Supplementary Materials for

Helminth Infection Reactivates Latent γ-herpesvirus Via Cytokine Competition at a Viral Promoter

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Materials and Methods

Mice, Infections, and Injections. Mice were infected with MHV68 between 7 and 10 weeks of age. C57BL6/J, R26-stop-eYFP (B6.129X1-Gt(ROSA)26Sor$^{tm1(EYFP)Cos}$/J), Stat6KO(*31*), and Yarg (B6.129S4-Arg1^{tm1Lky}/J)(*17*) mice were purchased from Jackson and maintained in our specific pathogen free mouse colony at Washington University. R26-stop-tdRFP(*16*), PPARγ f/f x Lysozyme M-cre(*32*), Arginase-1 f/f x Tie2-cre(*31*, *33*); Stat1KO(*34*); have been previously described. Yarg mice were crossed with R26-stop-tdRFP mice to generate double reporter mice, Yarg/R26-stop-RFP.

MHV68 (WUSM strain), MHV68-M3-FL(*14*), and MHV68-cre were administered intranasally ($1x10^5$ pfu) or intraperitoneally ($1x10^6$ pfu). 200 L3 larvae of *H.polygyrus* were administered by oral gavage 42 days after MHV68 infection. Mice were sensitized by intraperitoneal injection 2500 *Sm* eggs and then challenged 14 day later with 5000 eggs given intravenously(*32*, *35*). *Sm* eggs lodge in the lung parenchyma following intravenous re-challenge(*35*). *Listeria monocytogenes* ($1x10^5$ cfu) was administered intraperitoneally. 250 mg of anti-IFNγ (clone H22)(*25*) or isotype control (clone PIP) was injected intraperitoneally on day 42 of MHV68 infection. For long-lasting IL-4 complexes, 5 mg of IL-4 (Peprotech) and 25 mg of anti-IL-4 (BioXcell, clone 11B11) were complexed as described(*26*) prior to injection into mice on days 42 and 44 after MHV68 infection. To quantify virus-encoded luciferase expression, mice were infected with MHV68-M3-FL(*14*), weighed and injected with 150 mg/kg of D-Luciferin (Calipur LifeSciences) prior to imaging using an Xenogen IVIS 200 (Calipur LifeSciences). Total flux (photons/second) of either the abdominal region or the entire mouse was determined using Living Image software (Xenogen)(*14*).

Construction of MHV68-cre virus. Cre-recombinase sequence with an engineered intron to prevent expression of cre in bacterial cells was cloned into a vector containing the ubiquitin C promoter (UbC-cre) (pUB6/V5-His, Invitrogen), and then ligated into a vector such that it was flanked by translational insulator sequences on either side of the transgene (pBluescriptKS+/ins-UbC-cre). The transgene was amplified by PCR with primers containing 70 bp homology arms, gel purified, and used for recombination using lambda-Red mediated recombination and *galK*/kanamycin positive/negative selection described previously(*36*, *37*). Transgene was inserted into position 55215 of BAC-MHV68, a kind gift of Ulrich Koszinowski(*38*, *39*). MHV68-cre DNA was transfected into NIH3T12 cells and resulting virus passaged in NIH3T12 cells. Self-excision of the loxP flanked BAC sequence was confirmed by loss of GFP expression (contained within the BAC sequence) and restriction digest.

Flow cytometric analysis and sorting of virus-infected cells. Peritoneal cells from 8-10 mice were harvested by lavage, pooled, and blocked with 10% mouse serum. Cells selected with CD11b MicroBeads (Miltenyi Biotec) were analyzed or sorted after staining with antibodies: CD11b-PerCP-Cy5.5 (clone M1/70, BioLegend), F4/80-APC-Alexa Fluor 750 (clone BM8, Invitrogen), CD19-PE-Cy7 (clone 1D3, BD Pharmigen).

For analysis cells were also stained with CD206-PE (clone C068C2, BioLegend), CD301-Alexa Fluor 647 (clone ER-MP23, AbD Serotec). Cells were sorted into Trizol Reagent (Invitrogen). 1000 to 2000 cells were obtained from each sort. RNA was quantified using Qubit RNA assay kits (Invitrogen). All of the RNA from virus-pos cells and 50 ng of RNA from virus-neg cells was prepared for RNA-seq using ScriptSeq v2 RNA-seq library preparation kit (Epicentre). Index Primers (Epicentre) were added and samples underwent Duplex-Specific thermostable nuclease (DSN) (Evrogen) treatment to remove ribosomal RNA. Samples were pooled and sequenced on HiSeq.

RNA-seq processing and comparative expression analysis. Sequencing reads were trimmed at the 3'end to mitigate an effect of C addition by template-switching enzyme used for preparation of small-input libraries. Then, data were aligned using Tophat(*40*) to mm9 assembly of mouse genome and expression of genes scored by using Cufflinks(*41*). Top 9000 expressed genes (representing stably expressed fraction of transcriptome) were used to create ranked list ordered by the differential expression between RFP positive (virus-positive) and RFP negative (virus-negative) macrophages. This list was then used to compare our data against external signatures by means of pre-ranked Gene Set Enrichment Analysis (GSEA)(*42*). Specifically, M1/M2 specific signatures were obtained using publicly available dataset in Gene Expression Omnibus – GSE21895 – that profiled murine bone-marrow derived macrophages at different conditions including IL-4 (M2) and LPS+IFNγ (M1) stimulations. M1 and M2 specific signatures were derived by looking at top 400 differentially expressed genes that were upregulated in M1 and top 400 differentially expressed genes that were upregulated in M2. Querry genes common between datasets are listed in Supplementary Table 1.

