, curves were first analyzed using an asymmetric (five parameters) logistic equation, and significance of each individual data point was determined by two-way ANOVA. Unless otherwise specified, results are represented as mean \pm SEM.

Supplemental Text

LA1 partially activates CD11bA to an intermediate affinity conformation

We previously showed that CD11b agonist LA1 binds to the ligand-binding domain of CD11b (CD11bA-domain) (Fig. S2C) and allosterically enhances ligand binding of both full-length CD11b/CD18 and the isolated, recombinant CD11bA (19). Studies using conformation-specific antibodies showed that LA1 does not induce large conformational changes in the integrin heterodimer (44). To gain additional molecular insights, we utilized molecular dynamics studies using published structures of CD11bA, as well as a model of LA1 docked into CD11bA (19, 45). Results (Figs. S2D-S2G), shown as a superposition of CD11bA in closed (yellow), open (red) and energy minimized LA1-docked structure (red), suggest that the LA1 bound structure adopts a partially active, intermediate affinity conformation (46), where the F- α 7 loop, α 7 helix and the α 1 helix showed structural shift halfway between the closed and the open conformation, thereby priming the integrin (Fig. S2G). To confirm, we used isothermal titration calorimetry (ITC) to directly assess the binding of LA1 with CD11bA. We measured the heat flow in the absence or presence of various metal ions (Mn^{2+} , Ca^{2+} and Mg^{2+}). In the absence of LA1, the observed thermodynamic data for the interaction of three metal ions with CD11bA was similar to the data reported in literature (26) (Table S2). However, a dramatic favorable enthalpy-driven increase in the binding affinity of all three metal ions was observed in the presence of LA1 with CD11bA (Fig. S3A), which suggests that LA1 creates a favorable environment for binding of metal ions. Next, the heat flow was measured by placing LA1 in the cell and titrating it with a solution of CD11bA bound to various metal ions. LA1 showed no binding to the metal ions alone.

Fitting the experimental data to a model for simple binding of LA1 to a single class of sites ($n=1$) on the protein displayed almost no LA1 binding to CD11bA in the absence of metal ions (Fig. S3B), but showed a 45-fold increase in the affinity of LA1 to CD11bA in the presence of all three metal ions which is largely driven by favorable enthalpy (Table S3). These data confirm direct LA1 binding to CD11bA, where its affinity for CD11bA is modulated by metal ions.

In vivo, circulating leukocytes adhere to the surface of inflamed endothelium under fluid shear stress. To examine the strength of LA1-stimulated adhesion of CD11b/CD18 to immobilized ligands, human ICAM-1-IgG₁ Fc fusion protein (ICAM-1) or fibrinogen (Fg), we utilized a parallel plate shear flow adhesion assay (41). CD11b/CD18-expressing cells (WT) were allowed to accumulate on the immobilized ligands at a wall shear stress of $0.3 \text{ dyne}\cdot\text{cm}^{-2}$ for 30s. Subsequently, the wall shear stress was incrementally increased every 10s, and the velocity of the cells that remained bound at each increment was determined and used to quantify the rolling and firmly adherent cells. We found that, as compared to the adhesion under control physiologic buffer condition (Ca^{2+} and Mg^{2+} , 1mM each) activation using the known integrin agonist Mn^{2+} (1mM) significantly increased the number of firmly adherent WT cells at the initial $0.3 \text{ dyne}\cdot\text{cm}^{-2}$ shear stress (Figs. S4A-S4B). LA1 treatment increased the number of both rolling and firmly adherent cells, as compared to the control. However, LA1-mediated increase in firmly adhered cells was significantly lower than the cells activated with Mn^{2+} , suggesting that LA1 may not fully activate the integrin. Moreover, under increasing shear stress conditions (Fig. S4C), the adhesive behavior of LA1-activated cells was halfway between that of the control condition (where low affinity integrin conformation primarily

mediates weak, rolling adhesion) and the Mn^{2+} activation condition (where high affinity conformation mediates firm adhesion that resists high shear stress), and greatly mimicked the behavior of integrins in an intermediate conformation (46). This further indicates that LA1 binding *per se* induces integrin priming or intermediate conformation, rather than full activation.

The I316G substitution in CD11b constitutively activates the integrin heterodimer. Conversely, the E320A substitution in CD11b suppresses integrin activation, by de-linking the CD11bA domain from the rest of the integrin chain. LA1, by binding to the CD11bA and inducing a conformational switch, is able to rescue ligand binding by the E320A mutant integrin (19). We utilized these two integrin mutants to further investigate the effects of LA1 on CD11b/CD18 activation. We found that under basal conditions, I316G expressing cells showed high firm adhesion to the two ligands (ICAM-1 and Fg), whereas both the WT and the E320A mutant expressing cells showed little binding (Figs. S4C-S4E). Activation with agonist Mn^{2+} ions slightly increased the level of adhesion by I316G expressing cells, but dramatically enhanced both firm and rolling adhesion by the WT cells. As has been shown before, Mn^{2+} did not increase binding by the E320A cells. As shown above, LA1 treatment of WT cells primarily induced rolling adhesion. Surprisingly, LA1 also dramatically increased the number of I316G cells showing rolling adhesion. Similarly, it significantly enhanced binding of E320A cells, primarily via rolling adhesion. In sum, these data establish that LA1 induces partial integrin activation and an intermediate affinity conformation in CD11bA.

CD11b activation via LA1 does not harm the vascular endothelium

Inflammatory activation of the vascular endothelium upregulates expression of $\beta 2$ integrin ligands (such as ICAM-1) on cellular surface that leads to increased leukocyte adhesion and typically results in endothelial cell damage due to the release of highly cytotoxic reactive oxygen species (ROS) and proteases by the adherent neutrophils. Therefore, a key concern with the development of therapeutics using integrin activation as a mechanism of action has been whether the subsequent enhancement in neutrophil (and other leukocyte) cell adhesion would lead to increased localized damage of the endothelium. To address this issue, we performed two sets of experiments. *One*, we used an arterial balloon injury model to determine local effects of LA1 treatment on endothelial injury *in vivo*. As previously reported, LA1 reduces neointimal hyperplasia in a dose-dependent fashion post balloon angioplasty (19, 44). We examined vascular re-endothelialization in balloon-injured Fisher male rats treated with either LA1 or vehicle. Endothelial damage was measured using Evan's blue vital staining, where the denuded vascular regions show blue staining due to high permeability of the albumin-bound Evan's Blue dye, whereas intact endothelium does not (47). Seven days after balloon angioplasty, arteries from control animals showed high blue staining (Fig. 6B), whereas, minimal blue staining was observed in injured arteries of LA1-treated rats. Quantification showed a significantly reduced uptake of the Evan's blue dye by LA1 treated arteries (Fig. 6C). Immunohistochemical staining with anti-von Willebrand factor (vWF) antibody, which stains the vascular endothelium (48), showed significant re-endothelialization at the site of balloon injury with LA1 treatment (Fig. 6D), suggesting that LA1 may accelerate the process of endothelial regeneration (49). Additionally, we analyzed

animals that received a high dose of LA1 (2mg/kg/d for three weeks) and did not observe any signs of systemic vascular injury or leakage, edema or systemic vascular compromise in the liver, spleen, kidney, lung and heart (not shown), mitigating the concern of systemic vascular toxicity of LA1. *Two*, we co-incubated neutrophils with human vein endothelial cells (HUVECs) *in vitro* in the absence or presence of LA1 and measured HUVEC cytotoxicity. We did not observe increases in DNA damage (Fig. S14A-S14B) or apoptosis (Fig. S14C) in the HUVEC monolayer incubated with neutrophils in the presence of LA1 over untreated, control cells. Together, these results show that LA1 treatment does not harm the endothelium. Similarly, previously studies by others using knock-in animals that express constitutively active mutants of integrins CD11a/CD18 (50, 51) or $\alpha4\beta7$ (52) have not reported any signs of vascular injury in the various experimental models, suggesting that integrin activation, *per se*, may not harm the vasculature or have any harmful consequences for animals under normal conditions.

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Supplemental Figures and Figure Legends

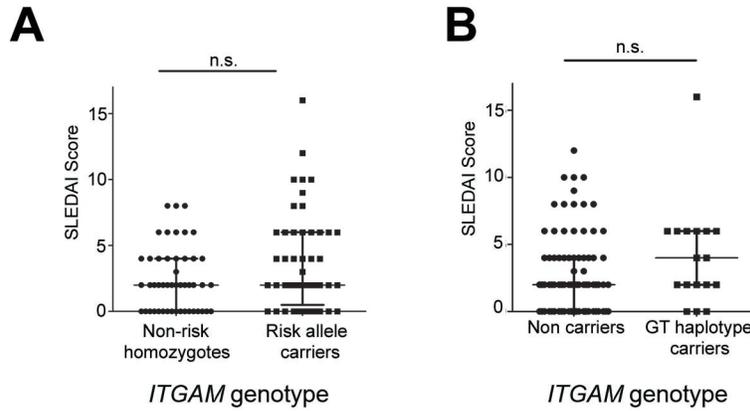


Figure S1. SLE Disease Activity Index (SLEDAI) scores in SLE patients at the time of blood sampling, stratified by *ITGAM* genotype. Patients are separated using the same groups in panels A. and B. as was done in Figure 1A and 1B respectively. SLEDAI scores are compared between genotype groups using the Mann-Whitney U test, with no significant differences observed (n.s.). Central tendency is represented by the median, and error bars show the interquartile range.

Figure S2. Molecular dynamics simulations show that LA1 induces partially active, intermediate affinity conformation in the CD11bA. **A.** A diagram showing domain organization of the CD11b and the CD18 chains. Sites of mutations encoded by the three ITGAM SNPs under study here are also depicted. **B.** A ribbon model of integrin CD11b/CD18 in its bent conformation based on the published structure of $\alpha X\beta 2$ (53). The model also depicts the proposed locations of the three mutations encoded by the three ITGAM SNPs under study here. **C.** Chemical structure of LA1. Also shown is a computational model of the LA1 bound CD11bA, displaying LA1 (red stick model) docked present in the activation-sensitive allosteric pocket near the F- $\alpha 7$ region of CD11bA (white ribbon). A metal ion at the MIDAS site is shown as a blue sphere. **D.** Graph showing computed root-mean-square-deviation (RMSD) of the CD11bA domain after removal of LA1 from the LA1-docked structure. Molecular dynamics simulation of LA1-docked CD11bA structure was performed for 30ns, after removal of LA1 from the binding pocket, and it showed conformational changes in the LA1-removed CD11bA that stabilized after 8ns of simulation, into a conformation that resembled the closed form. These molecular dynamics studies suggest that LA1 induces intermediate affinity conformation in the CD11bA, thereby priming the integrin for ligand binding. **E.** Graph showing computed RMSD values of different regions of the CD11bA domain (amino acid residue numbers on x-axis), after molecular dynamics simulation of various forms. It shows a large movement in the F- $\alpha 7$ loop, $\alpha 7$ helix and the $\alpha 1$ helix regions between the LA1-docked and LA1-removed structures that stabilized after 8ns of simulation, into a conformation that resembled the closed form. **F.** Table showing calculated RMSD values between LA1-docked and LA1-removed forms of CD11bA for various regions of

CD11bA. **G.** A superposition of the most representative structures of different forms of the CD11bA domain derived from MD simulations. The superimposed ribbon diagrams show structures of x-ray derived CD11b in the closed conformation (yellow ribbon) (27) and open conformation (28) (blue ribbon) were superimposed with an energy minimized structure of LA1-bound CD11bA (19) (LA1 is omitted for clarity) prior to molecular dynamics (MD) simulation (left figure, CD11bA is shown as red ribbon) and after a 30ns MD simulation (right figure, CD11bA is shown as pink ribbon). A zoomed-in view of the activation-sensitive F- α 7 region is presented in the inset, where all four structures have been superimposed to show the conformational changes upon MD simulation.

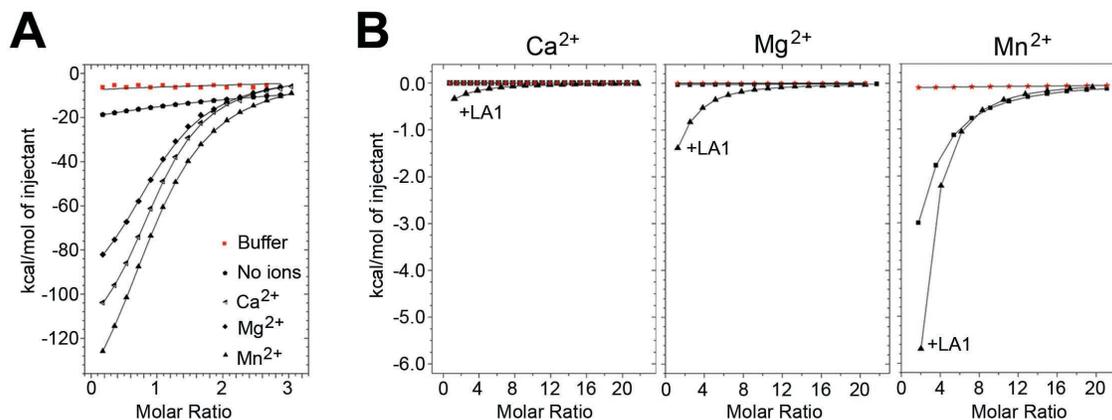


Figure S3. Isothermal titration calorimetry (ITC) based measurement of LA1 binding to CD11bA. **A.** Results of isothermal titration calorimetry (ITC) based measurements of LA1 binding to CD11bA in the absence or presence of various divalent ions at 298K (25°C). The graph shows integrated heats of reaction derived from the binding of LA1, in the reaction cell, when titrated with CD11bA in the presence of various metal ions, as shown. The solid lines represent the least square fit to a single binding model. **B.** The graphs show integrated heats of reaction derived from the binding of CD11bA in the reaction cell, in the absence or presence of three different metal ions, as indicated, when titrated with a solution of LA1. The solid lines represent the least square fit to a single binding model.

