Supplementary Materials for

Senolytics reduce coronavirus-related mortality in old mice

Christina D. Camell†, Matthew J. Yousefzadeh†, Yi Zhu†, Larissa G. P. Langhi Prata†, Matthew A. Huggins, Mark Pierson, Lei Zhang, Ryan D. O’Kelly, Tamar Pirtskhalava, Pengcheng Xun, Keisuke Ejima, Ailing Xue, Utkarsh Tripathi, Jair Machado Espindola-Netto, Nino Giorgadze, Elizabeth J. Atkinson, Christina L. Inman, Kurt O. Johnson, Stephanie H. Cholensky, Timothy W. Carlson, Nathan K. LeBrasseur, Sundeep Khosla, M. Gerard O’Sullivan, David B. Allison, Stephen C. Jameson, Alexander Meves, Ming Li, Y. S. Prakash, Sergio E. Chiarella, Sara E. Hamilton*, Tamara Tchkonia*, Laura J. Niedernhofer*, James L. Kirkland*, Paul D. Robbins*

†These authors contributed equally to this work.
*Corresponding author. Email: probbins@umn.edu (P.D.R.); kirkland.james@mayo.edu (J.L.K.); lniedern@umn.edu (L.J.N.); tchkonia.tamar@mayo.edu (T.T.); hamil062@umn.edu (S.E.H.)

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Figure S1: Senescence-Associated Secretory Phenotype (SASP) factor expression is amplified by Pathogen-Activated Molecular Pattern (PAMP). As in Fig. 1A, human adipocyte progenitors isolated from subcutaneous fat biopsies (n=5 subjects) were induced to undergo senescence with 10 Gy of ionizing radiation (SnC) or not (non-SnC). Then cells were treated with different concentrations of LPS for 3 hr. Gene expression was measured by qPCR. mRNA expression was normalized to vehicle-treated non-SnC. Means ± SEM, mixed effects model. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 for comparison SnC vs. non-SnC at the same concentration of LPS.

Figure S2: Senescence-Associated Secretory Phenotype (SASP) factors are amplified in kidneys of mice after Pathogen-Activated Molecular Pattern (PAMP) exposure. Kidney data from the same experiment as Figure 1B. Young (2-month-old) and old (26-month) mice were treated with PBS (n=5y and 5o) or LPS (n=4y and 3o) and tissues collected 24 hr later. RNA was isolated from kidney and gene expression measured by qPCR. Expression was normalized to vehicle-treated young mice. Means ± SEM, two-way ANOVA and post-hoc comparison Tukey’s Honestly Significant Difference used to compare the two animal cohorts within a treatment group. Arrows and asterisks: grey=vehicle-treated old vs. young; black=LPS-treated old vs. young; red=old ± LPS. **p<0.01, ***p<0.001, ****p<0.0001.

Figure S3: Senescence-Associated Secretory Phenotype (SASP) factors are amplified in tissues of Ercc1¬/¬ progeroid mice after Pathogen-Activated Molecular Pattern (PAMP) exposure. Three-month-old progeroid Ercc1¬/¬ mice and WT littermates were treated with PBS or
LPS (n=4/group), then euthanized and tissues collected 24 hours later. A. RNA was isolated from kidney and liver and the following measured by qPCR: \( p16^{ink4a} \) and \( p21^{Cip1} \), \( Il1a \), \( Il1b \), \( Il6 \), \( Mcp1 \), and \( Tnfa \). B. IL-6 and MCP-1 protein levels in serum from the same mice, measured by ELISA 24 hr later. Expression was normalized to vehicle-treated age-matched WT mice. Means ± SEM, two-way ANOVA and post-hoc comparison Tukey’s Honestly Significant Difference used to compare the two animal cohorts within a treatment group. Arrows and asterisks: grey=vehicle-treated \( Ercc1^{-/-} \) vs. age-matched WT; black=LPS-treated \( Ercc1^{-/-} \) vs. age-matched WT; red=\( Ercc1^{-/-} \) ± LPS. **p<0.01, ***p<0.001, ****p<0.0001.

Figure S4: Irradiated human kidney endothelial cells express markers of cellular senescence and SASP factors. Extended data for Fig. 2A. Primary human kidney endothelial cells were induced to undergo senescence by 10 Gy of ionizing radiation (SnC) or not (non-SnC) (n=9 biological replicates) and 20 days later, expression of senescence and SASP markers was measured by qPCR. Means ± SEM, mixed effects model,****p<0.0001.

Figure S5: The SARS-CoV2 spike protein-1 (S1) exacerbates the secretory phenotype of replicative senescent human endothelial cells. Primary human kidney endothelial cells (n=6 biological replicates) were induced to undergo senescence (SnC) with subculturing then treated with 500 ng recombinant S1 or PBS vehicle for 24 hr. SASP-related proteins were measured in the conditioned media (CM) by Luminex xMAP technology, similar to Figure 2A. Mean abundance (pg/mL) of secreted factors that were significantly induced by S1 is illustrated in the heat map and Supplemental Table 3. A mixed effects model was used to test the effect of S1, senescence, and their interaction, taking into account replicate measures for each protein.
**Figure S6: SARS-CoV2 spike protein-1 (S1) exacerbates the secretory phenotype of senescent human pre-adipocytes.** Analogous to Figure 2A, human adipocyte progenitors isolated from subcutaneous fat biopsies (n=10 subjects) were induced to undergo senescence with 10 Gy of ionizing radiation (SnC) or not (non-SnC). Cells were then treated with 500 ng recombinant S1 for 24 hr. Gene expression was measured by qPCR. Means ± SEM, two-way ANOVA. Arrows and asterisks: grey=vehicle-treated SnC vs. non-SnC; black=S1-treated SnC vs. non-SnC; red=SnC vehicle vs. S1-treated. *p<0.05, **p<0.01, ****p<0.0001.