Bone marrow-derived macrophage cultures and infections. BMDMs were harvested from C57BL6/J mice and differentiated for 7 days with 10% CMG-14 supernatants(*43*) in complete Dulbecco's modified Eagle's medium (DMEM) (10% FCS, 1% HEPES, 2mM L-glutamine). At day 7 $1.5x10^5$ cells were plated/well in 24-well plates, rested for 2-3 days cells, pretreated with cytokines (IL-4 (Peprotech) 10 ng/ml unless otherwise noted, IL-13 (Peprotech) 50 ng/ml, IL-5 (Peprotech) 50 ng/ml, IFNγ (R&D Systems) doses indicated in legends) or 200 mM Etomoxir (Sigma Aldrich) for 16 hours, infected with MHV68 (multiplicity of infection (MOI)=5, one hour), washed, and resuspended in media containing cytokines. Cells were harvested for FACS 24 hours after infection. Infected macrophages were fixed with 4% formaldehyde, blocked with 10% mouse serum and 1% Fc Block (CD16/32, BioLegend), then stained with polyclonal rabbit antibody to MHV68(*44*, *45*) (1:1000), followed by secondary goat anti-rabbit Alexa Fluor-647 (Invitrogen). For viral growth cells were infected, frozen, and then titered on NIH 3T12 cells as described(*27*).

RT-PCR. BMDMs were treated with 10 ng/ml IL-4 and/or IFNγ at indicated doses for 16 hours, subsequently infect with MHV68 (MOI=5), and RNA were prepared using Trizol (Invitrogen) 24 hours later for RT-PCR analysis of *gene 50* and *Gapdh* as

described(*3*). For expression of *Arg1*, *Relma/Fizz1, Nos2,* and *Eif2b1* Taqman probes from Applied Biosystems were used.

Promoter Luciferase assays. RAW 264.7 cells were transfected with LT-1 transfection reagent (Mirus) according to manufactures instructions. 6 well plates were seeded with $1x10^6$ RAW 264.7 cells 24 hours prior to transfection in complete DMEM (10% FCS, 2mM L-glutamine, 100 U/ml of streptomycin, 100 U/ml of penicillin). 2.5 μg of reporter plasmid was tranfected (pGL4.10[Luc] was used as a negative control, pGL4.13[Luc] was used as a positive control, and the green fluorescent protein pMaxGFP was used to determine transfection efficiency). For assays in which IL-4, IL-13 or IFNγ was used, 24 hours post transfection 10 ng/ml IL-4, 10 ng/ml IL-13 or 1 ng/ml IFNγ was added to each well. All cells were collected 48 hours post transfection and lysed. Luciferase assays were performed using 50 ml lab made luciferase agent (1.5 mM HEPES, pH 8, 0.4 mM DTT, 10.6 mM ATP, 80 mM MgSO4, 5.4 mM Coenzyme A, 2 mM EDTA, and 9.4 mM beetle Luciferin) and 10 ml of lysed cells from each condition. Luciferase assays were read using a TD-20/20 luminometer (Turner Biosystems). All transfections were repeated in triplicate and presented as a fold over empty pGL4.10 vector ratio.

Reporter Plasmids Construction. Promoters were amplified from WT MHV68 DNA and cloned into the pGL4.10[luc2] (Promega) luciferase plasmid. The E1 proximal promoter was amplified with forward primer E1-410F (5'-gatcggctagctctttataggtaccagggaa-3') and reverse primer E1-410R (5'-gatcgaagctggtcacatctgacagagaaa-3'); the E0 distal promoter was amplified with forward primer E0-250F (5'-gatcggctagcttaatcctatatggagat-3') and reverse primer E0ATGR (5'-gatcgaagcttgtgctgggttgtgaag-3'); the N3 promoter was amplified with forward primer N3FNhe1 (5'- agtcgctagctcaggatgcagttaagca-3') and reverse primer N3RBgl2 (5'-cgatagatctagcctggggcatagttctt-3'); the N4/N5 promoter was amplified with forward primer N4_N5F1000Nhe1 (5'- agtcgctagcaatcgtccggggggttaa-3') and reverse primer N4_N5RBgl2 (5'- cgatagatctaagccgtggtcagcaggt-3'). Point mutation in promoters were introduced by PCR and confirmed by sequencing.

Ex vivo limiting dilution assay (LDA) for latency and persistent replication. Reactivation from latency and preformed virus was assayed as described(*27*). Briefly, peritoneal exudate cells (PECs) or splenocytes were plated in 2-fold serial dilutions (24-wells per dilution) onto permissive mouse embryonic fibroblast (MEF) monolayers (maintained in DMEM with 10% FCS), and scored for cytopathic effect (CPE) 3 weeks later. Cells that reactivate and produce virus will lead to complete CPE of a well by this time. To distinguish preformed infectious virus in the sample from virus that reactivates *ex vivo* from live cells, parallel samples of PECs were mechanically disrupted to kill the cells, but keep any infectious virus intact. These samples were plated on parallel plates of MEFs and scored for cytopathic effect. By plating 2-fold serial dilutions of cells we can determine the frequency of 1 reactivation event per well. The 63.2% Poisson

distribution line represents the frequency at which one reactivation event is likely to have occurred per well.

Limiting Dilution (LD)-PCR to detect viral genome. To compare the frequency of cells harboring viral genome, PECs and splenocytes were assayed by nested PCR for viral genome as described(*5*). 63.2% Poisson distribution line represents the frequency at which one genome was detected per well.

Western Blot analysis. BMDMs were collected in laemmli buffer and analyzed as previously described(*45*).

Stat6 ChIP. ChIP assay was performed as previously described(*46*). Immunoprecipitations were performed with rabbit polyclonal antibodies (control IgG or Stat6 [M-200])(Santa Cruz Biotechnology Inc.). Quantification of binding DNA was performed with SYBR Green Fast PCR Master Mix using the ABI 7500 Fast Real-time PCR System (both from Applied Biosystems). N4/N5 primers were as follows: (forward) 5' GCC-GTC-CCT-TAT-CTA-CAG-TCA 3' and (reverse) 5' CTA-TCA-TGG-GGG-CCA-GGC 3'. VEGF primers were as follows: (forward) 5' CGG-GAT-TGC-ACG-GAA-ACT-TTT-CGT 3' and (reverse) 5'CTC-CCT-TCT-GGA-ACC-GAG-GCC 3'. To quantify immunoprecipitated DNA, a standard curve was generated from serial dilutions of input DNA. To calculate ChIP results as a perentage of input, the amount of the immunoprecipiated DNA from the IgG control was subtracted from the amount of the immunoprecipitated DNA from the Stat6 antibody, followed by normalizing against the amount of the input DNA.