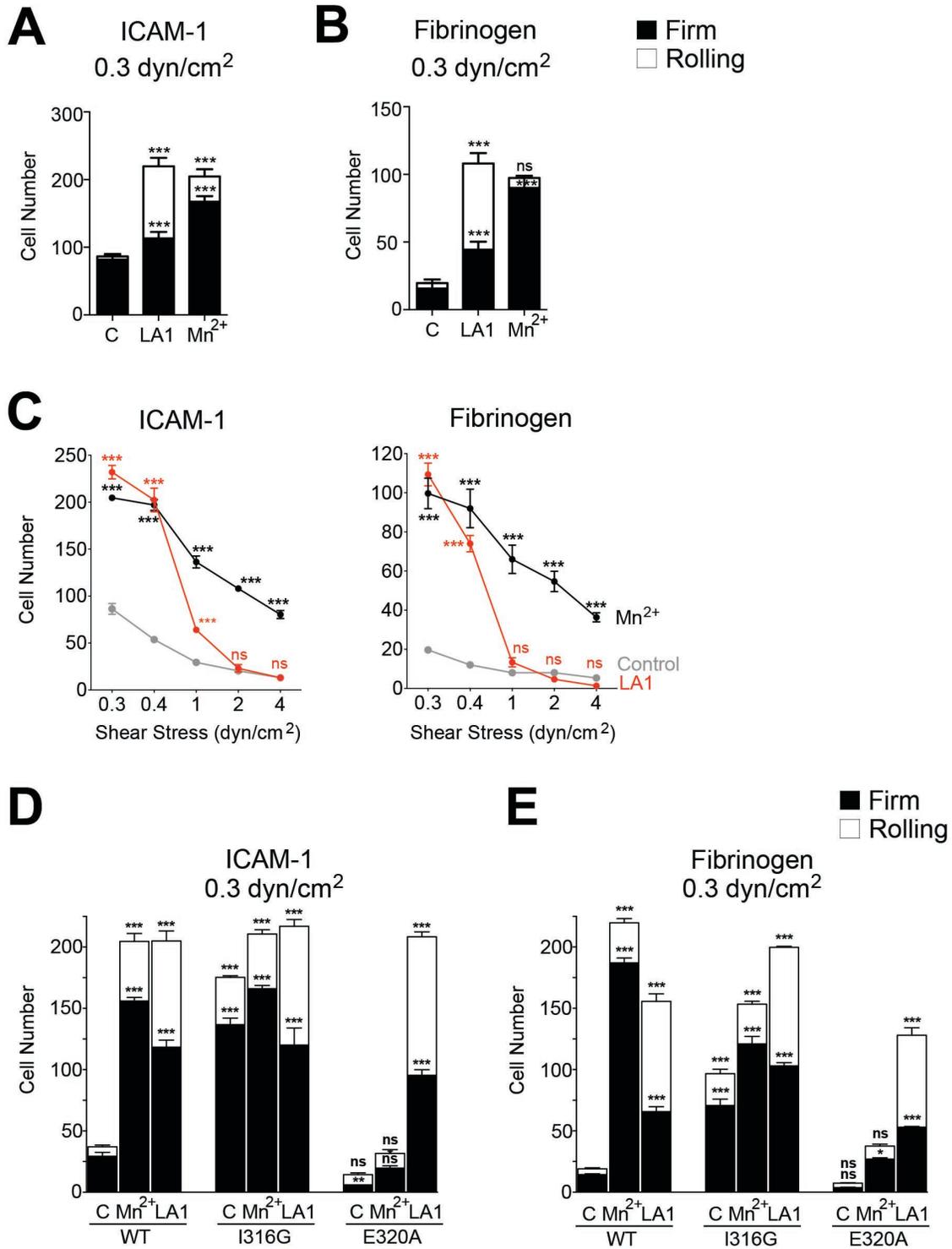


Figure S4. LA1 binding enhances rolling adhesion of CD11b-expressing cells under shear stress. **A-B.** Adhesive behavior of vehicle (C), Mn²⁺, or LA1-treated

CD11b/CD18-expressing cells to immobilized ligand ICAM-1 (**A**) or to fibrinogen (**B**) under the wall shear stress of 0.3 dyn/cm^2 . Bars show mean \pm SD (n=3) from one of at least three independent experiments. ($***P < 0.001$, ns = not significant, Student's t-test).

C. Cell resistance to detachment in shear flow. Graphs show total number of CD11b/CD18-expressing cells remaining bound at the end of each shear stress. Each data point shows the number of cells remaining bound (mean \pm SD) (n=3) from one of at least three independent experiments. ($***P < 0.001$, ns = not significant, Student's t-test).

D. Graph showing adhesion of cells expressing CD11bWT/CD18, CD11bI316G/CD18 or CD11bE320A/CD18 to immobilized ligand ICAM-1 in DMSO (C), Mn^{2+} or LA1 under a constant wall shear stress of 0.3 dyn/cm^2 . Bars show mean \pm the standard deviation (SD) (n=3) of cumulative number of firmly adherent and rolling cells. Data is from one of at least three independent experiments. ($***P < 0.001$, ns = not significant, Student's t-test).

E. Graph showing adhesion of cells expressing CD11bWT/CD18, CD11bI316G/CD18 or CD11bE320A/CD18 to immobilized ligand Fibrinogen in DMSO (C), Mn^{2+} or LA1 under a constant wall shear stress of 0.3 dyn/cm^2 . Bars show mean \pm the standard deviation (SD) (n=3) and are from one of at least three independent experiments. ($***P < 0.001$, ns = not significant, Student's t-test).

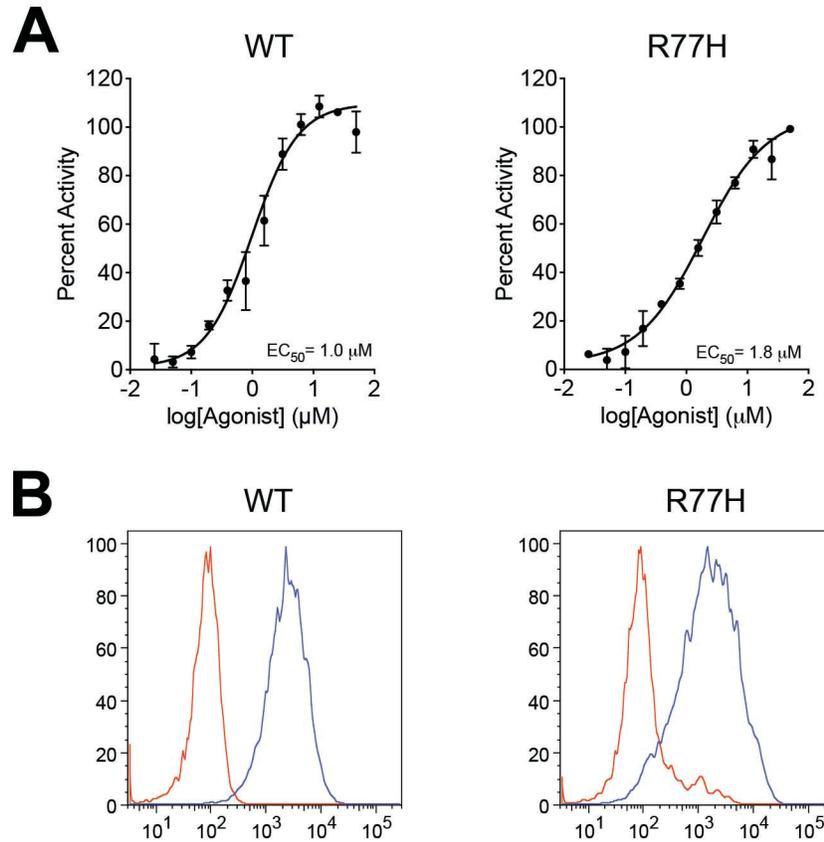


Figure S5. LA1 increases adhesion of WT and R77H mutant integrin CD11b/CD18 to similar levels. **A.** Dose-response curves showing the percentages of input K562 CD11b/CD18 WT (**A**) or R77H (**B**) CD11b/CD18 cells (with similar expression levels, see **B** below) adhering to immobilized fibrinogen in the presence of increasing concentration of LA1. EC_{50} values are indicated on each graph. Data shown are means \pm SEM ($n = 3$ replicates per data point) and are from one of at least three independent experiments. **B.** Flow cytometric analysis showing similar level of CD11b/CD18 surface expression on live K562 cells stably transfected with CD18 and CD11b WT or CD11b R77H and analyzed using the anti-CD11b/CD18 mAb IB4 (blue trace) or an IgG2a isotype control (red trace). Data shown are representative of at least two independent experiments.

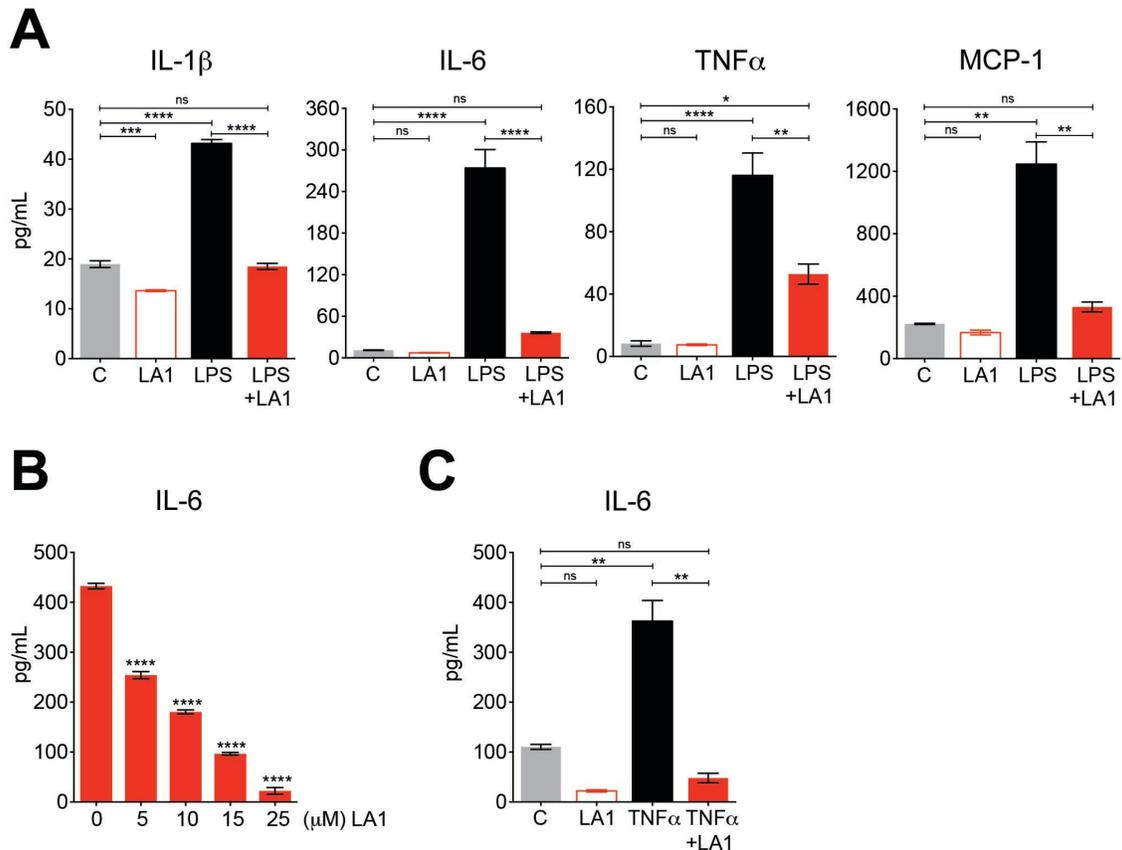


Figure S6. LA1 treatment suppresses synthesis of pro-inflammatory chemokines and cytokines in TLR4-stimulated primary neutrophils and macrophages. A. ELISA-based quantification of IL-1 β , IL6, TNF and MCP-1 levels in supernatants of mouse neutrophils treated with vehicle DMSO (C), LA1 (15 μ M), LPS (100ng/mL) or LPS (100ng/mL) and LA1 (15 μ M) for 8 hrs (IL-1 β , IL6 and MCP-1) or 12 hrs (TNF). Bars show mean \pm the standard error of the mean (SEM) (n=3) from one of at least two independent experiments. (* P <0.05, ** P <0.01, **** P <0.0001, ns = not significant, One-way ANOVA, Tukey's test). **B.** Bar graph showing ELISA based quantification of IL6 levels in supernatants of C57BL/6 WT bone marrow derived macrophages stimulated with LPS (100ng/mL) in the presence of various concentrations of LA1 for 12 hrs. Bars show mean \pm SEM (n=3) from one of at least two independent experiments. (**** P

<0.0001, ns = not significant, Student's t-test). **C.** Bar graph (mean \pm SEM) showing ELISA based quantification of IL6 levels in supernatants of C57BL/6 WT mouse neutrophils treated with vehicle DMSO (C), LA1 (15 μ M), TNF α (20ng/mL) or TNF α (20ng/mL) and LA1 (15 μ M) for 12 hrs. Data are from one of at least two independent experiments. (** P < 0.01, ns = not significant, One-way ANOVA, Tukey's test).