**Figure S7: Expression of viral entry genes in SnC vs. non-SnC.** A. Primary human lung epithelial cells were treated with recombinant IL-1α (200 µg) for 48 hr or vehicle only. ACE2 and TMPRSS2 mRNA were measured by qPCR (n=4 biological replicates). Means ± SEM; mixed effects model. ****p<0.0001. B. Primary human kidney endothelial cells were treated with recombinant IL-1α (200 µg) for 48 hr or vehicle only. Gene expression was measured by qPCR 24 hr after treatment and expression is shown relative to vehicle-treated samples. Means ± SEM; mixed effects model; ****p<0.0001. C. Human adipocyte progenitors isolated from subcutaneous fat tissue biopsies were induced to undergo senescence by 10 Gy of ionizing radiation (SnC) or not (non-SnC) (n=8 subjects). Gene expression was measured by RNA microarray. Means ± SEM, unpaired Student’s t-tests, not significant. D. Primary human kidney endothelial cells were induced to undergo senescence by 10 Gy of ionizing radiation (SnC) or not (non-SnC) (n=5 biological replicates). TMPRSS2 mRNA was measured by qPCR and expressed relative to non-senescent kidney endothelial cells. Means ± SEM; unpaired Student’s t-test. **p<0.01.
Figure S8: NME induces rapid death in old mice of both sexes. A. Extended data for Fig. 3A. Survival curve for 20-24-month-old old male (n=10) and female (n=8) WT mice that were exposed to NME bedding contaminated with murine β-coronavirus MHV for 7 days. B. Frequency of tissue resident cells (CD45+, intra-vascular stain negative) in the livers of SPF (n=3 young; n=20 old) and NME (n=8 young; n=17 old) mice. Means ± SEM, two-way ANOVA and post-hoc comparison Tukey’s Honestly Significant Difference were used to compare the two animal cohorts within a treatment group. ***p<0.001, ****p<0.0001. Arrows and asterisks: grey=SPF old vs young; black=NME old vs young; red=old SPF vs old NME. C. Extended data from Fig. 3E. Representative hematoxylin & eosin stain (1) and immunohistochemistry for MHV surface antigen (2) in sections of the intestinal tract of a 20-month-old WT NME mouse. Scale bar=50 μm.

Figure S9: Fisetin improved survival and reduced inflammation in old mice exposed to NME. Extended data from Fig. 4. A. Schematic diagram of the survival experiment. Old mice were administered Fisetin 20 mg/kg/day or vehicle only by oral gavage daily x 3 days starting on day 3 following initiation of NME. The 3 days of treatment were repeated every week for 3 weeks (3 days on, 4 days off). Animals were fed standard chow with Fisetin added (500 ppm) ad libitum once treatment was initiated. Survival curve for 20-24-month-old male (n=10/group) and female (n=8 vehicle; n=9 Fisetin) WT mice exposed to NME bedding contaminated with the murine β-coronavirus, mouse hepatitis virus (MHV) for 7 days. Log-rank (Mantel Cox test). Separate analyses were run for each sex in order to determine a p value for the effect of Fisetin treatment within a given sex. B. A cohort of young (2-month-old) and old (20-month-old) female mice (n=8-10 young + vehicle; 7-10 young + Fisetin; 8-11 old + vehicle; 12-13 old + Fisetin) were exposed to NME as described in Figure 4 for molecular analysis. Tissues were harvested 8-9 days post-
initiation of NME. SASP factor mRNA expression was measured in liver, spleen, kidney, and lung. All expression data were normalized to young mice treated with vehicle. Means ± SEM, two-way ANOVA and post-hoc comparison Tukey’s Honestly Significant Difference (HSD) used to compare the two animal cohorts within a treatment group. Arrows and asterisks: grey=vehicle-treated young vs. old; black=Fisetin-treated young vs. old; red=old ± Fisetin. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Figure S10: Genetic ablation of SnC suppresses inflammation/SASP in vivo. A. Extended sex-based survival analysis of NME-exposed old INK-ATTAC mice (n=8 old female + vehicle; n=9 old female + AP20187; n=11 old male + vehicle; n=10 old male + AP20187) from Fig. 5D. Log-rank (Mantel Cox) test. B. Extended data for Fig. 5A-D. Young (4 month-old) and old (22-30 month-old) male INK-ATTAC mice (n=5 young; n=3-4 old + vehicle; n=4 old + AP20187) were exposed to NME ± AP20187 to ablate SnC as described in Figure 5 and tissues were collected on day 7 post-initiation of NME. Quantification of SASP factor mRNA in multiple tissues. All expression data were expressed relative to vehicle-treated young mice. Means ± SEM. One-way ANOVA. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Figure S11: Fisetin suppresses mortality and improves adaptive immunity in aged mice challenged with environmental pathogens. Extended data for Fig. 5F-G. A. Old (22-26-month-old) mice were treated with Fisetin prior to exposure to NME to determine if senolytics prevent mortality caused by β-coronavirus infection. Mice were pretreated with 20 mg/kg Fisetin (n=19) by oral gavage daily x 2 days or vehicle (n=20). Animals were fed standard chow with Fisetin added (500 ppm) upon initiation of NME. Survival was measured for 45 days post-initiation of
NME. Log-rank (Mantel Cox) test. **B.** Analysis of survival in panel A by sex (n=10/group, except for old female + Fisetin n=9). Log-rank (Mantel Cox) test. Separate analyses were run for each sex to determine a p value for the effect of Fisetin treatment. **C.** Relative MHV antibody score in 22-26-month-old mice in the lifespan cohort on days 16 (n=8) and 21 (n=6) following initiation of NME.
Supplementary Figure 2