KSHV gene expression. BCBL-1 cells were cultured as previously described(*47*). At indicated times post IL-4 or 12-O-tetradecanoylphorbol 13-acetate (TPA) treatment, total RNA was extracted using RNA-Bee (Tel-Test) according to the manufacturer's instructions. RNA was reverse transcribed using SuperScript III (Invitrogen) according to the manufacturer's suggestions. Quantitative PCR (qPCR) analysis was carried out using an ABI StepOne Plus system along with ABI Fast SYBR reagent (Applied Biosystems, Carlsbad, CA). Expression of all genes was normalized to GAPDH expression. Primers are as follows: Orf57 FWD-ACGAATCGAGGGACGACG, REV-CGGGTTCGGACAATTGCT(*48*); Orf45 FWD-GCTTTGCGGCTTAAGTTTGG, REV- CGCCTCCTCTGGTAGCGA(*48*); RTA FWD-CACAAAAATGGCGCAAGATGA, REV-TGGTAGAGTTGGGCCTTCAGTT(*49*); Orf59 FWD-TTAGAAGTGGAAGGTGTGCC, REV-TCCTGGAGTCCGGTATAGAATC(*50*); Orf19 FWD-GGCGAAAAAGTCAGCGGTGGT, REV-CGGCGCGTCTTCCCTAAAGA(*51*); GAPDH FWD- CCCCTGGCCAAGGTCATCCA, REV-ACAGCCTTGGCAGCGCCAGT(*52*).

KSHV isolation and quantitation. Virus particles were harvested from PEL cells at indicated times post IL-4 treatment. After clearing from cellular debris, media supernatant was passed through a 0.45 μM filter. Virus particles were then pelleted by ultra-centrifugation using a Beckman SW-40 rotor at 100,000 x g for 1 hr. Virus pellets were resuspended and DNA was extracted using DNAzole (Molecular Research Center, Inc.). Viral genome copy number was determined by qPCR assay for LANA N-terminus (FWD- GCGCCCTTAACGAGAGGAAGTT, REV- TTCCTTCGCGGTTGTAGATG) using a serial diluted LANA expression plasmid as a standard curve.

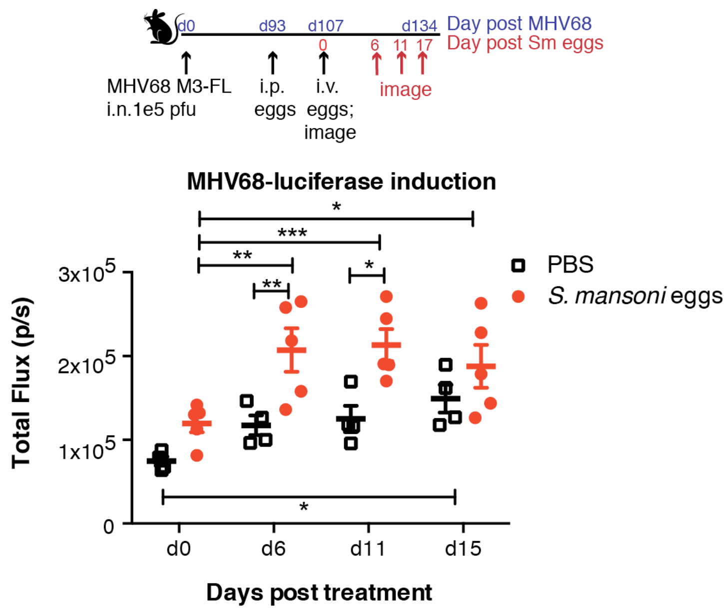

Fig. S1. Reactivation of MHV68 upon treatment with *Sm* eggs over 100 days after MHV68 infection. Mice infected with MHV68-M3-FL were challenged according to the timecourse depicted above with *Sm* eggs more than 3 months after infection with MHV68. Luciferase expression was measured. Each symbol represents an individual mouse. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ by 2-way repeated measures ANOVA with Tukey's and Bonferroni's post-test.

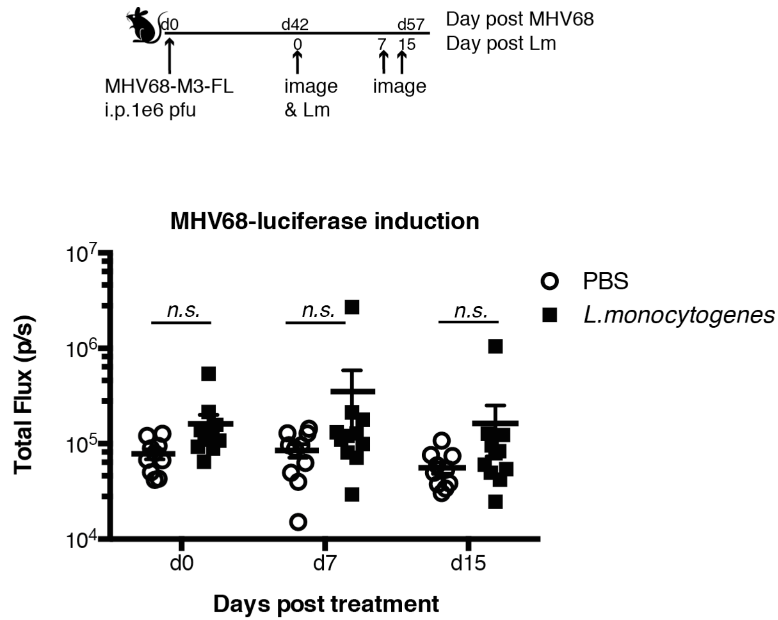

Fig. S2. *L. monocytogenes* does not reactivate MHV68. Mice were infected with MHV68-M3-FL for 42 days, and challenged with *L. monocytogenes*. Mice were imaged for luciferase expression either directly before infection with *L. monocytogenes* (d0) or at the indicated days after *L. monocytogenes* infection (d7 and d15). Total flux was quantitated. Two independent experiments were done and symbols are individual mice, bars are the means, and error bars are standard error. Neither time nor treatment was significant by 2-way repeated measures ANOVA. n.s. not significant.