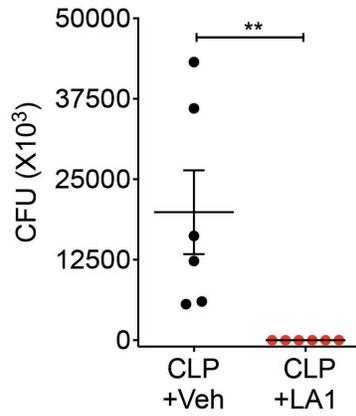


Figure S7. CFU count in CLP mice. Graph showing polymicrobial load (CFUs) in blood of B6 WT animals undergoing CLP and treated with vehicle or LA1 24 hr post-CLP. Each circle represents data from individual animal. Horizontal lines indicate arithmetic mean \pm SEM. (** $P < 0.01$, Student's t-test).

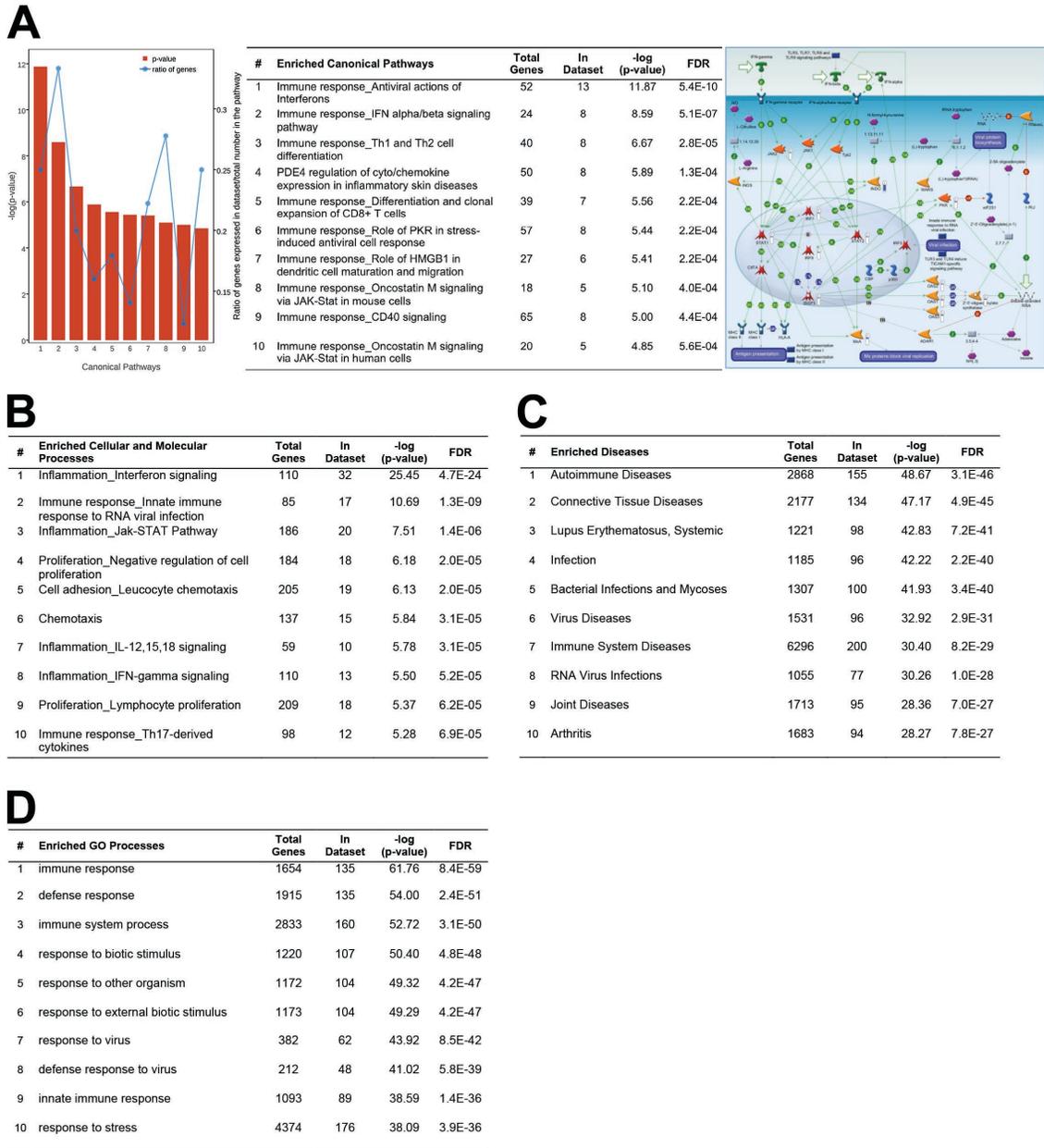


Figure S8. Antiviral immune response canonical pathways are enriched in LPS-stimulated human macrophages treated with LA1. A. Graph (left) of a table (middle) showing the top 10 significant canonical pathways that are enriched in the 416 genes that were significantly changed in macrophages treated with LPS+LA1 vs LPS, upon analysis of microarray data using GeneGo. The bar graph (left) shows P-value associated with enrichment. A graphical representation of the enriched pathway from GeneGo is

presented on the right. The blue hexagon denotes the ratio of number of genes present in our dataset over the total number of genes in that particular pathway. **B.** A table showing the top 10 significant Cellular and Molecular Processes that are enriched in the 416 genes that were significantly changed in macrophages treated with LPS+LA1 vs LPS, upon analysis of microarray data using GeneGo. **C.** A table showing the top 10 significantly enriched disease categories in the 416 genes that were significantly changed in macrophages treated with LPS+LA1 vs LPS, upon analysis of microarray data using GeneGo. Autoimmune diseases and SLE are among the top. **D.** A table showing the top 10 significantly enriched GO categories in the 416 genes that were significantly changed in macrophages treated with LPS+LA1 vs LPS, upon analysis of microarray data using GeneGo. Immune response is at the top.

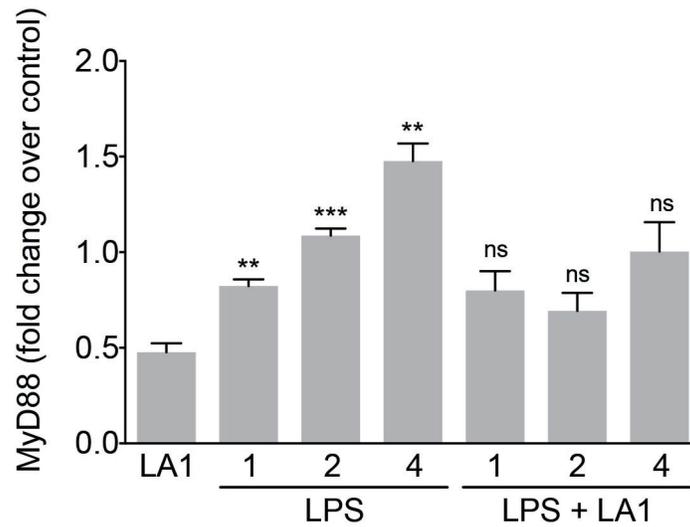


Figure S9. LA1-mediated CD11b activation reduces LPS-stimulated expression of MyD88. Bar graph (mean \pm SEM (n=3)) showing densitometric quantification of MyD88 levels in the immunoblots from lysates of RAW macrophages stimulated with LPS for 0-4h in the absence or presence of LA1, as presented in Figure 3D in the main text, showing that LA1-mediated CD11b activation significantly reduced MyD88 levels. Expression was normalized relative to GAPDH levels. (** $P < 0.01$, *** $P < 0.001$, ns = not significant, Student's t-test).

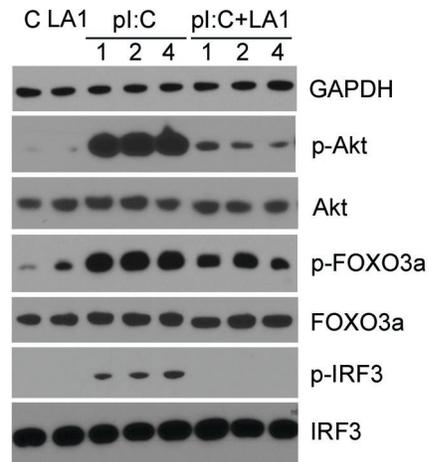


Figure S10. LA1-mediated CD11b activation suppresses TLR3-dependent IFN signaling via Akt-FOXO3-IRF3 axis. Immunoblot analysis of various phosphorylated (p-) and total proteins in lysates of RAW macrophages stimulated with pI:C for 0-4h in the absence or presence of LA1. GAPDH was used as loading control.

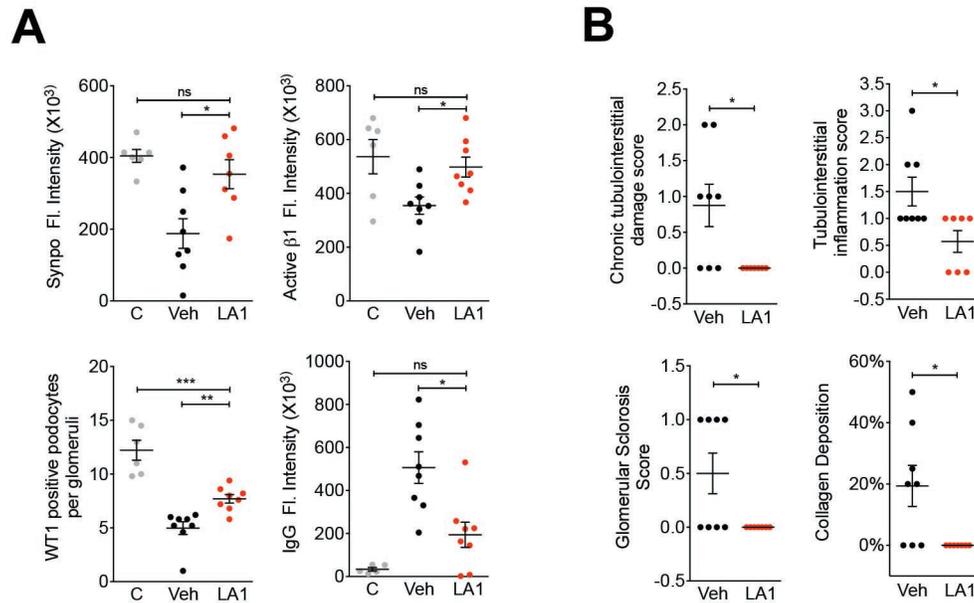


Figure S11. LA1-treated lupus-prone mice show reduced glomerular damage. A.

Graphs showing quantification of immunostaining in fluorescently-labeled kidney sections from 19-week old control (MRL/*Mpj*) and lupus-prone MRL/*lpr* mice, treated with either vehicle or LA1 (as shown in Fig. 4E). Kidney sections stained with antibodies against the podocyte markers synaptopodin, WT1, active integrin β 1 or anti-IgG (to quantify immune complex deposition) were quantified. Individual data points are displayed and line represents mean \pm SEM (n=5 for MRL/*Mpj*, n=7 LA1-treated MRL/*lpr* mice and n=8 vehicle-treated MRL/*lpr* mice); C is MRL/*Mpj*, veh is vehicle treated MRL/*lpr*, **B.** Kidney damage scores from kidney tissue from MRL/*lpr* vehicle versus LA1 treated mice, as assessed by histochemical analyses for tubulointerstitial damage, glomerulosclerosis and collagen deposition. Individual data points are shown. Line indicates mean \pm SEM (n=7 LA1-treated MRL/*lpr* mice and n=8 vehicle-treated MRL/*lpr* mice). (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$, ns = not significant, Student's t-test).

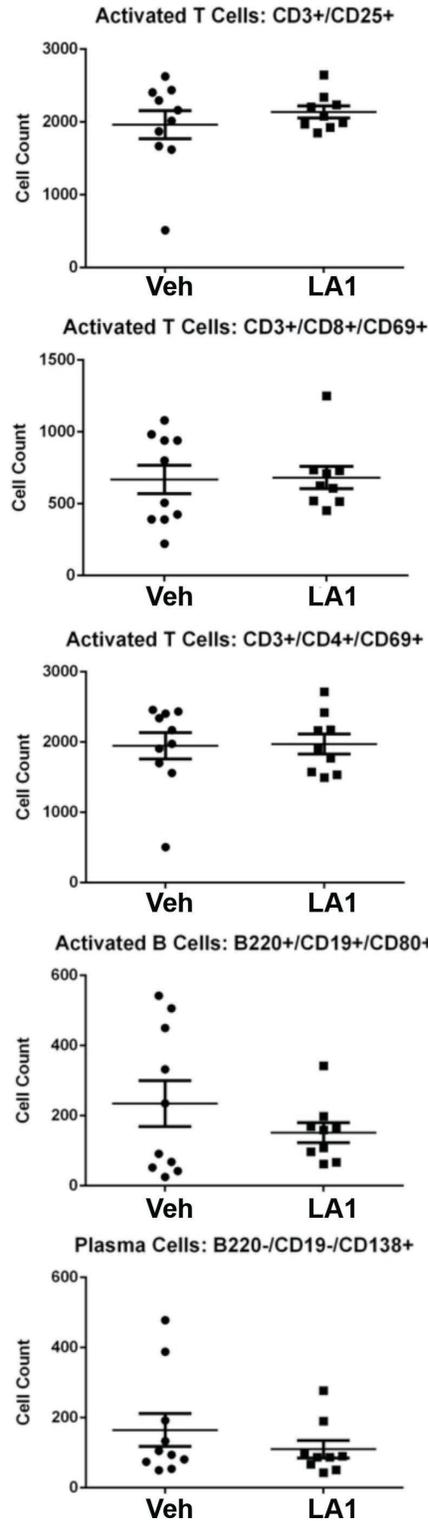


Figure S12. Effect of LA1 on splenic cell subsets. Graphs represent splenic cell counts for specific cell subsets in individual mice from LA1-treated and vehicle-treated MRL/lpr

mice, at euthanasia, at 19 weeks of age (n=10 in vehicle-treated and n=9 in LA1-treated). Y-axis represents cell counts of specific cell subset/ 1×10^6 splenocytes. Horizontal lines are mean+SEM and the dots represent values in individual mice. All comparisons are non-significant.