**Gene Expression**

- **p16**<sub>ink4a</sub>
- **p21**<sub>Cip1</sub>
- **Il1α**
- **Il1β**
- **Il6**
- **Il10**
- **Tnfa**
- **Mcp1**
- **Pai1**
- **Pai2**

**Comparative Analysis**

- Young WT vs. Old WT
- Effects of LPS vs. Veh

**Significance Levels**

- ****: p < 0.0001
- ***: p < 0.001
- **: p < 0.01
- *: p < 0.05

**Kidney:** Relative expression measured in both young and old WT mice under LPS and Veh conditions.
Supplementary Figure 7

A) Lung epithelial cells

ACE2

TMPRSS2

B) Kidney endothelial cells

Vehicle

IL-1α 200 ng

****

****

****

****

C) Adipocyte progenitor cells

D) Kidney endothelial cells

ACE2

TMPRSS2

Non-SnC

SnC

****

**

****

****
**A**

Supplementary Figure 8

Survival (%)

Days

Old Male

Old Female

**B**

Liver

% CD45 + Live Cells

Old

Young

SPF NME

**C**

H&E

MHV IHC

Old
**A**

Day

Fisetin Chow (500 ppm)

20mg/kg Fisetin or Vehicle

20mg/kg Fisetin or Vehicle

NME

0 10 20 30 40

Day

Survival (%)

100 75 50 25 0

Old + Control

Old + Fisetin

p<0.0001

100 75 50 25 0

Survival (%)

Days

**B**

Day

Male Control

Male Fisetin

Female Control

Female Fisetin

p<0.0001

p=0.0005

0 10 20 30 40

Percent survival

**C**

Relative MHV Antibody Scores

Fisetin (d16)

Fisetin (d21)

A59 (L)

A59 (N)

S (L)

LOD

0 10 20 30

Rel. MHV Antibody Scores

Supplementary Figure 11
### Supplemental Table 1. Statistical analysis and p values

|                      | IL-1a | IL-1b | IL-6 | MCP-1 | IL-10 | PAI1 | PAI2 | p16 | p21 |
|----------------------|-------|-------|------|-------|-------|------|------|-----|-----|
| Veh vs LPS in SC     | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.0227 | <0.0001 | 0.386 | 0.1049 |
| Veh Non-SC vs SC     | <0.0001 | <0.0001 | <0.0001 | 0.0138 | 0.5155 | 0.2375 | 0.0679 | <0.0001 | 0.0093 |
| LPS Non-SC vs SC     | <0.0001 | <0.0001 | <0.0001 | 0.0027 | <0.0001 | 0.0004 | <0.0001 | <0.0001 | 0.004 |

Note: +, zero-skewness log transformed

|                      | IL-1a | IL-1b | IL-6 | MCP-1 | IL-10 | PAI1 | PAI2 | p16 | p21 |
|----------------------|-------|-------|------|-------|-------|------|------|-----|-----|
| Veh vs LPS in Old WT | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.0133 | 0.419 | 0.9885 | <0.0001 |
| Veh Young vs Old     | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| LPS Young vs Old     | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.0005 | <0.0001 | <0.0001 | 0.0064 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

|                      | IL-6 | MCP-1 | TNFa |
|----------------------|------|-------|-------|
| Veh vs LPS in Old WT | <0.0001 | <0.0001 | <0.0001 |
| Veh Young vs Old     | <0.0001 | <0.0001 | <0.0001 |
| LPS Young vs Old     | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed

|                      | IL-2 | IL-3 | IL-5 | IL-6 | IL-8 | IL-10 | IL-12p40 | IL-12p70 | IL-13 | IL-17F |
|----------------------|------|------|------|------|------|-------|----------|----------|-------|--------|
| Veh vs S1 in SC      | <0.0001 | 0.0017 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Effects of S1 in SC vs effects in NonSc | 0.0032 | 0.0094 | 0.0451 | 0.5482 | 0.7491 | 0.0153 | 0.1601 | 0.2668 | 0.0801 | 0.0007 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

|                      | IL-18 | IL-22 | IL-27 | IP-10 | MIG/CXCL9 | DGFB-AB/BB | RANTES | TGFa | TNFa | TNFb |
|----------------------|-------|-------|-------|-------|-----------|-------------|--------|------|------|------|
| Veh vs S1 in Sc      | <0.0001 | <0.0001 | 0.0004 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Effects of S1 in SC vs effects in NonSc | 0.0618 | 0.2376 | 0.0809 | 0.3385 | 0.3084 | 0.7493 | 0.7852 | 0.0027 | 0.4246 | 0.0954 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

|                      | IFITM1 | IFITM2 | IFITM3 |
|----------------------|--------|--------|--------|
| NonSc CM vs. Sc. CM  | 0.6453 | <0.0001 | <0.0001 |
| Sc CM vs. Sc CM+ anti-IL-1a | 0.7049 | 0.0816 | 0.0901 |
| Sc CM vs. Sc CM+ anti-IL-18 | 0.7638 | 0.479 | 0.1046 |
| Sc CM vs. Sc CM+ anti-IL-1a+anti-IL-18+Anti-PAI1 | 0.2169 | 0.002 | 0.0011 |