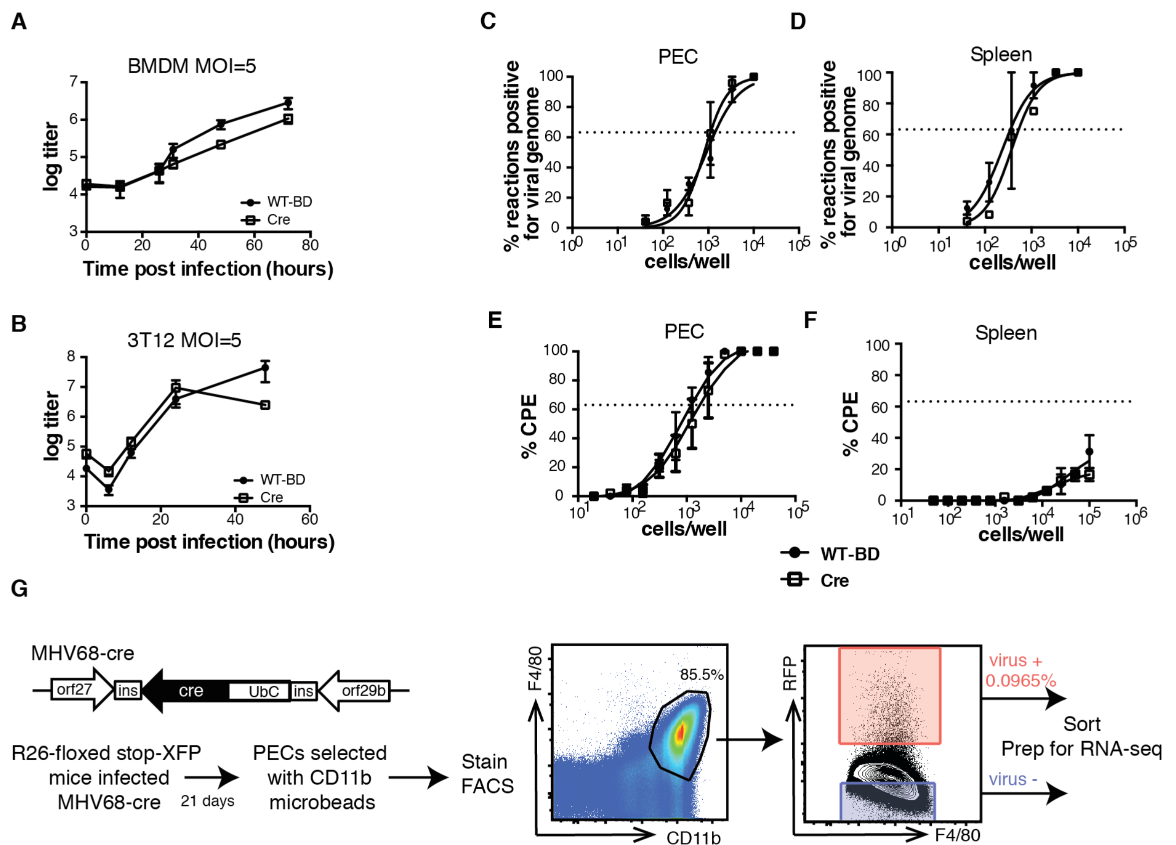

Fig. S3. Characterization of MHV68-cre virus and design of RNAseq experiment. **(A)** Growth curve of infected BMDMs comparing WT-BAC-derived (WT-BD) virus with MHV68-cre. Three independent experiments. **(B)** Growth curves of WT-BD and MHV68-cre in NIH3T12 cells. Three independent experiments. **(C-D)** Limiting dilution (LD)-PCR analysis at day 16 of PECs (C) or splenocytes (D) from mice infected intraperitoneally with either WT-BD (wild type MHV68 BAC derived) or MHV68-cre. Data points indicate the percentage of wells that were positive by nested-PCR for MHV68 gene 50 over a set of serial dilutions of cells. 12-24 wells per dilution were assayed. **(E-F)** Limiting dilution assay (LDA) for frequency of reactivation from latency of PECs (E) or splenocytes (F). Percent of wells that have cytopathic effect (CPE) was plotted against number of cells that were added per well. 24 wells per dilution were scored. Dotted horizontal lines represent 63.2% Poisson distribution. Parts C-F represent 2 independent experiments. **(G)** Diagram of MHV68-cre and sorting analysis of virus-positive and virus-negative cells from R26-stop-XFP mice infected i.p. with MHV68-cre. Peritoneal cells (PECs) were harvested as a source of infected macrophages. Three independent experiments were performed in each of which cells from at least eight mice were pooled and sorted as shown. Open reading frame (orf), insulator sequence (Ins), Ubiquitin C promoter (UbC).