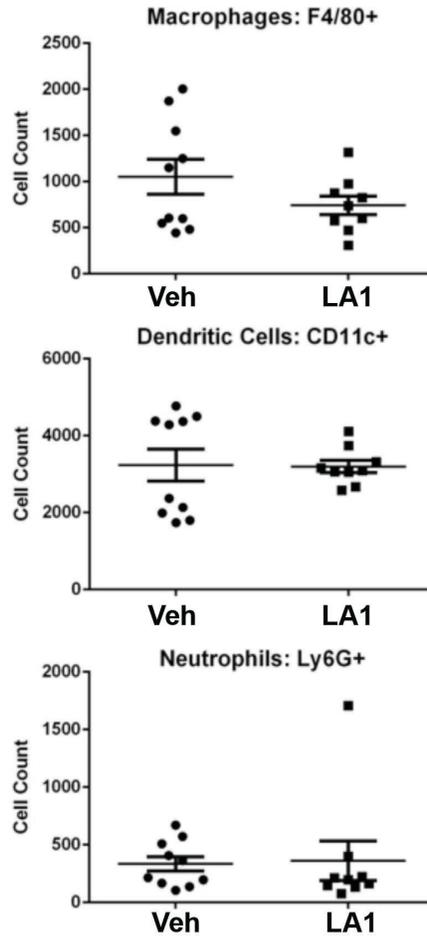


Figure S13. Effect of LA1 on splenic myeloid cell subsets. Graphs represent splenic cell counts for specific cell subsets in individual mice from LA1-treated and vehicle-treated MRL/lpr mice, at euthanasia, at 19 weeks of age (n=10 in vehicle-treated and n=9 in LA1-treated). Y-axis represents cell counts of specific cell subset/ 1×10^6 splenocytes. Horizontal lines are mean+SEM and the dots represent values in individual mice. All comparisons are non-significant.

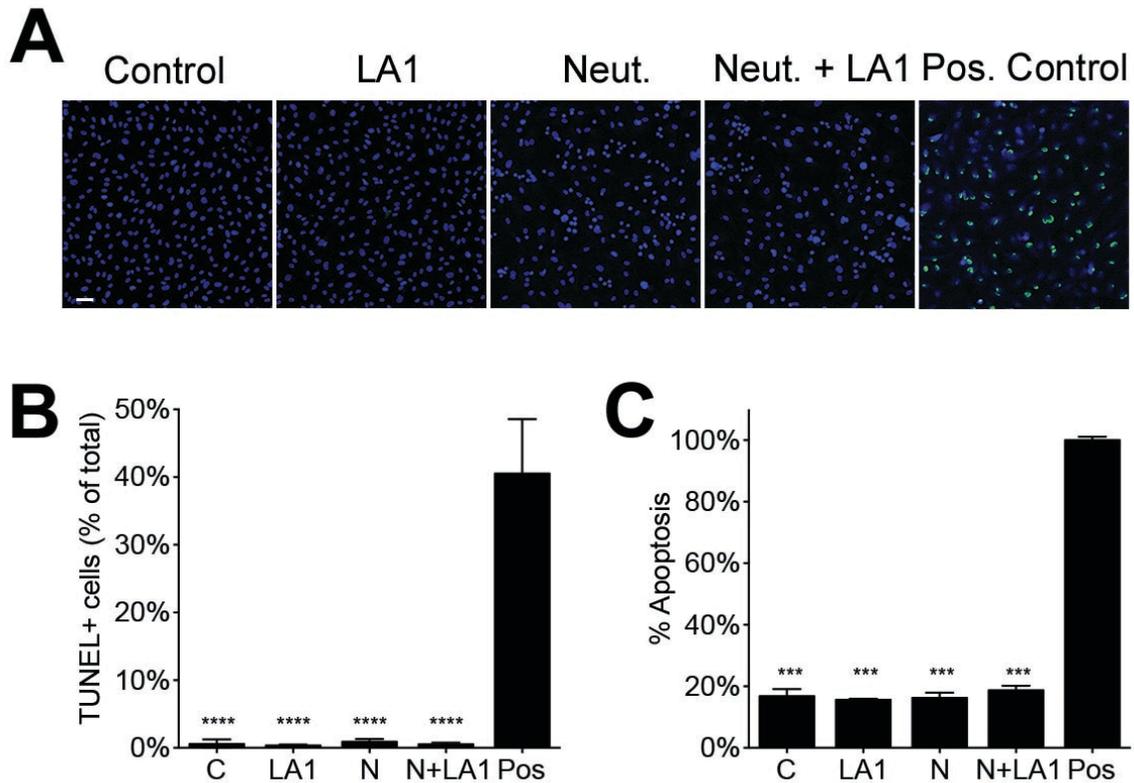


Figure S14. LA1 does not damage endothelial cells. **A.** Representative confocal images of human umbilical vein endothelial cells (HUVECs) cultured in the absence or presence of LA1 and neutrophils (DAPI-stained nuclei (blue), TUNEL staining (green)). H_2O_2 -treated HUVECS serve as positive control. Scale bar=50 μ m. **B.** Quantification of TUNEL-positive cells as a percentage of total HUVECs from (A). Data shown are mean \pm SEM from at least 5 independent fields, from duplicate experiments. **C.** Quantification of HUVEC apoptosis under various conditions (as in A) using LDH release assay and expressed as a percentage of total LDH in a positive control (cells lysed with 2% Triton-100). Data shown are mean \pm SEM (n=3). (***) P <0.001, (****) P <0.0001, ns = not significant, Student's t-test).

Supplemental Tables

Table S1: Clinical and serologic characteristics of the SLE patients

	Clinical Feature	SLE Cases
		n=171
Demographic characteristics	Age, years*	50 (37-63)
	Female, no (%)	148 (87)
ACR Clinical Criteria for SLE	Malar rash, no (%)	89 (52)
	Discoid rash, no (%)	55 (32)
	Photosensitivity, no (%)	96 (56)
	Oral ulcers, no (%)	57 (33)
	Arthritis, no (%)	144 (84)
	Serositis, no (%)	57 (33)
	Renal disorder, no (%)	61 (36)
	Neurological disorder, no (%)	19 (11)
	Hematological disorder, no (%)	64 (30)
	Immunological disorder, no (%)	118 (69)
Prevalence of Specific Autoantibody Profiles	ANA, no (%)	160 (94)
	Ro, no (%)	63 (37)
	La, no (%)	30 (18)
	Sm, no (%)	34 (20)
	RNP, no (%)	47 (27)
	DNA, no (%)	94 (55)

* the age values are the median (interquartile range), other values represent the number of patients who have that categorical finding, followed by the percentage in parentheses.

Metal ion	CD11bA alone				CD11bA + LA1			
	K_d (μ M)	ΔS^0 (kcal/mol/deg)	ΔH^0 (kcal/mol)	ΔG^0 (kcal/mol)	K_d (μ M)	ΔS^0 (kcal/mol/deg)	ΔH^0 (kcal/mol)	ΔG^0 (kcal/mol)
Ca ²⁺	2041 ±500	3.629 ±0.02	-0.069 ±0.02	-3.698	43.8±12	0.34±0.01	-5.64±1.14	-5.980
Mg ²⁺	1096 ±306	3.349 ±0.01	-0.720 ±0.2	-4.069	27.5±8	0.02±0.001	-6.289±1.98	-6.269
Mn ²⁺	41.7 ±5	0.18 ±0.22	-6.19 ±1.20	-6.010	12.58±2	1.47±0.21	-8.29±1.30	-6.820

Table S2. Binding energy of CD11bA in the absence or presence of pre-bound LA1 to various metal ions.

CD11bA with metal ions	LA1 Binding			
	K_d (μ M)	ΔS^0 (kcal/mol/deg)	ΔH^0 (kcal/mol)	ΔG^0 (kcal/mol)
None	47 \pm 9	-0.402 \pm 0.071	-127.1 \pm 1.07	-7.304
Ca ²⁺	0.9 \pm 0.02	-0.283 \pm 0.043	-92.69 \pm 0.12	-8.356
Mg ²⁺	1 \pm 0.07	-0.311 \pm 0.064	-100.9 \pm 1.01	-8.222
Mn ²⁺	1.6 \pm 0.2	-0.541 \pm 0.093	-169.3 \pm 1.56	-8.082

Table S3. Binding energy of LA1 to CD11bA in the absence or presence of various metal ions.

Table S4. mRNA expression of 416 genes is affected by LA1.

Table S4. mRNA expression of 416 genes is affected by LA1

	ProbeID	Accession	Entrez Gene_ID	Probe_id	Symbol	[LPS](normalized)	[LPS + LA1](normalized)	p (Corr)	Fold Change	FC (abs)	Regulation	Significant
1	5570711	NM_002164.4	3620	ILMN_32399	IDO1	5.52	0.30	0.00	-37.03	37.03	down	yes
2	5570278	NM_002416.1	4283	ILMN_17453	CXCL9	4.75	-0.05	0.00	-27.76	27.76	down	yes
3	380259	NM_002164.3	3620	ILMN_16563	INDO	5.05	0.25	0.00	-27.72	27.72	down	yes
4	6270553	NM_001565.2	3627	ILMN_17917	CXCL10	5.73	0.98	0.00	-26.86	26.86	down	yes
5	870202	NM_003810.2	8743	ILMN_18013	TNFSF10	4.42	0.02	0.00	-21.14	21.14	down	yes
6	6620121	NM_005623.2	6355	ILMN_17729	CCL8	4.49	0.36	0.00	-17.56	17.56	down	yes
7	1980524	NM_052941.3	115361	ILMN_17713	GBP4	4.24	0.29	0.00	-15.43	15.43	down	yes
8	1030204	NM_002981.1	6346	ILMN_20869	CCL1	3.92	-0.01	0.00	-15.26	15.26	down	yes
9	3360343	NM_080657.4	91543	ILMN_16578	RSAD2	4.03	0.28	0.00	-13.46	13.46	down	yes
10	6520523	NM_145659.3	246778	ILMN_17537	IL27	3.56	0.00	0.00	-11.79	11.79	down	yes
11	1510364	NM_052942.2	115362	ILMN_21145	GBP5	3.98	0.48	0.00	-11.30	11.30	down	yes
12	4900435	NM_006573.3	10673	ILMN_17584	TNFSF13B	2.82	-0.64	0.00	-11.01	11.01	down	yes
13	3370349	NM_001710.4	629	ILMN_17742	CFB	3.74	0.37	0.00	-10.29	10.29	down	yes
14	1980750	NM_145641.1	80833	ILMN_17568	APOL3	3.03	-0.31	0.00	-10.12	10.12	down	yes
15	6330132	NM_002201.4	3669	ILMN_16599	ISG20	4.28	0.95	0.00	-10.00	10.00	down	yes
16	7320546	NM_014398.2	27074	ILMN_21708	LAMP3	3.37	0.21	0.00	-8.94	8.94	down	yes
17	6840020	NM_006573.3	10673	ILMN_20668	TNFSF13B	2.53	-0.57	0.00	-8.56	8.56	down	yes
18	7100646	NM_006274.2	6363	ILMN_17691	CCL19	3.22	0.12	0.00	-8.55	8.55	down	yes
19	4540709	NM_005409.3	6373	ILMN_20678	CXCL11	3.10	0.01	0.00	-8.51	8.51	down	yes
20	3180039	NM_015149.3	23179	ILMN_16543	RGL1	1.79	-1.27	0.00	-8.38	8.38	down	yes
21	1030333	NM_002982.3	6347	ILMN_17200	CCL2	1.82	-1.25	0.00	-8.37	8.37	down	yes
22	2190148	NM_002053.1	2633	ILMN_21487	GBP1	3.78	0.74	0.00	-8.24	8.24	down	yes
23	2810767	NM_005755.2	10148	ILMN_18026	EBI3	3.00	0.03	0.00	-7.86	7.86	down	yes
24	6840035	NM_002053.1	2633	ILMN_17011	GBP1	3.72	0.75	0.00	-7.83	7.83	down	yes
25	3710243	NM_024625.3	56829	ILMN_17299	ZC3HAV1	3.39	0.42	0.00	-7.80	7.80	down	yes
26	3870338	NM_006820.1	10964	ILMN_17239	IFI44L	2.91	-0.02	0.00	-7.63	7.63	down	yes
27	7400743	NM_020954.2	57714	ILMN_22890	KIAA1618	2.94	0.04	0.00	-7.47	7.47	down	yes
28	2000148	NM_001548.3	3434	ILMN_17076	IFIT1	4.06	1.22	0.00	-7.14	7.14	down	yes
29	5700725	NM_033255.2	94240	ILMN_23885	EPST11	2.91	0.08	0.00	-7.12	7.12	down	yes
30	5360156	NM_003641.3	8519	ILMN_18012	IFITM1	2.81	0.04	0.00	-6.83	6.83	down	yes
31	1690066	NM_002462.2	4599	ILMN_16623	MX1	3.33	0.64	0.00	-6.44	6.44	down	yes
32	7650097	NM_198213.1	8638	ILMN_16748	OASL	4.12	1.47	0.00	-6.27	6.27	down	yes
33	5490470	NM_002463.1	4600	ILMN_22319	MX2	2.94	0.30	0.00	-6.21	6.21	down	yes
34	6280543	NM_003733.2	8638	ILMN_16817	OASL	2.99	0.38	0.00	-6.09	6.09	down	yes
35	580678	NM_001080535.1	93082	ILMN_22358	LINC1	3.03	0.42	0.00	-6.08	6.08	down	yes
36	4040181	NM_001042483.1	26471	ILMN_24046	NUPR1	2.39	-0.22	0.00	-6.08	6.08	down	yes
37	1770593	NM_003956.3	9023	ILMN_17410	CH25H	2.56	-0.03	0.00	-6.00	6.00	down	yes
38	520408	NM_001549.2	3437	ILMN_22397	IFIT3	3.62	1.04	0.00	-5.97	5.97	down	yes
39	540670	NM_172374.1	259307	ILMN_16599	IL411	2.04	-0.51	0.00	-5.88	5.88	down	yes
40	2760500	NM_001775.2	952	ILMN_22337	CD38	2.56	0.03	0.00	-5.79	5.79	down	yes
41	5550035	NM_178452.3	123872	ILMN_17769	LRRC50	2.57	0.08	0.00	-5.63	5.63	down	yes
42	4760703	NM_014314.3	23586	ILMN_17970	DDX58	2.81	0.33	0.00	-5.58	5.58	down	yes
43	3940520	NM_001002010.1	51251	ILMN_23521	NT5C3	2.52	0.09	0.00	-5.41	5.41	down	yes
44	240053	NM_001024071.1	2643	ILMN_18127	GCH1	2.84	0.42	0.00	-5.36	5.36	down	yes
45	1770072	XM_001133269.2	730249	ILMN_31932	IRG1	3.38	0.97	0.00	-5.30	5.30	down	yes
46	5490068	NM_153259.2	255231	ILMN_16604	MCOLN2	2.53	0.14	0.00	-5.24	5.24	down	yes
47	4570768	NM_005658.3	7185	ILMN_16982	TRAF1	3.16	0.78	0.00	-5.19	5.19	down	yes
48	450189	NM_199139.1	54739	ILMN_17426	XAF1	2.50	0.13	0.00	-5.17	5.17	down	yes
49	7000398	NM_001002010.1	51251	ILMN_17697	NT5C3	2.47	0.11	0.00	-5.13	5.13	down	yes
50	7550242	NM_003865.1	8820	ILMN_17429	HEX1	2.28	-0.06	0.00	-5.05	5.05	down	yes
51	5390239	NM_005191.3	941	ILMN_17167	CD80	2.57	0.27	0.00	-4.94	4.94	down	yes
52	1010360	NM_001024070.1	2643	ILMN_23358	GCH1	2.56	0.26	0.00	-4.91	4.91	down	yes