Note: +, zero-skewness log transformed

|                      | IFITM1 | IFITM2 | IFITM3 |
|----------------------|--------|--------|--------|
| Veh vs. IL1a (200ng) | 0.3900 | <0.0001 | <0.0001 |
| Veh vs. IL1a (1 ug)  | 0.1234 | <0.0001 | <0.0001 |
Figure 2F

| TMPRSS2 | ACE2 | TMPRSS2 | ACE2 |
|---------|------|---------|------|
| CM of NonSc preadipocytes vs. CM of Sc preadipocytes | 0.9908 | 0.7911 | 0.9908 | 0.7911 |
| CM of NonSc Kidney endothelial cells vs. CM of Sc kidney endothelial cells | <0.0001 | 0.0014 | <0.0001 | 0.0259 |

Note: +, zero-skewness log transformed

Figure 2F-1

| TMPRSS2 | ACE2 | TMPRSS2 | ACE2 |
|---------|------|---------|------|
| NonSc CM vs. Sc. CM | <0.0001 | 0.0014 | <0.0001 | 0.0259 |
| Sc CM vs. Sc CM+ anti-PAI1 | 0.1199 | <0.0001 | 0.1202 |
| Sc CM vs. Sc CM+ anti-IL-1a | <0.0001 | 0.0259 |
| Sc CM vs. Sc CM+ anti-IL-18 | <0.0001 | 0.0259 |

Note: +, zero-skewness log transformed

Figure 2F-2

| TMPRSS2 | ACE2 | TMPRSS2 | ACE2 |
|---------|------|---------|------|
| Veh vs. IL-1a (200ng) | <0.0001 | 0.0014 | <0.0001 | 0.0259 |
| Veh vs. IL-1a (1 ug) | <0.0001 | 0.0014 | <0.0001 | 0.0259 |

Note: +, zero-skewness log transformed

Figure 2H

CORRELATION OF P16 AND TMPRSS2 with ID controlled

r=0.7233

Regress tmpRSS again P16 with ID controlled

R-squared=0.65

Adj R-squared=0.55

Figure 3B

| Liver | Lung | Kidney | Liver | Lung | Kidney |
|------|------|--------|------|------|--------|
| p16  | p16  | p16    | p21  | p21  | p21    |
| SPF vs NME in Old | 0.0272 | 0.1743 | 0.6427 | 0.0006 | 0.0148 | 0.1081 |
| SPF Young vs Old | 0.0028 | 0.2695 | <0.0001 | 0.7542 | 0.4048 | 0.0021 |
| NME Young vs Old | 0.0034 | 0.0327 | <0.0001 | 0.0015 | 0.1229 | 0.0146 |

Note: +, zero-skewness log transformed

Figure 3C

| Liver | Lung | Kidney | Liver | Lung | Kidney | Liver | Lung | Kidney |
|------|------|--------|------|------|--------|------|------|--------|
| p16  | p16  | p16    | p21  | p21  | p21    | p16  | p16  | p16    |
| SPF vs NME in Old | 0.0013 | 0.2113 | 0.0003 | 0.0009 | 0.0057 | 0.0001 | 0.0042 | 0.1611 | 0.0002 |
| SPF Young vs Old | 0.2609 | 0.2288 | 0.0017 | 0.1167 | 0.0391 | 0.1184 | 0.1312 | 0.2166 | 0.1843 |
| NME Young vs Old | 0.0336 | 0.5996 | 0.0001 | 0.5117 | 0.1229 | 0.0132 | 0.6855 | 0.8083 | 0.0017 |

Note: +, zero-skewness log transformed

Figure 3D

| Liver | Lung | Kidney | Liver | Lung | Kidney |
|------|------|--------|------|------|--------|
| p16  | p16  | p16    | p21  | p21  | p21    |
| SPF vs NME in Old | 0.0024 | 0.0872 | <0.0001 | 0.0056 |
| SPF Young vs Old | 0.3077 | 0.7975 | 0.9316 | 0.8639 |
| NME Young vs Old | 0.0030 | 0.2706 | 0.0002 | 0.0034 |

Note: +, zero-skewness log transformed, ++, box cox transformed, +++ rank transformed

Figure 4D

| Liver | Lung | Kidney | Liver | Lung | Kidney |
|------|------|--------|------|------|--------|
| IL-6 | IL-10 | CCL11 | TNF |
| SPF vs NME in Old | 0.0024 | 0.0872 | <0.0001 | 0.0056 |
| SPF Young vs Old | 0.3077 | 0.7975 | 0.9316 | 0.8639 |
| NME Young vs Old | 0.0030 | 0.2706 | 0.0002 | 0.0034 |

Note: +, zero-skewness log transformed

Figure 4E

| Liver | Lung | Kidney |
|------|------|--------|
| MHV  |      |        |
| Veh vs Fisetin in Old | 0.1627 |
| Fisetin Young vs Old | <0.0001 |
| Veh Young vs Old | <0.0001 |

Note: +, zero-skewness log transformed
|                  | Liver | Kidney | Lung | Spleen | Liver | Kidney | Lung | Spleen |
|------------------|-------|--------|------|--------|-------|--------|------|--------|
| Veh vs Fisetin in Old | 0.0023 | 0.0846 | 0.0345 | 0.7789 | 0.0085 | <0.0001 | 0.2120 | 0.0198 |
| Fisetin Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