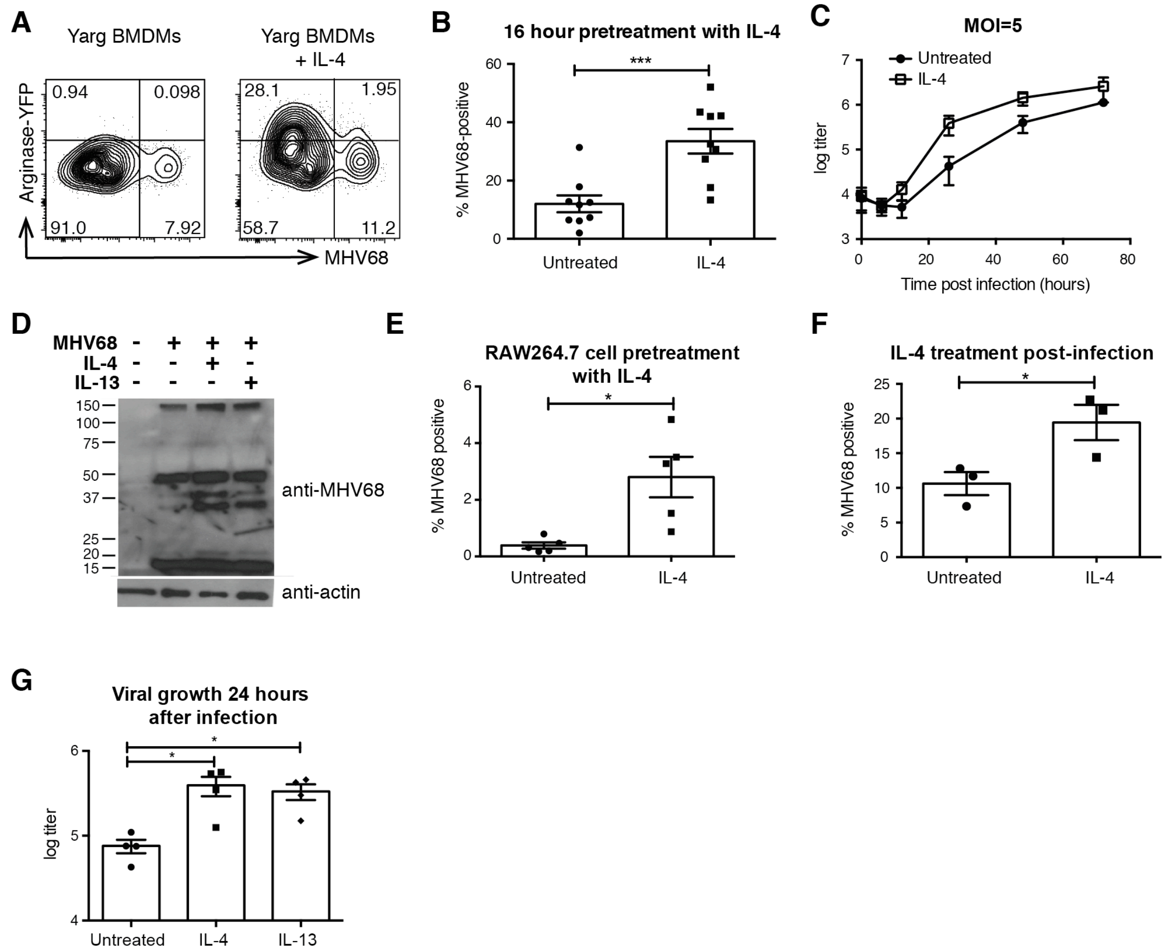

Fig. S4. IL-4 promotes virus replication in BMDMs and RAW264.7 cells. (A) Yarg BMDMs were either untreated or treated with IL-4 and infected with MHV68 at a multiplicity of infection (MOI)=5. Cells were analyzed 24 hours by flow cytometry for MHV68 lytic antigen expression and YFP (arginase) expression. **(B)** BMDMs were pretreated with IL-4 for 16 hours then infected with MHV68 at MOI=5. 24 hours later cells were analyzed by FACS as in Fig. 3A for expression of MHV68 lytic viral antigens. Shown is the average across multiple experiments of MHV68-positive cells. **(C)** BMDMs were treated with IL-4 and infected with MHV68 at a MOI=5. Viral titer was determined by plaque assay at the indicated timepoints. **(D)** BMDMs were treated with IL-4 or IL-13 and infected with MHV68 as in B. Lysates were analyzed by Western for expression of MHV68 proteins. **(E)** RAW264.7 macrophages were pretreated with IL-4 and infected with MHV68 for 24 hours. Cells were analyzed by flow cytometry for expression of MHV68 lytic viral proteins. **(F)** BMDMs were infected with MHV68. After virus inoculum was washed off, IL-4 was added to the cultures. Cells were analyzed 24 hours later by flow cytometry for expression of lytic viral proteins. **(G)** BMDMs were treated with either IL-4 or IL-13 and infected at an MOI=5. Viral titer was determined by plaque assay 24 hours after infection. In B, E - G symbols represent individual experiments. * $p<0.05$ by t test.