53	4670114 XM_001133269.1	730249 ILMN_18383LOC730249	3.81	1.52	0.00	-4.90	4.90	down	yes
54	1740360 NM_017414.3	11274 ILMN_32404 USP18	2.39	0.11	0.00	-4.86	4.86	down	yes
55	7160373 NM_002033.2	2526 ILMN_17920 FUT4	1.89	-0.38	0.00	-4.81	4.81	down	yes
56	6590445 NM_018993.2	54453 ILMN_17695 RIN2	1.85	-0.40	0.00	-4.78	4.78	down	yes
57	2510220 NM_005533.2	3430 ILMN_17453 IFI35	2.38	0.13	0.00	-4.75	4.75	down	yes
58	990768 NM_006187.2	4940 ILMN_17453 OAS3	2.43	0.19	0.00	-4.73	4.73	down	yes
59	4290189 NM_012385.1	26471 ILMN_18105 P8	2.06	-0.18	0.00	-4.73	4.73	down	yes
60	4540382 NM_020119.3	56829 ILMN_17248 ZC3HAV1	2.73	0.49	0.00	-4.72	4.72	down	yes
61	5720482 NM_016323.2	51191 ILMN_17297 HERC5	3.25	1.04	0.00	-4.64	4.64	down	yes
62	7200168 NM_006207.1	5157 ILMN_16803 PDGFRL	2.26	0.05	0.00	-4.62	4.62	down	yes
63	6650242 NM_021034.2	10410 ILMN_18057 IFITM3	2.22	0.04	0.00	-4.52	4.52	down	yes
64	2360392 NM_031212.3	81894 ILMN_17904 SLC25A28	2.02	-0.14	0.00	-4.49	4.49	down	yes
65	1260270 NM_004833.1	9447 ILMN_16813 AIM2	2.30	0.15	0.00	-4.42	4.42	down	yes
66	1410181 NM_022136.3	64092 ILMN_16848 SAMS1N1	2.05	-0.09	0.00	-4.41	4.41	down	yes
67	380201 NM_012108.2	26228 ILMN_32479 STAP1	2.15	0.02	0.00	-4.37	4.37	down	yes
68	4830471 NM_024873.3	79931 ILMN_17075 TNIP3	2.39	0.29	0.00	-4.31	4.31	down	yes
69	1090390 NM_001032409.1	4938 ILMN_24108 OAS1	2.19	0.10	0.00	-4.26	4.26	down	yes
70	5960343 NM_033405.2	85441 ILMN_17875 PRIC285	2.78	0.70	0.00	-4.22	4.22	down	yes
71	870408 NM_000585.2	3600 ILMN_17241 IL15	2.30	0.24	0.00	-4.19	4.19	down	yes
72	3180681 NR_003187.1	654817 ILMN_21129 NCF1C	1.60	-0.46	0.00	-4.19	4.19	down	yes
73	3170091 NM_153236.3	168537 ILMN_17766 GIMAP7	1.46	-0.60	0.00	-4.17	4.17	down	yes
74	3940438 NM_000265.4	653361 ILMN_16973 NCF1	1.39	-0.67	0.00	-4.17	4.17	down	yes
75	5260070 NM_021170.2	57801 ILMN_16534 HES4	2.61	0.55	0.00	-4.17	4.17	down	yes
76	3840593 NM_004510.2	3431 ILMN_24151 SP110	2.20	0.15	0.00	-4.16	4.16	down	yes
77	1340491 NM_004510.2	3431 ILMN_17314 SP110	2.19	0.14	0.00	-4.15	4.15	down	yes
78	3370138 NM_152854.2	958 ILMN_23678 CD40	2.25	0.20	0.00	-4.14	4.14	down	yes
79	3990170 NM_005532.3	3429 ILMN_20587 IFI27	1.96	-0.07	0.00	-4.07	4.07	down	yes
80	540671 NM_001080978.1	10288 ILMN_23123 LILRB2	1.14	-0.88	0.00	-4.05	4.05	down	yes
81	7040035 NM_001032409.1	4938 ILMN_16756 OAS1	2.14	0.14	0.00	-4.02	4.02	down	yes
82	4040576 NM_000600.1	3569 ILMN_16996 IL6	3.34	1.35	0.00	-3.96	3.96	down	yes
83	2480577 NM_002600.3	5142 ILMN_23402 PDE4B	2.05	0.07	0.00	-3.95	3.95	down	yes
84	620403 NR_003133.1	400759 ILMN_17824 LOC400759	2.06	0.10	0.00	-3.90	3.90	down	yes
85	1230767 NM_006435.2	10581 ILMN_16733 IFITM2	2.04	0.10	0.00	-3.86	3.86	down	yes
86	2690435 NM_001548.2	3434 ILMN_16993 IFIT1	2.04	0.12	0.00	-3.80	3.80	down	yes
87	3890609 NM_021105.1	5359 ILMN_17452 PLSCR1	1.98	0.06	0.00	-3.79	3.79	down	yes
88	5810136 NM_003037.1	6504 ILMN_17707 SLAMF1	2.30	0.38	0.00	-3.77	3.77	down	yes
89	630091 NM_181782.2	135112 ILMN_16877 NCOA7	1.70	-0.21	0.00	-3.77	3.77	down	yes
90	5870692 NM_013345.2	29933 ILMN_18111 GPR132	2.06	0.15	0.00	-3.75	3.75	down	yes
91	4730059 NM_138456.3	116071 ILMN_16902 BATF2	1.97	0.08	0.00	-3.73	3.73	down	yes
92	1450427 NM_022147.2	64108 ILMN_21739 RTP4	2.03	0.14	0.00	-3.72	3.72	down	yes
93	3450180 NM_002534.2	4938 ILMN_16582 OAS1	2.03	0.13	0.00	-3.72	3.72	down	yes
94	5960747 NM_006074.3	10346 ILMN_17792 TRIM22	1.92	0.04	0.00	-3.67	3.67	down	yes
95	2710575 NM_001781.1	969 ILMN_21883 CD69	1.87	0.02	0.00	-3.62	3.62	down	yes
96	4490053 NM_001558.2	3587 ILMN_16528 IL10RA	1.97	0.12	0.00	-3.60	3.60	down	yes
97	3830349 NM_002185.2	3575 ILMN_23425 IL7R	2.08	0.23	0.00	-3.60	3.60	down	yes
98	2690689 NM_002214.2	3696 ILMN_17329 ITGB8	1.93	0.11	0.00	-3.55	3.55	down	yes
99	4390059 NM_176796.1	5031 ILMN_16600 P2RY6	1.11	-0.70	0.00	-3.52	3.52	down	yes
100	650328 NM_003327.2	7293 ILMN_21122 TNFRSF4	1.71	-0.10	0.00	-3.52	3.52	down	yes
101	1570484 NM_012068.3	22809 ILMN_16691 ATF5	1.75	-0.07	0.00	-3.52	3.52	down	yes
102	770538 NM_153374.1	256586 ILMN_17244 LYSMD2	1.32	-0.48	0.00	-3.49	3.49	down	yes
103	2100196 NM_005101.1	9636 ILMN_20540 ISG15	3.28	1.48	0.00	-3.48	3.48	down	yes
104	1440564 NM_004350.2	864 ILMN_17874 RUNX3	1.13	-0.67	0.00	-3.47	3.47	down	yes
105	2360348 NM_207315.2	129607 ILMN_17836 CMPK2	1.85	0.06	0.00	-3.47	3.47	down	yes
106	1190026 NM_021822.1	60489 ILMN_18021 APOBEC3G	1.69	-0.10	0.00	-3.45	3.45	down	yes
107	4290368 NM_024430.2	9050 ILMN_17130 PSTPIP2	1.47	-0.30	0.00	-3.42	3.42	down	yes