**Figure 4F**

|                  | Ifnr | Il1a | Il1b | Il6 | Il17 | Tnfa | Cxcl1 | Cxcl2 | Cxcl10 | Mcp1 |
|------------------|------|------|------|-----|------|------|-------|-------|--------|------|
| Veh vs Fisetin in Old | 0.0149 | 0.0004 | 0.0058 | 0.1128 | 0.0038 | 0.0087 | 0.0139 | 0.0327 | 0.0018 |
| Fisetin Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

**Figure 4G**

|                  | IL-1b | IL-6 | MCP-1 | INFa |
|------------------|-------|------|-------|------|
| Veh vs Fisetin in Old | 0.0027 | 0.0273 | 0.0125 | 0.0012 |
| Fisetin Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

**Figure 5B**

|                  | MHV |
|------------------|-----|
| Young Veh vs Old Veh | 0.005 |
| Old Veh vs Old SP20187 | 0.048 |

**Supplemental Figure 1**

|                  | Il1a | Il1b | Il6 | Il10 | Mcp1 | P411 | P412 | p16 | p21 |
|------------------|------|------|-----|------|------|------|------|-----|-----|
| Non-SC vs SC 0 ug LPS | 0.0004 | 0.0001 | 0.0002 | 0.0041 | 0.0002 | 0.7391 | 0.2947 | <0.0001 | 0.007 |
| Non-SC vs SC 0.1 ug LPS | 0.002 | 0.0009 | 0.0001 | 0.0002 | 0.0042 | 0.3076 | 0.2175 | <0.0001 | 0.0396 |
| Non-SC vs SC 1 ug LPS | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.1551 | 0.0128 | <0.0001 | 0.0001 |
| Non-SC vs SC 10 ug LPS | 0.0011 | 0.0017 | <0.0001 | 0.0005 | <0.0001 | 0.1726 | 0.0005 | <0.0001 | 0.0029 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

**Supplemental Figure 2**

|                  | Il1a | Il1b | Il6 | Il10 | Mvp1 | P411 | P412 | Lps | Tnf |
|------------------|------|------|-----|------|------|------|------|-----|-----|
| Veh vs LPS in Old WT | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | 0.0001 | 0.0001 | <0.0001 | 0.6998 |
| Veh Young vs Old | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.0001 | <0.0001 |
| LPS Young vs Old | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.0001 | 0.0029 |

Note: +, zero-skewness log transformed

**Supplemental Figure 3A Liver**

|                  | p16 | p21 | Il1a | Il1b | Il6 | Mkp1 | Tnf |
|------------------|-----|-----|------|------|-----|------|-----|
| Veh vs LPS in Erccl-Δ | 0.7497 | 0.5939 | <0.0001 | <0.0001 | <0.0001 | 0.0002 | <0.0001 |
| Veh WT vs Erccl-Δ | 0.8699 | 1 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| LPS WT vs Erccl-Δ | 0.0004 | 0.0024 | 0.0005 | 0.0001 | <0.0001 | 0.0027 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

**Supplemental Figure 3A Kidney**

|                  | p16 | p21 | Il1a | Il1b | Il6 | Mkp1 | Tnf |
|------------------|-----|-----|------|------|-----|------|-----|
| Veh vs LPS in Erccl - A versus B | 0.8771 | 0.5881 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
|          |       |       |       |       |       |       |
|----------|-------|-------|-------|-------|-------|-------|
| A vs. C  | 0.8011 | 0.3447 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| B vs. D  | <0.0001 | 0.001 | 0.0002 | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed.

**Supplemental Figure 3B Serum**

|          | IL6   | MCP1  |
|----------|-------|-------|
| Veh vs LPS in Ercc1 - A versus B | <0.0001 | <0.0001 |
| LPS effect in Ercc1 vs effect in WT - Slope of line 1 versus 2 | 0.4245 | 0.0282 |
| A vs. C  | <0.0001 | <0.0001 |
| B vs. D  | 0.0089 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed.

**Supplemental Figure 4**

|          | p16  | p21  | IL-1α | IL-1β | IL-6  | IL-8  | PAI-1 |
|----------|------|------|-------|-------|-------|-------|-------|
| Non-SC vs SC | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed.

**Supplemental Figure 5**

|          | sCD40L | GM-CSF | IL-1β | IL-17F |
|----------|--------|-------|-------|--------|
| Veh vs S1 in Scns | 0.0357 | 0.0576 | 0.008 | 0.0185 |
| S1 effect in Scns vs effect in NonScns | 0.3461 | 0.5992 | 0.041 | 0.3755 |
| Veh vs S1 in Non Scns | 0.0381 | 0.0314 | 0.0617 | 0.0132 |
| Scns Veh vs. Non Scns Veh | <0.0001 | 0.0342 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed.

**Supplemental Figure 6**

|          | IL-1α | IL-1β | IL-6  | IL-8  | MCP-1 |
|----------|-------|-------|-------|-------|-------|
| Veh vs S1 in Sc - A versus B | 0.0034 | 0.046 | 0.0858 | 0.0865 | 0.709 |
| Veh Non-SC vs SC | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| S1 Non-SC vs SC | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

Note: +, zero-skewness log transformed.