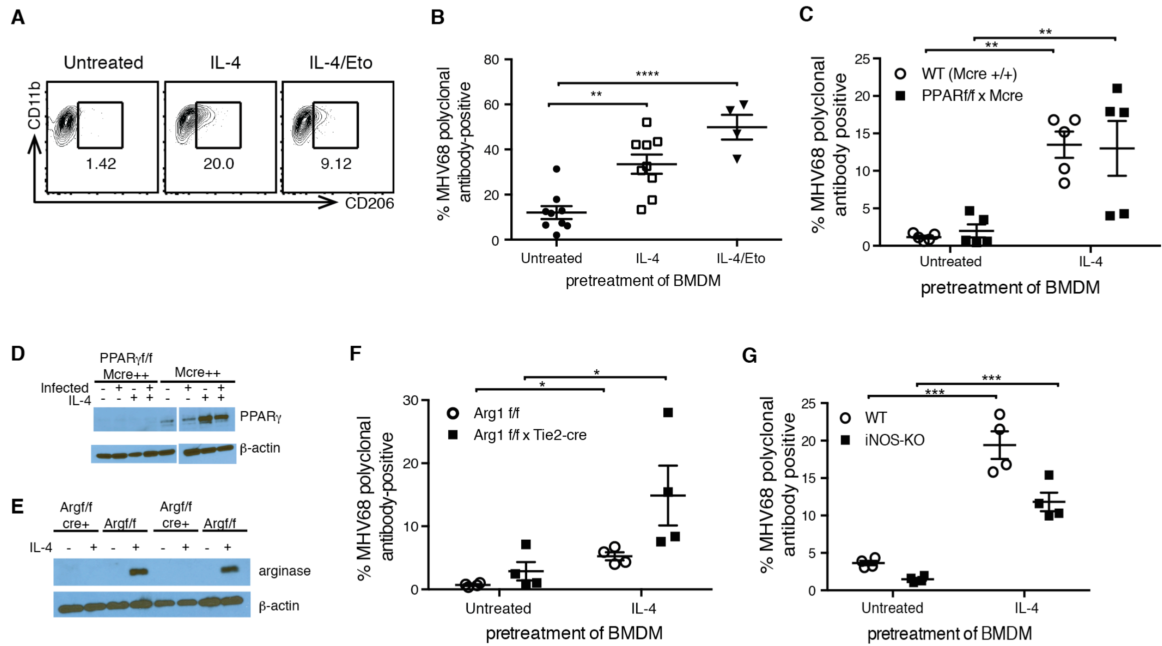

Fig. S5. Pathways involved in alternative macrophage activation are not required for IL-4-induced increase in MHV68 replication. (A-B) BMDMs were pretreated with either IL-4 (10ng/ml) or IL-4/Etomoxir (Eto)(200mM). Cells were infected with MHV68 and analyzed by flow cytometry for CD206 (A) and MHV68 infection (B) 24 hours later. **(C)** PPARγ f/f x Lysozyme M (Mcre) BMDMs and WT (Mcre++) BMDMs were infected and stained as in (A). **(D)** Deletion of PPARg was confirmed by western blot of BMDM lysates. (**E-F)** Arginase-1 (Arg1) f/f x Tie2 cre and WT (Arg f/f) BMDMs were infected and stained as in (A). (**E)** Deletion of arginase-1 was confirmed by western flot of BMDM lysates. **(F)** Flow cytometric analysis of MHV68 infection as in (A). (**G)** iNOS-deficient BMDMs were treated and stained as in (A). For B, C, F, and G percentage of cells that were positive for MHV68 staining is plotted. Symbols in graphs represent individual experiments. * $p<0.05$, ** $p< 0.01$, *** $p<0.001$, **** $p<0.0001$ by either one-way ANOVA or two-way ANOVA with Sidak's multiple comparison test.

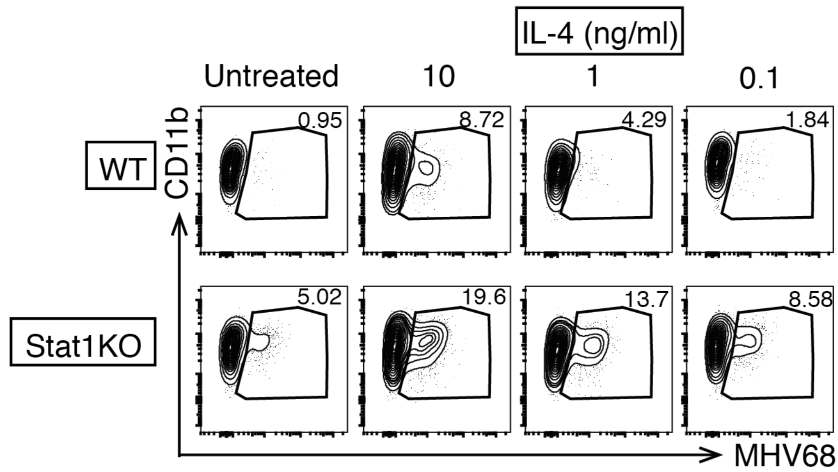

Fig. S6. Stat1 is not required for IL-4 induced MHV68 replication. Stat1KO or WT BMDMs were pretreated with IL-4 and then infected with MHV68. 24 hours later cells were analyzed for MHV68 infection by flow cytometry. Represents two independent experiments.

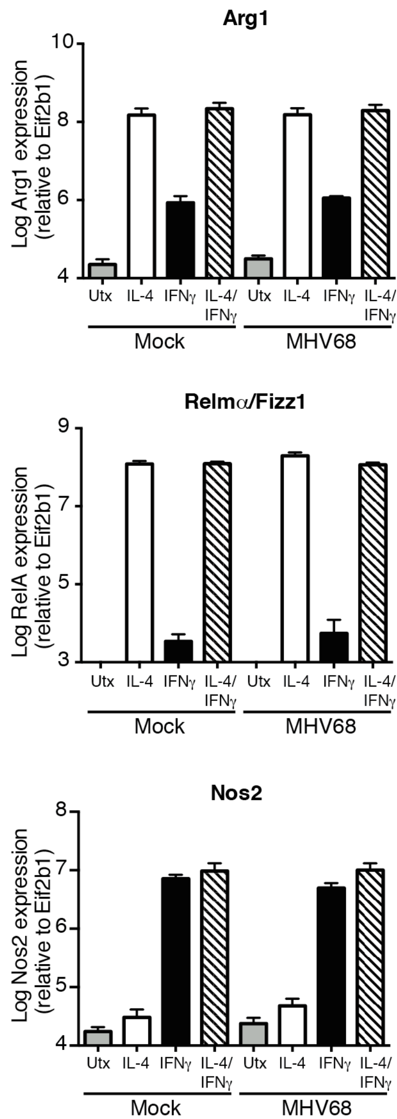

Figure S7. Gene expression analysis of BMDMs treated with IL-4 and IFNγ. BMDMs were treated with IL-4, IFNγ, or a combination of the two prior to infection with MHV68 at MOI=5. 24-hours later RNA was harvested and gene expression analysis was performed to quantitate expression of Arginase-1 (Arg1), Resistin-like molecule alpha (Relma/Fizz1), and Nitric oxide synthase-2, inducible (Nos2). Expression was normalized to Eif2b1. Data represents 3 independent experiments.

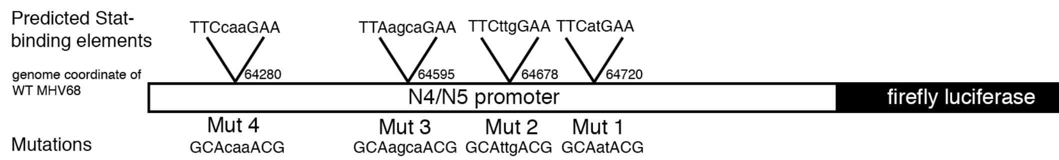

Fig. S8. Schematic of N4/N5 luciferase construct with potential Stat-binding mutants.