108	940356 NM_002189.2	3601 ILMN_16656 IL15RA	1.86	0.09	0.00	-3.42	3.42	down	yes
109	4610364 NM_006273.2	6354 ILMN_16834 CCL7	1.69	-0.08	0.00	-3.41	3.41	down	yes
110	1190040 NM_175571.2	155038 ILMN_17473 GIMAP8	1.21	-0.55	0.00	-3.40	3.40	down	yes
111	2120079 NM_002759.1	5610 ILMN_17065 EIF2AK2	1.86	0.10	0.00	-3.39	3.39	down	yes
112	6420520 NM_001250.4	958 ILMN_17792 CD40	1.97	0.21	0.00	-3.39	3.39	down	yes
113	1240142 NM_017654.2	54809 ILMN_18143 SAMD9	1.92	0.17	0.00	-3.35	3.35	down	yes
114	6200672 NM_016118.3	51667 ILMN_16652 NUB1	1.72	-0.02	0.00	-3.35	3.35	down	yes
115	2900725 NM_000785.3	1594 ILMN_17404 CYP27B1	1.78	0.04	0.00	-3.34	3.34	down	yes
116	6060468 NM_002964.3	6279 ILMN_17298 S100A8	0.30	-1.43	0.00	-3.34	3.34	down	yes
117	7560440 NM_000675.3	135 ILMN_18073 ADORA2A	2.27	0.53	0.00	-3.33	3.33	down	yes
118	2320598 NM_000266.1	4693 ILMN_17948 NDP	1.60	-0.13	0.00	-3.31	3.31	down	yes
119	3890523 XM_937367.1	3575 ILMN_16913 IL7R	2.02	0.29	0.00	-3.30	3.30	down	yes
120	3870594 NM_005531.1	3428 ILMN_17109 IFI16	1.56	-0.16	0.00	-3.30	3.30	down	yes
121	7320561 NM_016817.2	4939 ILMN_16740 OAS2	2.30	0.58	0.00	-3.30	3.30	down	yes
122	7040431 NM_020226.3	56978 ILMN_18020 PRDM8	1.81	0.09	0.00	-3.28	3.28	down	yes
123	2370639 NM_138441.2	115004 ILMN_17066 C6orf150	1.66	-0.04	0.00	-3.25	3.25	down	yes
124	4040397 NM_002608.1	5155 ILMN_17758 PDGFB	1.73	0.04	0.00	-3.23	3.23	down	yes
125	5290465 NM_033339.3	840 ILMN_23737 CASP7	1.74	0.06	0.00	-3.22	3.22	down	yes
126	3930681 NM_024119.2	79132 ILMN_16784 DHX58	2.01	0.33	0.00	-3.20	3.20	down	yes
127	5670465 NM_001124.1	133 ILMN_17089 ADM	1.77	0.10	0.00	-3.19	3.19	down	yes
128	1510193 NM_152858.1	9589 ILMN_17489 WTAP	2.09	0.42	0.00	-3.18	3.18	down	yes
129	2070646 NM_020370.1	53831 ILMN_17853 GPR84	1.95	0.28	0.00	-3.16	3.16	down	yes
130	1500280 NM_001031683.1	3437 ILMN_17017 IFIT3	3.29	1.63	0.00	-3.15	3.15	down	yes
131	5220204 NM_018381.2	55337 ILMN_17504 C19orf66	1.65	-0.01	0.00	-3.15	3.15	down	yes
132	5490240 NM_181509.1	84557 ILMN_17761 MAP1LC3A	1.71	0.06	0.00	-3.14	3.14	down	yes
133	7160010 NM_015435.3	25897 ILMN_23811 RNF19A	1.63	-0.01	0.00	-3.12	3.12	down	yes
134	7320370 NM_003151.2	6775 ILMN_17852 STAT4	2.06	0.42	0.00	-3.12	3.12	down	yes
135	4830437 NM_199344.2	375035 ILMN_33076 SFT2D2	1.65	0.02	0.00	-3.10	3.10	down	yes
136	4900086 NM_178232.2	145864 ILMN_16543 HAPLN3	1.61	-0.01	0.00	-3.08	3.08	down	yes
137	5670440 NM_001561.4	3604 ILMN_18133 TNFRSF9	1.62	0.03	0.00	-3.01	3.01	down	yes
138	6510026 NM_016584.2	51561 ILMN_17156 IL23A	2.20	0.62	0.00	-3.00	3.00	down	yes
139	520360 NM_152851.1	64231 ILMN_17210 MS4A6A	0.34	-1.24	0.00	-2.99	2.99	down	yes
140	7560471 NM_145279.4	148932 ILMN_17982 MOBKL2C	1.31	-0.26	0.00	-2.96	2.96	down	yes
141	3800398 NM_018438.4	26270 ILMN_17014 FBXO6	1.65	0.09	0.00	-2.95	2.95	down	yes
142	4120369 NM_021822.1	60489 ILMN_22324 APOBEC3G	1.48	-0.08	0.00	-2.95	2.95	down	yes
143	4150692 NM_017554.1	54625 ILMN_16917 PARP14	1.75	0.19	0.00	-2.94	2.94	down	yes
144	5870180 NM_021994.2	11179 ILMN_16816 ZNF277	1.56	0.01	0.00	-2.93	2.93	down	yes
145	7510414 NM_001552.2	3487 ILMN_16658 IGFBP4	1.43	-0.12	0.00	-2.93	2.93	down	yes
146	4280497 NM_021181.3	57823 ILMN_17109 SLAMF7	2.00	0.45	0.00	-2.92	2.92	down	yes
147	7320176 NM_001295.2	1230 ILMN_16788 CCR1	0.59	-0.96	0.00	-2.92	2.92	down	yes
148	1990397 NM_004510.2	3431 ILMN_16726 SP110	1.62	0.08	0.00	-2.92	2.92	down	yes
149	3170064 NM_005931.2	4277 ILMN_17080 MICB	1.22	-0.31	0.00	-2.89	2.89	down	yes
150	4610433 NM_139314.1	51129 ILMN_17077 ANGPTL4	1.65	0.12	0.00	-2.88	2.88	down	yes
151	520059 NM_014398.2	27074 ILMN_21708 LAMP3	1.53	0.01	0.00	-2.88	2.88	down	yes
152	5310100 NM_014290.1	23424 ILMN_17052 TDRD7	1.67	0.15	0.00	-2.87	2.87	down	yes
153	6220195 NM_006399.2	10538 ILMN_16688 BATF	1.39	-0.12	0.00	-2.86	2.86	down	yes
154	3170136 NM_152703.2	219285 ILMN_17994 SAMD9L	1.77	0.26	0.00	-2.85	2.85	down	yes
155	5700735 NM_031458.1	83666 ILMN_17312 PARP9	1.71	0.20	0.00	-2.84	2.84	down	yes
156	1940064 NM_001048183.1	65979 ILMN_17365 PHACTR4	1.42	-0.06	0.00	-2.79	2.79	down	yes
157	7330523 NM_001014279.1	389289 ILMN_20986 C5orf39	1.44	-0.04	0.00	-2.79	2.79	down	yes
158	5820035 NM_004289.5	9603 ILMN_20497 NFE2L3	1.22	-0.26	0.00	-2.78	2.78	down	yes
159	3830762 NM_181724.1	338773 ILMN_17381 TMEM119	-0.24	-1.72	0.00	-2.78	2.78	down	yes
160	240722 NM_002535.2	4939 ILMN_17367 OAS2	1.67	0.21	0.00	-2.76	2.76	down	yes
161	2510672 NM_003199.2	6925 ILMN_18141 TCF4	1.18	-0.28	0.00	-2.76	2.76	down	yes
162	1940162 NM_004120.3	2634 ILMN_17740 GBP2	1.65	0.19	0.00	-2.75	2.75	down	yes

163	6130138 NM_006468.6	10623 ILMN_17956 POLR3C	1.53	0.07	0.00	-2.75	2.75	down	yes
164	1770152 NM_152851.1	64231 ILMN_23598 MS4A6A	0.32	-1.14	0.00	-2.75	2.75	down	yes
165	2120612 XM_938742.1	130367 ILMN_18113 SGPP2	1.94	0.48	0.00	-2.75	2.75	down	yes
166	6110343 NM_145898.1	6368 ILMN_16861 CCL23	1.49	0.03	0.00	-2.74	2.74	down	yes
167	4280678 NM_005410.2	6414 ILMN_17850 SEPP1	-0.15	-1.61	0.00	-2.74	2.74	down	yes
168	5490408 NM_005195.3	1052 ILMN_17820 CEBPD	1.47	0.02	0.00	-2.73	2.73	down	yes
169	3940189 NM_004972.2	3717 ILMN_16831 JAK2	1.53	0.09	0.00	-2.72	2.72	down	yes
170	1470091 NM_172174.1	3600 ILMN_23692 IL15	1.54	0.10	0.00	-2.71	2.71	down	yes
171	5080021 NM_001165.3	330 ILMN_17761 BIRC3	1.97	0.53	0.00	-2.71	2.71	down	yes
172	4220431 NM_000127.2	2131 ILMN_21299 EXT1	1.61	0.18	0.00	-2.69	2.69	down	yes
173	1030743 NM_000595.2	4049 ILMN_17954 LTA	1.47	0.05	0.00	-2.69	2.69	down	yes
174	2230204 NM_001032731.1	4939 ILMN_22489 OAS2	1.37	-0.05	0.00	-2.68	2.68	down	yes
175	3060255 NM_182962.1	330 ILMN_24056 BIRC3	1.79	0.38	0.00	-2.67	2.67	down	yes
176	6330725 NM_005178.2	602 ILMN_17105 BCL3	0.95	-0.47	0.00	-2.67	2.67	down	yes
177	6860482 NM_017912.3	55008 ILMN_16546 HERC6	1.94	0.53	0.00	-2.66	2.66	down	yes
178	4890707 NM_002856.2	5819 ILMN_17183 PVRL2	1.42	0.02	0.00	-2.64	2.64	down	yes
179	1450370 NM_018403.4	55802 ILMN_18092 DCP1A	1.45	0.06	0.00	-2.63	2.63	down	yes
180	130519 NM_005419.2	6773 ILMN_16909 STAT2	1.50	0.10	0.00	-2.63	2.63	down	yes
181	870767 NM_001130963.1	23306 ILMN_33064 TMEM194A	1.63	0.23	0.00	-2.63	2.63	down	yes
182	5390102 NM_015278.3	23328 ILMN_21859 SASH1	1.33	-0.05	0.00	-2.60	2.60	down	yes
183	6250064 NM_002198.1	3659 ILMN_17083 IRF1	2.05	0.67	0.00	-2.60	2.60	down	yes
184	2510239 NM_030961.1	81844 ILMN_16663 TRIM56	1.32	-0.05	0.00	-2.59	2.59	down	yes
185	70121 XR_040455.1	645638 ILMN_32001 LOC645638	0.91	-0.45	0.00	-2.58	2.58	down	yes
186	4880626 NM_018326.2	55303 ILMN_17484 GIMAP4	0.87	-0.50	0.00	-2.58	2.58	down	yes
187	4900239 NM_014143.2	29126 ILMN_17019 CD274	1.46	0.10	0.00	-2.57	2.57	down	yes
188	160148 NM_013410.2	205 ILMN_23380 AK3L1	1.42	0.06	0.00	-2.56	2.56	down	yes
189	2650379 NM_013372.5	26585 ILMN_17529 GREM1	1.50	0.14	0.00	-2.56	2.56	down	yes
190	2260615 NM_004698.1	9129 ILMN_17153 PRPF3	1.18	-0.18	0.00	-2.56	2.56	down	yes
191	2030767 NM_001778.2	962 ILMN_20610 CD48	1.50	0.15	0.00	-2.56	2.56	down	yes
192	1690184 NM_183419.1	25897 ILMN_18123 RNF19A	1.38	0.02	0.00	-2.56	2.56	down	yes
193	5900253 NM_018664.1	55509 ILMN_17632 BAF3	1.38	0.03	0.00	-2.55	2.55	down	yes
194	2060047 NM_004776.2	9334 ILMN_16858 B4GALT5	1.58	0.24	0.00	-2.53	2.53	down	yes
195	4610066 NM_015257.2	23306 ILMN_32288 TMEM194A	1.68	0.34	0.00	-2.53	2.53	down	yes
196	4780044 XR_037483.1	389386 ILMN_32954 LOC389386	1.31	-0.03	0.00	-2.53	2.53	down	yes
197	7610440 NM_199139.1	54739 ILMN_23705 XAF1	1.36	0.03	0.00	-2.52	2.52	down	yes
198	5810176 NM_182664.2	83593 ILMN_23629 RASSF5	1.50	0.17	0.00	-2.52	2.52	down	yes
199	6180465 NM_017585.2	11182 ILMN_17783 SLC2A6	1.59	0.26	0.00	-2.52	2.52	down	yes
200	1820053 NM_152346.1	124935 ILMN_17871 SLC43A2	0.83	-0.49	0.00	-2.51	2.51	down	yes
201	6220673 NM_015278.3	23328 ILMN_17126 SASH1	1.23	-0.09	0.00	-2.51	2.51	down	yes
202	1990487 NM_019001.2	54464 ILMN_18090 XRN1	1.32	0.01	0.00	-2.48	2.48	down	yes
203	7560593 NM_020530.3	5008 ILMN_17805 OSM	1.04	-0.26	0.00	-2.46	2.46	down	yes
204	7330392 NM_000593.5	6890 ILMN_17510 TAP1	1.53	0.23	0.00	-2.46	2.46	down	yes
205	1570129 NM_006700.1	10906 ILMN_17582 TRAFD1	1.35	0.05	0.00	-2.45	2.45	down	yes
206	1440064 AK126405	ILMN_1913060	0.41	-0.88	0.00	-2.45	2.45	down	yes
207	4640392 NM_005937.3	4302 ILMN_17187 MLLT6	0.91	-0.38	0.00	-2.45	2.45	down	yes
208	2570300 NM_006417.3	10561 ILMN_17600 IFI44	1.98	0.69	0.00	-2.44	2.44	down	yes
209	3940133 NM_017633.2	55603 ILMN_17404 FAM46A	1.13	-0.15	0.00	-2.44	2.44	down	yes
210	1240097 NM_013448.2	11177 ILMN_16583 BAZ1A	1.43	0.15	0.00	-2.44	2.44	down	yes
211	1240440 NM_006472.2	10628 ILMN_16974 TXNIP	0.07	-1.22	0.00	-2.44	2.44	down	yes
212	4570441 NM_022168.2	64135 ILMN_17813 IFIH1	1.86	0.58	0.00	-2.44	2.44	down	yes
213	650692 NM_207332.1	157697 ILMN_21046 ERICH1	1.24	-0.04	0.00	-2.43	2.43	down	yes
214	6180056 NM_014506.1	27348 ILMN_17243 TOR1B	1.31	0.03	0.00	-2.43	2.43	down	yes
215	6510735 NM_001012967.1	91351 ILMN_32439 DDX60L	1.56	0.28	0.00	-2.43	2.43	down	yes
216	6660398 NM_002003.2	2219 ILMN_16680 FCN1	0.00	-1.28	0.00	-2.43	2.43	down	yes
217	5310053 NM_002341.1	4050 ILMN_23762 LTB	1.19	-0.09	0.00	-2.42	2.42	down	yes