**Supplemental Figure 7A**

|          | ACE2  | TMPRSS2 |
|----------|-------|---------|
| Veh vs. IL-1α (200ng) | <0.0001 | <0.0001 |

**Supplemental Figure 7B**

|          | IL-6  | IL-8  | IP10  | MCP1  |
|----------|-------|-------|-------|-------|
| Vehicle vs IL-1α tx | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

**Supplemental Figure 7C**

|          | ACE2  | TMPRSS2 |
|----------|-------|---------|
| Non-SC vs. SC | 0.2342 | 0.4994 |

**Supplemental Figure 7D**

|          | TMPRSS2 |
|----------|---------|
| Non-SC vs. SC | 0.0011 |

**Supplemental Figure 8B**

|          | CD45+ cells |
|----------|-------------|
| SPF vs NME in Old | <0.0001 |
| SPF Young vs Old | <0.0001 |
| NME Young vs Old | 0.0001 |

**Supplemental Figure 9B**

|          | Liver | Liver | Liver | Liver | Liver | Liver |
|----------|-------|-------|-------|-------|-------|-------|
| II2     | II7   | II10  | Mpl1a | Pail  | Pail  | Pail  |
| Veh vs Fisetin in Old | 0.0193 | 0.3649 | 0.2438 | 0.6787 | 0.0598 | 0.0033 |
|                    | Spleen | Spleen | Spleen | Spleen | Spleen | Spleen |
|--------------------|--------|--------|--------|--------|--------|--------|
| Veh vs Fisetin in Old | 0.5773 | 0.2322 | 0.6524 | 0.0055 | 0.0493 | 0.0279 |
| Fisetin Young vs Old | <0.0001 | 0.8516 | 0.0047 | <0.0001 | <0.0001 | 0.0007 |
| Veh Young vs Old | <0.0001 | 0.1100 | 0.0378 | <0.0001 | <0.0001 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | + | + | + | +++ | + | + |

|                    | Spleen | Spleen | Spleen | Spleen | Spleen | Spleen |
|--------------------|--------|--------|--------|--------|--------|--------|
| Veh vs Fisetin in Old | 0.1815 | 0.0027 | 0.0669 | 0.0669 | 0.5973 | 0.2660 |
| Fisetin Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.028 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | + | + | + | +++ | + | + |

|                    | Kidney | Kidney | Kidney | Kidney | Kidney | Kidney |
|--------------------|--------|--------|--------|--------|--------|--------|
| Veh vs Fisetin in Old | 0.0173 | 0.0628 | 0.3457 | 0.0573 | 0.2116 | 0.0950 |
| Fisetin Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.0535 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.0138 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | + | + | + | + | + | + |

|                    | Kidney | Kidney | Kidney | Kidney | Kidney | Kidney |
|--------------------|--------|--------|--------|--------|--------|--------|
| Veh vs Fisetin in Old | 0.0070 | 0.0740 | 0.3080 | 0.0018 | 0.0357 | 0.1547 |
| Fisetin Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | 0.0039 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | +++ | + | + | + | + | +++ |

|                    | Kidney | Kidney |
|--------------------|--------|--------|
| Veh vs Fisetin in Old | 0.0084 | 0.8260 |
| Fisetin Young vs Old | 0.0002 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | +++ | |

|                    | Lung | Lung | Lung | Lung | Lung | Lung |
|--------------------|------|------|------|------|------|------|
| Veh vs Fisetin in Old | 0.4869 | 0.2290 | 0.2332 | 0.4918 | 0.9646 | 0.0521 |
| Fisetin Young vs Old | 0.0001 | 0.0004 | <0.0001 | <0.0001 | 0.0025 | <0.0001 |
| Veh Young vs Old | 0.0011 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | + | + | + | + | + | + |

|                    | Lung | Lung | Lung | Lung | Lung | Lung |
|--------------------|------|------|------|------|------|------|
| Veh vs Fisetin in Old | 0.0189 | 0.1465 | 0.3793 | 0.0199 | 0.6119 | 0.2253 |
| Fisetin Young vs Old | 0.0011 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Veh Young vs Old | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed | + | + | + | + | + | + |

Lung
|                  |          |
|------------------|----------|
| Veh vs Fisetin in Old | 0.2809   |
| Fisetin Young vs Old | <0.0001  |
| Veh Young vs Old   | <0.0001  |

Note: +, zero-skewness log transformed; ++, box cox transformed; +++ rank transformed

**Figure 10B**

|                |       |       |       |       |
|----------------|-------|-------|-------|-------|
| Kidney         |       |       |       |       |
| Young Veh vs Old Veh | <0.001 | 0.001 | <0.001 | 0.005 |
| Old Veh vs Old SP20187 | 0.001  | 0.001 | 0.001  | 0.633 |

|                |       |       |       |       |
| Colon          |       |       |       |       |
| Young Veh vs Old Veh | 0.024  | 0.002 | 0.028  | 0.065 |
| Old Veh vs Old SP20187 | 0.287  | 0.224 | 0.233  | 0.009 |

|                |       |       |       |       |
| Brain          |       |       |       |       |
| Young Veh vs Old Veh | <0.001 | <0.001 | <0.001 | <0.001 |
| Old Veh vs Old SP20187 | 0.941  | 0.026 | 0.001  | 0.011 |