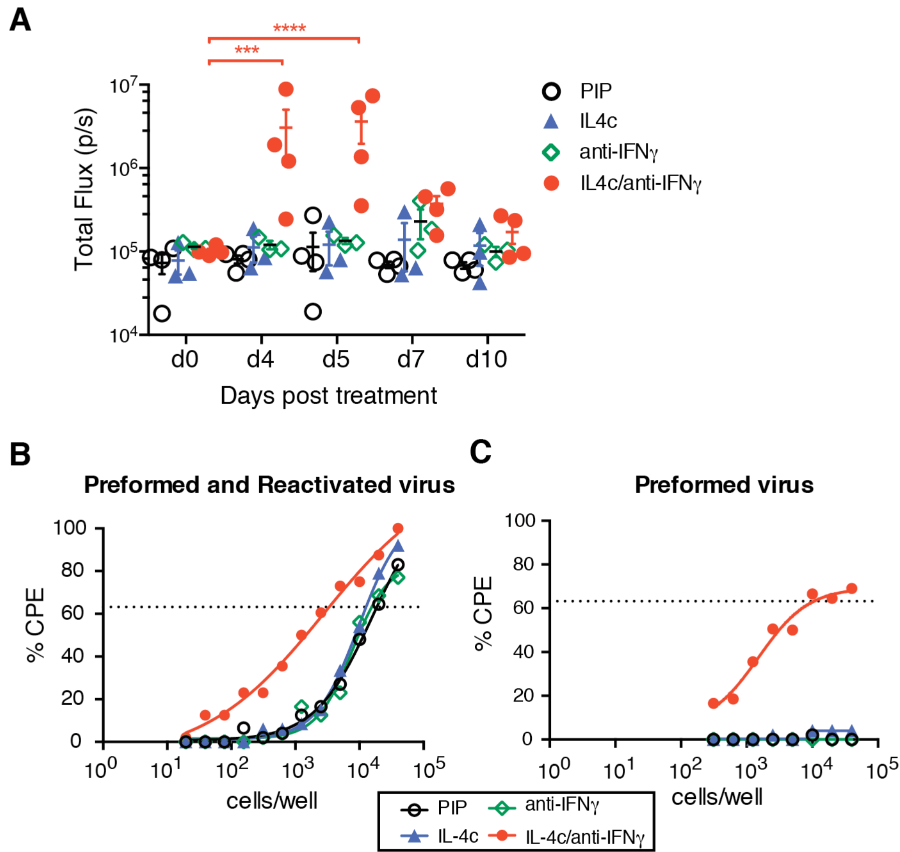

Fig. S9. Timecourse and LDA analysis of anti-IFNγ/IL4c-induced reactivation of MHV68. (A) Mice were infected with MHV68-M3-FL. 42 days later mice were imaged for luciferase expression (d0) and received isotype control (PIP), anti-IFNγ, IL4 complexes (IL4c), or anti- IFNγ plus IL4c. Mice were imaged on the indicated days for luciferase expression and total flux (photons/second) was measured in the abdominal region. Symbols are individual mice from one experiment. **(B)** Live PECs were isolated from 3 mice per experiment in a), pooled, and plated in 2-fold serial dilutions on MEF monolayers. CPE from 24-wells per dilution was counted and plotted against the number of cells per well. **(C)** Parallel samples to those in (B) were disrupted to kill cells but keep preformed virus intact, and were plated as in (B). ***p<0.001, ****p<0.0001 by 2-way repeated measures ANOVA and Tukey's post-test. For LDA analysis: Fit curve represents a sigmoidal dose response curve with variable slope. Dotted horizontal line represents 63.2% Poisson distribution. One representative experiment of two is shown.

Table S1. M1 and M2 signatures in virus-pos and virus-neg macrophages. List of differentially expressed genes in virus-pos and virus-neg macrophages that overlap with M1 and M2 signatures (table included at the end of the file).

Supplementary Table 1: M1 and M2 signatures in virus-pos and virus-neg macrophages.

M1 signature genes overlapping with virus-pos	M2 signature genes overlapping with virus-neg
1110018G07Rik	1500031L02Rik
1110038F14Rik	1810034E14Rik
1190005F20Rik	1810063B05Rik
1810029B16Rik	2310003L22Rik
2010106G01Rik	3110001D03Rik
2010109K11Rik	4930455F23Rik
3110001I22Rik	5830432E09Rik
3110003A17Rik	6230427J02Rik
4933426M11Rik	9830001H06Rik
A530032D15Rik	Aagab
Acot9	Abhd14b
Acp2	Acap3
Acsl1	Acot2
Adar	Acp6
Adora2a	Actr6
Aftph	Acy1
Agrn	Acyp1
AI607873	Adcy9
Akna	Add3
Ankrd33b	Aimp2
Ap3m2	Ak3
Arfgap3	Ak8
Arhgef3	Akr1c12
Arl4a	Alkbh7
Ass1	Amacr
AW112010	Ang
Axl	Ank
B2m	Ankmy2
Batf	Ap1b1
Batf2	Arg1
Bbip1	Arhgap39
BC006779	Arl15
BC013712	Arntl
Bcl2a1b	B230118H07Rik
Bcl3	Batf3
Bcl9	Bcs1l
Bcor	Brwd1
Birc3	Btbd2
C130026I21Rik	Btbd6
C1s	C130050O18Rik
C4b	C2cd2l
Calcrl	Cbr2
Casp1	Ccdc88c
Casp4	Ccl24
Ccdc25	Ccnf
Ccdc88b	Cd163
Ccl3	Cd200r1
Ccl4	Cd24a
Ccl5	Cd300lb
Ccrl2	Cd300lg
Cd14	Cdan1
Cd2ap	Cdc25b
Cd40	Cdc42ep3
Cds1	Cdk4
Cebpb	Cebpa
Cenpj	Chek2
Cfb	Chst12
Cflar	Ckap2
Clcn7	Clec10a
Clec4e	Cluap1
Cmpk2	Cox7a1
Cpne3	Csgalnact2