218	6280725 NR_003697.1	285958 ILMN_32487 C7orf40	1.29	0.02	0.00	-2.41	2.41	down	yes
219	2680079 NM_024576.3	79627 ILMN_17158 OGFRL1	1.52	0.26	0.00	-2.41	2.41	down	yes
220	1660010 NM_033034.1	85363 ILMN_17049 TRIM5	1.28	0.01	0.00	-2.40	2.40	down	yes
221	160270 NM_022003.1	53826 ILMN_17688 FXVD6	1.17	-0.09	0.00	-2.40	2.40	down	yes
222	3130358 AK096179	ILMN_1898124	1.19	-0.07	0.00	-2.39	2.39	down	yes
223	270601 NM_033055.2	64645 ILMN_17630 HIAT1	1.24	-0.01	0.00	-2.39	2.39	down	yes
224	2650564 NM_004585.3	5920 ILMN_17016 RARRES3	1.26	0.01	0.00	-2.38	2.38	down	yes
225	510520 NM_021226.2	58504 ILMN_16763 ARHGAP22	1.15	-0.11	0.00	-2.38	2.38	down	yes
226	1230224 NM_005494.2	10049 ILMN_24024 DNAJB6	1.30	0.05	0.00	-2.38	2.38	down	yes
227	6400647 NM_139265.2	30844 ILMN_17200 EHD4	1.18	-0.06	0.00	-2.38	2.38	down	yes
228	3120474 XM_371461.4	85379 ILMN_17728 KIAA1671	1.21	-0.03	0.00	-2.36	2.36	down	yes
229	1400026 XM_001714786.1	728127 ILMN_32363 CTGLF7	1.44	0.20	0.00	-2.36	2.36	down	yes
230	6580189 XR_019393.1	387820 ILMN_16908 LOC387820	1.18	-0.06	0.00	-2.36	2.36	down	yes
231	7380243 XM_001133059.1	728772 ILMN_17519 LOC728772	1.32	0.09	0.00	-2.35	2.35	down	yes
232	4880408 NM_006378.2	10507 ILMN_16875 SEMA4D	0.97	-0.26	0.00	-2.34	2.34	down	yes
233	2680100 NM_006058.3	10318 ILMN_17036 TNIP1	1.59	0.36	0.00	-2.34	2.34	down	yes
234	7210717 NM_173558.2	221472 ILMN_21150 FGD2	1.05	-0.18	0.00	-2.34	2.34	down	yes
235	7610053 NM_017631.4	55601 ILMN_17951 DDX60	1.75	0.52	0.00	-2.34	2.34	down	yes
236	2470603 NM_016374.5	51742 ILMN_22695 ARID4B	1.07	-0.15	0.00	-2.33	2.33	down	yes
237	2470092 NM_013272.2	28232 ILMN_16547 SLCO3A1	0.91	-0.31	0.00	-2.32	2.32	down	yes
238	20521 NM_032844.1	84930 ILMN_16823 MASTL	1.12	-0.10	0.00	-2.32	2.32	down	yes
239	6110020 XM_036729.5	373856 ILMN_16903 USP41	1.19	-0.03	0.00	-2.32	2.32	down	yes
240	4120114 NM_000882.2	3592 ILMN_16713 IL12A	1.19	-0.02	0.00	-2.31	2.31	down	yes
241	1940343 NM_015368.3	24145 ILMN_16978 PANX1	1.31	0.10	0.00	-2.31	2.31	down	yes
242	4150270 NM_144590.1	118932 ILMN_21325 ANKRD22	1.19	-0.01	0.00	-2.30	2.30	down	yes
243	3190433 NM_181900.2	80765 ILMN_17843 STARD5	1.19	-0.02	0.00	-2.30	2.30	down	yes
244	1440360 NM_181791.1	353345 ILMN_20923 GPR141	1.13	-0.08	0.00	-2.30	2.30	down	yes
245	1820750 NM_007315.2	6772 ILMN_16901 STAT1	1.20	0.00	0.00	-2.30	2.30	down	yes
246	7040142 NM_001032998.1	8942 ILMN_17375 KYNU	1.40	0.20	0.00	-2.30	2.30	down	yes
247	3610343 NM_002485.4	4683 ILMN_17348 NBN	1.75	0.55	0.00	-2.29	2.29	down	yes
248	1170349 NM_005558.3	3898 ILMN_17823 LAD1	1.22	0.03	0.00	-2.29	2.29	down	yes
249	1570156 NM_016817.2	4939 ILMN_17093 OAS2	1.22	0.04	0.00	-2.28	2.28	down	yes
250	6860382 NM_007346.2	11054 ILMN_17282 OGFR	1.03	-0.16	0.00	-2.27	2.27	down	yes
251	730010 NM_017825.1	54936 ILMN_18114 ADPRHL2	0.98	-0.20	0.00	-2.27	2.27	down	yes
252	5670717 NM_207332.1	157697 ILMN_17310 ERICH1	1.20	0.02	0.00	-2.27	2.27	down	yes
253	1980672 NM_000575.3	3552 ILMN_16584 IL1A	2.43	1.25	0.00	-2.27	2.27	down	yes
254	1110494 NM_015257.1	23306 ILMN_21313 TMEM194	1.36	0.18	0.00	-2.27	2.27	down	yes
255	6400176 NM_004029.2	3665 ILMN_17981 IRF7	1.90	0.72	0.00	-2.26	2.26	down	yes
256	2570079 NM_139266.1	6772 ILMN_16913 STAT1	1.21	0.04	0.00	-2.26	2.26	down	yes
257	4210630 XM_290799.7	57636 ILMN_17645 ARHGAP23	0.92	-0.26	0.00	-2.26	2.26	down	yes
258	3140707 NM_031458.1	83666 ILMN_20535 PARP9	1.23	0.06	0.00	-2.25	2.25	down	yes
259	1710753 NM_178815.3	221079 ILMN_21200 ARL5B	1.42	0.26	0.00	-2.24	2.24	down	yes
260	2470601 NM_173842.1	3557 ILMN_16897 IL1RN	0.96	-0.21	0.00	-2.24	2.24	down	yes
261	2060121 NM_000147.3	2517 ILMN_17527 FUCA1	0.02	-1.14	0.00	-2.24	2.24	down	yes
262	6660369 NM_001491.2	2651 ILMN_16803 GCNT2	1.00	-0.16	0.01	-2.23	2.23	down	yes
263	3290292 NM_015907.2	51056 ILMN_16837 LAP3	1.06	-0.10	0.00	-2.23	2.23	down	yes
264	6020255 NM_000399.2	1959 ILMN_17431 EGR2	0.24	-0.92	0.00	-2.23	2.23	down	yes
265	2850576 NM_022367.2	64218 ILMN_17027 SEMA4A	0.14	-1.02	0.00	-2.22	2.22	down	yes
266	2470093 NM_201629.1	9414 ILMN_16649 TJP2	1.05	-0.10	0.00	-2.22	2.22	down	yes
267	2320220 NM_032029.1	83953 ILMN_18017 FCAMR	1.22	0.07	0.00	-2.21	2.21	down	yes
268	7160593 NM_152542.2	152926 ILMN_20700 PPM1K	1.27	0.12	0.00	-2.21	2.21	down	yes
269	6560075 NM_003141.3	6737 ILMN_16780 TRIM21	1.27	0.13	0.00	-2.21	2.21	down	yes
270	2140746 NM_001042724.1	5819 ILMN_23373 PVRL2	1.15	0.01	0.00	-2.20	2.20	down	yes
271	1410279 NM_001006666.1	200316 ILMN_22969 APOBEC3F	1.10	-0.03	0.00	-2.19	2.19	down	yes
272	4890451 NM_023927.1	65983 ILMN_20656 GRAMD3	1.40	0.26	0.00	-2.19	2.19	down	yes

273	1190750 NM_032148.2	84102 ILMN_17471 SLC41A2	1.24	0.11	0.00	-2.18	2.18	down	yes
274	2690324 NM_033397.2	85450 ILMN_18051 ITPRIP	0.81	-0.31	0.00	-2.17	2.17	down	yes
275	4290192 NM_203464.1	205 ILMN_17640 AK3L1	1.09	-0.03	0.00	-2.17	2.17	down	yes
276	620112 NM_001079691.1	90634 ILMN_17994 N4BP2L1	1.47	0.36	0.00	-2.16	2.16	down	yes
277	7560037 NM_133471.1	170954 ILMN_17329 KIAA1949	0.88	-0.23	0.00	-2.16	2.16	down	yes
278	1030431 NM_001995.2	2180 ILMN_16845 ACSL1	1.42	0.30	0.00	-2.16	2.16	down	yes
279	6550288 NM_020231.3	56983 ILMN_18111 KTELC1	0.99	-0.12	0.00	-2.16	2.16	down	yes
280	5310358 NM_022173.1	7072 ILMN_23884 TIA1	0.94	-0.17	0.00	-2.16	2.16	down	yes
281	5810632 NM_014306.3	51493 ILMN_17959 C22orf28	1.08	-0.02	0.00	-2.16	2.16	down	yes
282	4860458 NM_023079.3	65264 ILMN_16921 UBE2Z	0.91	-0.20	0.00	-2.15	2.15	down	yes
283	2510356 NM_001974.3	2015 ILMN_17806 EMR1	1.01	-0.09	0.00	-2.15	2.15	down	yes
284	7040386 NM_001955.2	1906 ILMN_16827 EDN1	1.55	0.44	0.00	-2.15	2.15	down	yes
285	1410168 NM_001421.2	2000 ILMN_16520 ELF4	1.09	-0.01	0.00	-2.15	2.15	down	yes
286	6560373 NM_001031677.2	53917 ILMN_16778 RAB24	0.58	-0.52	0.00	-2.15	2.15	down	yes
287	4890598 NM_032430.1	84446 ILMN_21858 BRSK1	0.76	-0.34	0.00	-2.14	2.14	down	yes
288	770047 NM_018323.2	55300 ILMN_18151 PI4K2B	1.26	0.16	0.00	-2.14	2.14	down	yes
289	4200240 NM_001080391.1	6672 ILMN_22849 SP100	1.16	0.06	0.00	-2.14	2.14	down	yes
290	2070059 NM_032789.1	84875 ILMN_22620 PARP10	1.17	0.07	0.00	-2.14	2.14	down	yes
291	1690465 XR_018848.1	650369 ILMN_16836 LOC650369	1.01	-0.09	0.00	-2.14	2.14	down	yes
292	610537 NM_058184.1	54072 ILMN_16684 C21orf42	1.11	0.02	0.00	-2.13	2.13	down	yes
293	4570240 NM_004302.3	91 ILMN_22433 ACVR1B	0.79	-0.30	0.00	-2.13	2.13	down	yes
294	4560576 NM_002468.3	4615 ILMN_17385 MYD88	1.18	0.09	0.00	-2.13	2.13	down	yes
295	4570050 NM_172174.1	3600 ILMN_22730 IL15	1.09	0.01	0.00	-2.11	2.11	down	yes
296	6550133 NM_001079691.1	90634 ILMN_23446 N4BP2L1	1.48	0.40	0.00	-2.11	2.11	down	yes
297	5720039 NM_001511.1	2919 ILMN_17878 CXCL1	2.61	1.53	0.02	-2.11	2.11	down	yes
298	5360079 NM_018384.3	55340 ILMN_17693 GIMAP5	0.61	-0.46	0.00	-2.11	2.11	down	yes
299	6180253 NM_006779.2	10435 ILMN_16527 CDC42EP2	1.11	0.03	0.00	-2.11	2.11	down	yes
300	2940403 NM_001135811.1	58516 ILMN_32726 FAM60A	1.03	-0.04	0.00	-2.11	2.11	down	yes
301	1050356 NM_057159.2	1902 ILMN_17014 LPAR1	0.78	-0.29	0.00	-2.10	2.10	down	yes
302	1470382 NM_004029.2	3665 ILMN_23490 IRF7	1.56	0.50	0.00	-2.10	2.10	down	yes
303	3830709 NR_002726.1	10151 ILMN_21745 HNRNPA3P1	1.22	0.15	0.00	-2.09	2.09	down	yes
304	3870458 NM_012108.1	26228 ILMN_17810 BRDG1	1.05	-0.01	0.00	-2.09	2.09	down	yes
305	2190452 XM_938171.2	415116 ILMN_17077 PIM3	1.52	0.46	0.00	-2.08	2.08	down	yes
306	1740050 XM_495863.3	387751 ILMN_16685 GVIN1	0.84	-0.22	0.00	-2.08	2.08	down	yes
307	7400465 NM_032172.1	84132 ILMN_21156 USP42	0.98	-0.07	0.00	-2.08	2.08	down	yes
308	4280482 NM_018370.2	55332 ILMN_16693 DRAM1	1.29	0.23	0.00	-2.08	2.08	down	yes
309	2060300 NM_198467.1	222194 ILMN_17120 RSBN1L	0.96	-0.09	0.00	-2.08	2.08	down	yes
310	1740382 NM_000161.2	2643 ILMN_17888 GCH1	1.15	0.10	0.00	-2.07	2.07	down	yes
311	6840347 NM_024576.3	79627 ILMN_20957 OGFRL1	1.40	0.35	0.00	-2.07	2.07	down	yes
312	1440341 NM_172369.2	714 ILMN_17859 C1QC	-0.21	-1.25	0.00	-2.07	2.07	down	yes
313	5390615 NM_033016.1	5155 ILMN_23943 PDGFB	1.07	0.02	0.00	-2.07	2.07	down	yes
314	1260497 NM_015150.1	23180 ILMN_18007 RFTN1	1.08	0.04	0.00	-2.06	2.06	down	yes
315	4060017 NM_001080973.1	54756 ILMN_24078 IL17RD	1.26	0.22	0.00	-2.06	2.06	down	yes
316	2000022 NM_006084.4	10379 ILMN_17454 IRF9	1.09	0.05	0.00	-2.06	2.06	down	yes
317	4810187 NM_007315.2	6772 ILMN_17773 STAT1	0.93	-0.11	0.00	-2.05	2.05	down	yes
318	2320358 NM_022154.5	64116 ILMN_22335 SLC39A8	1.06	0.02	0.00	-2.05	2.05	down	yes
319	2070392 NM_018042.2	55106 ILMN_17282 SLFN12	0.80	-0.23	0.00	-2.05	2.05	down	yes
320	6400681 NM_001005176.1	11262 ILMN_22468 SP140	1.02	-0.01	0.00	-2.05	2.05	down	yes
321	3140438 NM_020895.2	57655 ILMN_17371 GRAMD1A	1.68	0.64	0.00	-2.05	2.05	down	yes
322	6100521 NM_001040443.1	51131 ILMN_17767 PHF11	1.06	0.03	0.00	-2.05	2.05	down	yes
323	6200019 NM_002258.2	3820 ILMN_20796 KLRB1	0.86	-0.17	0.00	-2.04	2.04	down	yes
324	4560541 NM_152649.1	197259 ILMN_16678 MLKL	0.91	-0.12	0.00	-2.04	2.04	down	yes
325	1740075 NM_153698.1	195827 ILMN_17172 C9orf21	0.89	-0.14	0.00	-2.04	2.04	down	yes
326	1010487 NM_006763.2	7832 ILMN_17700 BTG2	0.86	-0.17	0.00	-2.04	2.04	down	yes
327	130181 NM_144590.2	118932 ILMN_17998 ANKRD22	1.01	-0.01	0.00	-2.03	2.03	down	yes