|                |       |       |
| Pancreas       |       |       |
| Young Veh vs Old Veh | 0.035  | 0.01  |
| Old Veh vs Old SP20187 | 0.076  | 0.174 |
**Supplemental Table 2.** Primary human kidney endothelial cells (n=9 biological replicates) were induced to undergo senescence with 10 Gy of ionizing radiation (SnC) or not (non-SnC) then treated with 500 ng recombinant S1 or PBS vehicle for 24 hr. Thirty SASP-related proteins were measured in the conditioned media (CM) by Luminex xMAP technology. Relative abundance induced by S1 (normalized to vehicle treated non-senescent cells (non-SnC + Veh)) is illustrated in the heat map. A mixed effects model was used to test the effect of S1, senescence, and their interaction, taking into account replicate measures within a subject for each protein as well as the composite score. Margin effects of SnC in the treatment group also were tested under the mixed effects model framework. Overall, the effect of S1 on SnC was significantly more pronounced than on non-SnC (composite score change p<0.0089). Note: ns not significant; + zero-skewedness log transformed; ++ box cox transformed; +++ rank transformed.
|                | Veh vs. S1 in SnC | Overall effects of S1 in SnC | Overall effects in Non-SnC vs. Overall effects in Non-SnC | Veh vs. S1 in SnC | Overall effects of S1 in SnC | Overall effects in Non-SnC vs. Overall effects in Non-SnC |
|----------------|-------------------|-----------------------------|-----------------------------------------------------------|-------------------|-----------------------------|-----------------------------------------------------------|
| **Non-SnC + Veh** |                   |                             |                                                           |                   |                             |                                                           |
| sCD40L         | 5.04 ± 1.15       |                             |                                                           | 14.00 ± 4.89      | <0.0001                    | 0.0032                                                    |
| Fractalkine    | 16.24 ± 2.59      |                             |                                                           | 20.35 ± 9.07      | <0.0001                    | 0.0094                                                    |
| Eotaxin        | 4.02 ± 0.54       |                             |                                                           | 5.04 ± 0.67       | <0.0001                    | 0.0451                                                    |
| G-CSF          | 22.80 ± 4.79      |                             |                                                           | 23.86 ± 4.09      | <0.0001                    | 0.5482                                                    |
| GM-CSF         | 3.62 ± 0.58       |                             |                                                           | 4.37 ± 0.55       | <0.0001                    | 0.7491                                                    |
| INFα2          | 0.29 ± 0.06       |                             |                                                           | 0.69 ± 0.07       | <0.0001                    | 0.1601                                                    |
| INFy           | 2.20 ± 0.44       |                             |                                                           | 3.08 ± 0.40       | <0.0001                    | 0.8081                                                    |
| IL-1α          | 0.41 ± 0.05       |                             |                                                           | 0.46 ± 0.04       | <0.0001                    | 0.0007                                                    |
| IL-2           | 0.05 ± 0.01       |                             |                                                           | 0.03 ± 0.01       | <0.0001                    | 0.0018                                                    |
| IL-3           | 0.11 ± 0.06       |                             |                                                           | 0.19 ± 0.03       | <0.0001                    | 0.2146                                                    |
| IL-5           | 0.07 ± 0.01       |                             |                                                           | 0.08 ± 0.01       | <0.0001                    | 0.0039                                                    |
| IL-6           | 413.49 ± 146.76   |                             |                                                           | 548.96 ± 165.30   | <0.0001                    | 0.9905                                                    |
| IL-8           | 2140.10 ± 493.14  |                             |                                                           | 2167.84 ± 548.41  | <0.0001                    | 0.6694                                                    |
| IL-10          | 0.29 ± 0.07       |                             |                                                           | 0.55 ± 0.11       | <0.0001                    | 0.0542                                                    |
| IL-12p40       | 6.57 ± 0.74       |                             |                                                           | 7.38 ± 0.71       | <0.0001                    | 0.0105                                                    |
| IL-12p70       | 0.31 ± 0.10       |                             |                                                           | 0.43 ± 0.10       | <0.0001                    | 0.1076                                                    |
| IL-13          | 3.49 ± 0.97       |                             |                                                           | 5.10 ± 0.81       | <0.0001                    | 0.0021                                                    |
| IL-17F         | 0.84 ± 0.27       |                             |                                                           | 0.95 ± 0.25       | <0.0001                    | 0.0069                                                    |
| IL-18          | 0.16 ± 0.02       |                             |                                                           | 0.31 ± 0.07       | <0.0001                    | 0.0018                                                    |
| IL-22          | 1.02 ± 1.02       |                             |                                                           | 2.21 ± 0.50       | <0.0001                    | 0.2376                                                    |
| IL-27          | 43.40 ± 6.93      |                             |                                                           | 42.72 ± 6.40      | <0.0001                    | 0.0004                                                    |
| IP-10          | 2.73 ± 0.57       |                             |                                                           | 3.93 ± 0.97       | <0.0001                    | 0.3385                                                    |
| MIG/CXCL9      | 0.67 ± 0.10       |                             |                                                           | 0.52 ± 0.08       | <0.0001                    | 0.3084                                                    |
| PDGF-AB/BB     | 386.58 ± 128.88   |                             |                                                           | 385.43 ± 131.82   | <0.0001                    | 0.7493                                                    |
| RANTES         | 62.98 ± 4.15      |                             |                                                           | 68.21 ± 5.85      | <0.0001                    | 0.7852                                                    |
| TGFβa          | 1.40 ± 0.27       |                             |                                                           | 0.82 ± 0.19       | <0.0001                    | 0.0027                                                    |
| TNFα           | 16.09 ± 2.86      |                             |                                                           | 15.93 ± 3.05      | <0.0001                    | 0.4246                                                    |
| TNFβ0.1        | 2.60 ± 0.46       |                             |                                                           | 2.34 ± 0.42       | <0.0001                    | 0.0954                                                    |
| EGF            | 5724.33 ± 1052.49 |                             |                                                           | 4901.56 ± 676.40  | <0.0001                    | 1.0551                                                    |
| FGF-2          | 112.03 ± 64.12    |                             |                                                           | 1129.72 ± 52.46   | <0.0001                    | 0.0004                                                    |
| FLT-3L         | 1.53 ± 0.46       |                             |                                                           | 1.16 ± 0.24       | <0.0001                    | 0.15 ± 0.24                                                |
| GROα           | 1142.25 ± 139.30  |                             |                                                           | 1183.24 ± 126.26  | <0.0001                    | 0.7236                                                    |
| IL-4           | 0.12 ± 0.03       |                             |                                                           | 0.12 ± 0.03       | <0.0001                    | 0.17 ± 0.04                                                |
| IL-9           | 1.79 ± 0.39       |                             |                                                           | 1.68 ± 0.36       | <0.0001                    | 0.29 ± 0.57                                                |
| IL-15          | 5.73 ± 1.94       |                             |                                                           | 5.61 ± 1.85       | <0.0001                    | 0.73 ± 1.57                                                |
| MCP-1          | 1156.74 ± 128.61  |                             |                                                           | 877.49 ± 64.76    | <0.0001                    | 2288.87 ± 410.78                                          |
| MCP-3          | 85.21 ± 2.27      |                             |                                                           | 88.68 ± 3.43      | <0.0001                    | 131.66 ± 37.11                                           |
| M-CSF          | 132.45 ± 31.13    |                             |                                                           | 116.47 ± 24.23    | <0.0001                    | 210.55 ± 49.77                                           |
| PDGF-AA        | 795.06 ± 225.30   |                             |                                                           | 777.66 ± 211.66   | <0.0001                    | 416.70 ± 54.90                                           |
**Supplemental Table 3.** Primary human kidney endothelial cells (n=6 biological replicates) were induced to undergo senescence (SnC) with subculturing then treated with 500 ng recombinant S1 or PBS vehicle for 24 hr. Thirty SASP-related proteins were measured in the conditioned media (CM) by Luminex xMAP technology. Mean abundance (pg/mL) of secreted factors that were significantly induced by S1 is illustrated in the heat map. A mixed effects model was used to test the effect of S1, senescence, and their interaction, taking into account replicate measures for each protein. Note: + zero-skewness log transformed.