M1-cont.	M2- cont.
Crlf3	Dars2
Csrnp1	Ddx31
Cxcl10	Ddx59
Cxcl2	Deptor
Cxcl9	Dhx37
Cycs	Dna2
D14Ertd668e	Dnalc4
Daam1	Dnmbp
Daxx	Dok2
Dcp2	Dolpp1
Dnajb6	Dym
Dram1	Dyrk3
Dusp1	Echs1
Eapp	Enpp1
Ebi3	Ephx1
Ehd1	Eps8
Eif4g3	F13a1
Ell2	Fam117a
Enpp4	Fam195a
Etnk1	Fam43a
Fam26f	Fam58b
Fam82a2	Fam63a
Fas	Fam65a
Flnb	Fam98c
Fnbp1l	Fcrls
Fpr1	Fgfr1
Frmd4a	Fh1
Ftsjd2	Fli1
Fyb	Foxred2
Gadd45a	Gab3
Gbp4	Galc
Gbp5	Galnt9
Gbp6	Gamt
Gbp9	Gapt
Gca	Gas6
Gch1	Gfer
Gfpt1	Gins3
Ggct	Glcci1
Gm12185	Glod4
Gm12250	Glt25d1
Gm14446	Gng10
Gm4951	Gpn3
Gm6377	Gramd4
Gpd2	H2afj
Gpr18	Hadh
Gtf2b	Haus8
Gtpbp2	Hdac10
H2-M3	Hebp1
H2-Q8	Hfe
H2-T22	Hist1h2af
Hck	Hist1h2ai
Herc6	Hist1h2ak
Hinfp	Hrsp12
Hipk1	Hspe1
Hspbap1	Idh1
I830012O16Rik	Idh2
Icam1	Ifi27l1
Ifi203	Igf1
Ifi204	Imp3
Ifih1	Inpp5a
Ifit1	Kdelc2
Ifit2	Kif23
Ifitm3	Klhdc2
Ifnar2	Klhl17

M1-cont.	M2-cont.
Ift57	Ldlrad3
Igtp	Limk1
Iigp1	Lmnb1
Ikbke	Loh12cr1
Il12rb1	Lpin1
Il15ra	Ltb4r1
Il1a	Lyl1
Il1b	Mafb
Il27	Mctp1
Inpp5b	Mettl13
Irak2	Mgl2
Irg1	Miip
Irgm1	Mrc1
Irgm2	Mrpl42
Isg20	Mrps35
Itga5	Nat8l
Itgal	Ndufa12
Jam2	Nt5dc3
Kdm4a	Nthl1
Kif3c	Nudcd2
Klf6	Nudt2
Klra2	Olfm1
Larp1	Oxct1
Lcp2	Oxnad1
Leng9	Paip2b
Lmo4	Paox
Lnpep	Paqr7
Lpar1	Pcbd2
Lrch1	Pccb
Lrp10	Pcyox1l
Lrrc25	Pdcd4
Lrrc4	Pde12
Ly6a	Pdlim1
Ly6c2	Pecr
Ly6i	Peo1
Lztfl1	Phlda3
M6pr	Phtf1
Mafk	Plekhf1
March5	Plekhg3
Marcksl1	Plxnc1
Mgat4a	Polr2h
Mlkl	Polr3gl
Mmp14	Pot1a
Mnda	Pparg
Mocs1	Prkdc
Mrpl52	Prkrir
Ms4a4c	Prpsap2
Ms4a6b	Psmg2
Mtmr14	Ptgr1
Mtmr6	Ptgs1
Mtus1	Rab19
Mx1	Rab3il1
Myd88	Rasa3
N4bp1	Retnla
Ncf1	Rgs10
Nckap1l	Rnase4
Ncoa7	Rnf130
Nfkbia	Rpa3
Nfkbib	Rpl10a
Nfkbie	Rprd1b
Nfkbiz	Samd1
Nktr	Sesn1
Nlrc5	Slc45a4
Nod1	Slc46a3

M1-cont.

Nod2
Nt5c3
Nup98
Oasl1
Oasl2
Optn
Otud1
Parp10
Parp14
Parp8
Pfkfb3
Pgs1
Phf11
Pilra
Pilrb1
Pla2g16
Plagl2
Pld2
Plekhm3
Plscr1
Pml
Pnp
Ppm1k
Ppp4r2
Prdx5
Prpf39
Psmb9
Pstpip2
Ptges
Ptpn1
Pttg1
Pydc4
Rab10
Rab11fip1
Rab20
Rab22a
Rab32
Rap1b
Rapgef2
Rasa4
Rc3h1
Relb
Rhou
Riok3
Ripk2
Rnf114
Rnf135
Rnf14
Rnf31
Saa3
Sav1
Sbds
Scarf1
Senp1
Serpina3f
Serpina3g
Serpinb9
Sh3bp4
Skil
Slamf7
Slamf8
Slc11a1
Slc16a10
Slc25a12

M2-cont.

Smarca2
Smc4
Sulf2
Sult1a1
Surf2
Susd3
Taco1
Tarsl2
Tdp1
Tdp2
Tfrc
Tiam1
Tiam2
Timm17b
Timm8b
Tm7sf3
Tmem126b
Tmem18
Tmem37
Tmem64
Tmem81
Tob1
Tprkb
Trim47
Tspan5
Vat1
Vkorc1
Xrcc3
Yeats2
Zfand1
Zfp101
Zfp161
Zfp511
Zfp706
Zfp81
Zfyve21
Zmat3

M1-cont.

Slc25a37
Slc26a2
Slc28a2
Slc2a6
Slc31a2
Slc3a2
Slco3a1
Slfn3
Slfn4
Slfn8
Snx18
Snx20
Socs3
Sod2
Sp100
Spata13
Spata2
Sqstm1
St3gal1
Stard3
Stat2
Stat3
Stx11
Stx8
Stxbp1
Tagap1
Tbrg4
Tcirg1
Tdrd7
Tgs1
Tgtp1
Tle3
Tlk2
Tlr2
Tlr3
Tmcc3
Tmem131
Tmem2
Tnf
Tnfaip2
Tnfaip3
Tnfrsf1b
Tnfsf10
Tnip1
Tnip3
Tor1aip2
Traf1
Traf3ip2
Trex1
Trim21
Trim25
Txn1
Uba7
Ube2f
Ube2l6
Usp15
Usp18
Vav1
Vrk2
Wdfy1
Whamm
Xaf1
Xkr8
Ythdf1

M1-cont.

Zbp1
Zc3h12a
Zc3h12c
Zc3h7a
Zc3hav1
Zcchc2
Zcchc6
Zfp106
Zfp281
Zfp800
Zfp821
Znfx1
Znrf1
Zufsp