328	5390725 NM_001050.2	6752 ILMN_21522 SSTR2	1.13	0.11	0.00	-2.03	2.03	down	yes
329	2970347 NM_033397.2	85450 ILMN_32391 ITPRIP	0.76	-0.26	0.00	-2.03	2.03	down	yes
330	4480497 NM_033130.2	89790 ILMN_16555 SIGLEC10	0.09	-0.93	0.00	-2.02	2.02	down	yes
331	5910064 NM_033093.1	85363 ILMN_24046 TRIM5	1.03	0.02	0.00	-2.02	2.02	down	yes
332	4880215 NM_001514.3	2959 ILMN_17378 GTF2B	1.19	0.18	0.00	-2.02	2.02	down	yes
333	6480360 NM_138636.2	51311 ILMN_16578 TLR8	0.71	-0.31	0.00	-2.02	2.02	down	yes
334	6370441 NM_033338.4	840 ILMN_23629 CASP7	0.99	-0.02	0.00	-2.02	2.02	down	yes
335	5900471 NM_000956.2	5732 ILMN_17039 PTGER2	0.98	-0.03	0.00	-2.01	2.01	down	yes
336	2030309 NM_001032295.1	710 ILMN_16703 SERPING1	0.92	-0.09	0.00	-2.01	2.01	down	yes
337	2450152 NM_001042453.1	51765 ILMN_23287 MST4	1.13	0.13	0.00	-2.01	2.01	down	yes
338	7200435 NM_005170.2	430 ILMN_17234 ASCL2	0.89	-0.12	0.00	-2.00	2.00	down	yes
339	150180 NM_002425.1	4319 ILMN_17418 MMP10	0.07	3.49	0.00	10.72	10.72	up	yes
340	60079 NM_006145.1	3337 ILMN_17753 DNAJB1	-1.83	1.35	0.00	9.04	9.04	up	yes
341	2710064 XM_941665.2	387763 ILMN_16774 LOC387763	0.76	3.60	0.00	7.17	7.17	up	yes
342	4670390 NM_002089.3	2920 ILMN_16826 CXCL2	1.30	3.79	0.00	5.62	5.62	up	yes
343	6770630 NM_014475.3	27294 ILMN_16892 DHHD	-0.26	2.20	0.00	5.50	5.50	up	yes
344	6620528 NM_005952.2	4501 ILMN_17751 MT1X	-1.94	0.35	0.00	4.89	4.89	up	yes
345	3060750 NM_005047.2	5711 ILMN_17209 PSMD5	0.05	2.31	0.00	4.79	4.79	up	yes
346	6860465 NM_004997.2	4608 ILMN_17052 MYBPH	-0.36	1.74	0.00	4.29	4.29	up	yes
347	3850433 NM_005346.3	3304 ILMN_16604 HSPA1B	-1.04	1.03	0.00	4.21	4.21	up	yes
348	4010086 NM_013370.2	29948 ILMN_17959 OKL38	-1.63	0.42	0.00	4.12	4.12	up	yes
349	1340075 NM_004281.3	9531 ILMN_16597 BAG3	-0.85	1.11	0.00	3.88	3.88	up	yes
350	1440408 NM_181702.1	2669 ILMN_16770 GEM	-0.18	1.68	0.00	3.65	3.65	up	yes
351	1170246 NM_181702.1	2669 ILMN_23678 GEM	-0.26	1.60	0.00	3.64	3.64	up	yes
352	3400019 NM_002923.1	5997 ILMN_21973 RGS2	-1.75	0.11	0.00	3.61	3.61	up	yes
353	430050 NM_012342.2	25805 ILMN_16914 BAMB1	0.19	2.02	0.00	3.56	3.56	up	yes
354	160092 NM_002155.3	3310 ILMN_18061 HSPA6	-1.01	0.80	0.00	3.50	3.50	up	yes
355	4220605 NM_005239.4	2114 ILMN_17201 ETS2	-0.02	1.76	0.00	3.43	3.43	up	yes
356	1430280 NM_004364.2	1050 ILMN_17157 CEBPA	-1.99	-0.23	0.00	3.40	3.40	up	yes
357	2640719 NR_001445.1	125050 ILMN_20748 RN7SK	0.01	1.77	0.00	3.38	3.38	up	yes
358	5420564 NM_005384.2	4783 ILMN_17073 NFLI3	-0.58	1.10	0.00	3.21	3.21	up	yes
359	160598 NM_006644.2	10808 ILMN_17128 HSPH1	-1.22	0.45	0.00	3.18	3.18	up	yes
360	2680110 NM_014220.2	4071 ILMN_17703 TM4SF1	0.68	2.32	0.00	3.12	3.12	up	yes
361	7100639 NM_018948.2	54206 ILMN_16655 ERRF1	-0.61	1.02	0.00	3.11	3.11	up	yes
362	6760021 NR_003672.2	84973 ILMN_32270 SNHG7	-1.37	0.26	0.00	3.10	3.10	up	yes
363	6420040 NM_144607.3	124637 ILMN_16709 CYB5D1	-0.13	1.49	0.00	3.08	3.08	up	yes
364	5670367 NM_007350.3	22822 ILMN_32515 PHLDA1	-0.31	1.26	0.00	2.98	2.98	up	yes
365	6110736 NM_003749.2	8660 ILMN_20834 IRS2	-1.23	0.30	0.00	2.88	2.88	up	yes
366	4810520 NM_025195.2	10221 ILMN_18038 TRIB1	-0.97	0.55	0.00	2.86	2.86	up	yes
367	4070017 NM_002539.1	4953 ILMN_17485 ODC1	-1.20	0.28	0.00	2.78	2.78	up	yes
368	990176 NR_001445.1	125050 ILMN_17394 RN7SK	0.05	1.50	0.00	2.72	2.72	up	yes
369	780711 NM_194293.2	165904 ILMN_18021 XIRP1	0.25	1.66	0.00	2.65	2.65	up	yes
370	6270273 NM_006558.1	10656 ILMN_16917 KHDRBS3	-0.14	1.20	0.00	2.54	2.54	up	yes
371	430674 NM_015193.3	23237 ILMN_17111.ARC	-0.22	1.11	0.00	2.52	2.52	up	yes
372	7550066 NM_006343.2	10461 ILMN_21385 MERTK	-1.47	-0.15	0.00	2.49	2.49	up	yes
373	3180008 NM_207501.1	401281 ILMN_17974 FLJ27255	-0.18	1.14	0.00	2.49	2.49	up	yes
374	2970482 NR_004400.1	26863 ILMN_32366 RNU1-5	0.12	1.43	0.00	2.48	2.48	up	yes
375	380685 NR_006882.1	780854 ILMN_32423 SNORD3D	0.00	1.30	0.00	2.46	2.46	up	yes
376	940152 NM_017572.2	2872 ILMN_23470 MKNK2	-0.77	0.51	0.00	2.43	2.43	up	yes
377	2510164 NR_006880.1	780851 ILMN_32395 SNORD3A	0.01	1.28	0.00	2.42	2.42	up	yes
378	1240386 NM_014851.2	9903 ILMN_16927 KLHL21	-0.85	0.40	0.00	2.36	2.36	up	yes
379	6480091 NM_018602.2	55466 ILMN_17769 DNAJA4	-0.61	0.63	0.00	2.36	2.36	up	yes
380	3780717 NM_080725.1	140809 ILMN_18048 SRXN1	-0.86	0.36	0.00	2.34	2.34	up	yes
381	4570458 NM_001010990.1	9709 ILMN_23741 HERPUD1	-0.60	0.62	0.00	2.33	2.33	up	yes
382	2360091 NR_004426.1	26864 ILMN_32446 RNU1G2	0.00	1.22	0.00	2.33	2.33	up	yes

383	1440296 NM_005324.3	3021 ILMN_16957 H3F3B	-0.82	0.40	0.00	2.32	2.32 up	yes
384	160504 XR_041703.1	728537 ILMN_32985 LOC728537	-0.04	1.17	0.00	2.30	2.30 up	yes
385	430546 NM_003518.3	8339 ILMN_17161 HIST1H2BG	-0.23	0.97	0.00	2.29	2.29 up	yes
386	6200692 NM_201559.2	2309 ILMN_16817 FOXO3	-0.23	0.95	0.00	2.27	2.27 up	yes
387	4610189 NM_001010990.1	9709 ILMN_23741 HERPUD1	-0.66	0.53	0.00	2.27	2.27 up	yes
388	6380717 NM_005345.4	3303 ILMN_17890 HSPA1A	-0.60	0.58	0.00	2.26	2.26 up	yes
389	1690630 NM_153690.4	131583 ILMN_17060 FAM43A	-0.41	0.76	0.00	2.25	2.25 up	yes
390	3990497 NR_002987.1	677838 ILMN_32454 SNORA61	-1.34	-0.17	0.00	2.24	2.24 up	yes
391	5670152 NR_004408.1	26869 ILMN_32462 RNU1-3	0.05	1.20	0.00	2.22	2.22 up	yes
392	5270110 NM_014740.2	9775 ILMN_16670 EIF4A3	-0.63	0.52	0.00	2.22	2.22 up	yes
393	3890521 NM_133328.2	162989 ILMN_17680 DEDD2	-0.99	0.13	0.00	2.17	2.17 up	yes
394	2710402 NM_015144.2	23174 ILMN_17434 ZCCHC14	-0.84	0.28	0.00	2.17	2.17 up	yes
395	6620753 NM_006007.1	7763 ILMN_17952 ZFAND5	-1.02	0.10	0.00	2.17	2.17 up	yes
396	6370523 NM_032505.1	84541 ILMN_17162 KBTBD8	-0.35	0.77	0.00	2.17	2.17 up	yes
397	5720278 NR_003098.1	23642 ILMN_32367 SNHG1	-1.13	-0.01	0.00	2.17	2.17 up	yes
398	3440138 NM_004071.2	1195 ILMN_16797 CLK1	-0.69	0.42	0.00	2.16	2.16 up	yes
399	4850136 XR_018287.2	399988 ILMN_32003 LOC399988	-0.59	0.52	0.00	2.16	2.16 up	yes
400	4290072 NM_013376.3	29950 ILMN_17940 SERTAD1	-0.52	0.58	0.00	2.15	2.15 up	yes
401	4610021 NM_003259.2	7087 ILMN_18025 ICAM5	-0.09	1.00	0.00	2.14	2.14 up	yes
402	3180450 NM_014117.2	29035 ILMN_17734 C16orf72	-0.83	0.25	0.00	2.12	2.12 up	yes
403	2570220 NR_023371.1	100169760 ILMN_32347 RN5S9	0.22	1.30	0.00	2.12	2.12 up	yes
404	620202 NM_182980.2	29948 ILMN_23195 OSGIN1	-0.75	0.32	0.00	2.11	2.11 up	yes
405	3830653 NM_006736.5	3300 ILMN_23909 DNAJB2	-0.97	0.09	0.00	2.08	2.08 up	yes
406	830619 NM_004083.4	1649 ILMN_16769 DDIT3	-0.49	0.57	0.00	2.08	2.08 up	yes
407	3360224 NM_002421.2	4312 ILMN_17264 MMP1	0.02	1.05	0.00	2.05	2.05 up	yes
408	6620201 NM_017644.3	54800 ILMN_16786 KLHL24	-1.05	-0.02	0.01	2.04	2.04 up	yes
409	3800463 NM_018344.3	55315 ILMN_17173 SLC29A3	-1.09	-0.06	0.00	2.04	2.04 up	yes
410	4920110 NM_015675.2	4616 ILMN_17189 GADD45B	0.50	1.53	0.00	2.04	2.04 up	yes
411	2650390 NM_002309.2	3976 ILMN_17387 LIF	0.18	1.20	0.00	2.03	2.03 up	yes
412	5720059 NM_018988.2	54438 ILMN_17782 GFOD1	-1.01	0.00	0.00	2.02	2.02 up	yes
413	2970128 NM_025218.2	80329 ILMN_17384 ULBP1	-0.17	0.84	0.00	2.02	2.02 up	yes
414	2650019 NM_016605.1	51307 ILMN_17445 FAM53C	-0.40	0.62	0.00	2.02	2.02 up	yes
415	780528 NM_001827.1	1164 ILMN_20722 CKS2	-0.67	0.34	0.00	2.01	2.01 up	yes
416	4200379 NR_004407.1	26824 ILMN_32451 RNU11	-0.14	0.87	0.00	2.01	2.01 up	yes