| Protein   | Non-SnC + Veh | Non-SnC + S1 | SnC + Veh | SnC + S1 | Veh vs. S1 in SnC |
|-----------|---------------|--------------|-----------|----------|------------------|
| sCD40L    | 7.34167 ± 0.3852 | 9.25667 ± 1.7731 | 18.6833 ± 1.83973 | 23.5417 ± 1.61923 | 0.0357           |
| GM-CSF    | 7.4 ± 0.93531   | 9.81167 ± 2.057   | 9.75417 ± 0.63444 | 13.6125 ± 1.35175 | 0.0576           |
| IL-1β     | 3.25833 ± 0.31944 | 3.0933 ± 0.4049    | 7.9375 ± 0.95513  | 11.2917 ± 1.19025 | 0.008            |
| IL-17F    | 2.325 ± 0.08184  | 2.55167 ± 0.1537   | 5.36667 ± 0.28966  | 6.17083 ± 0.25629 | 0.0185           |
Supplemental Table 4. Viruses detected by PCR in oral swabs or fecal pellets of young (3-month-old) and old (20-24-month-old) female mice at day 7 post-exposure to NME. (MHV: mouse hepatitis virus; MNV: murine norovirus; TMEV: Theiler’s encephalomyelitis virus; PV: parvovirus)

|       | MHV | MNV | TMEV | PV  |
|-------|-----|-----|------|-----|
| Young | 7/7 | 7/7 | 7/7  | 1/7 |
| Old   | 7/7 | 7/7 | 7/7  | 0/7 |
**Supplemental Table 5.** Serological analysis of multiple viral infections in young (3-month-old) or old (21-22-month-old) female mice on day 21-23 that survived NME following prior immunization with a sublethal dose of MHV (see Fig. 3F). (MVM: minute virus of mice; MNV: murine norovirus; GDVII: TMEV: Theiler’s encephalomyelitis virus; PV: parvovirus)

|       | MVM   | MNV   | TMEV  | PV    |
|-------|-------|-------|-------|-------|
| Young | 3/26  | 13/26 | 23/26 | 0/26  |
| Old   | 1/24  | 12/24 | 6/24  | 1/24  |
### Supplemental Table 6. Primers and probes for qRT-PCR

| Human Taqman probes | Mouse Taqman probes |
|---------------------|---------------------|
| **TBP** Hs00427620_m1 | **Cdkn1a** Mm04205640_g1 |
| **IL6** Hs00174131_m1 | **Cdkn2a** Mm00494449_m1 |
| **IL8** CXCL Hs00174103_m1 | **Gapdh** Mm99999915_g1 |
| **MCP-1** CCL2 Hs00234140_m1 | **Il1a** Mm00439620_m1 |
| **IFITM1** Hs00705137_s1 | **Il6** Mm00446190_m1 |
| **IFITM2** Hs00829485_sH | **Tnfa** Mm00443258_m1 |
| **IFITM3** Hs03057129_s1 |             |
| **ACE2** Hs1085330_m1 |             |
| **TMPRSS2** Hs01122322_m1 |             |
| **P16** Hs00923894_m1 |             |
| **P21** Hs00355782_m1 |             |
| **IL1a** Hs00174092_m1 |             |
| **IL1b** Hs01555410_m1 |             |
| **PAI1** Serpine1 Hs01126607_g1 |             |
| **IL10** Hs00961622_m1 |             |
| **PAI2** Serpine2 Hs00299953_m1 |             |
Mcp1 Mm00441242_m1

Mouse primers

Cdkn1a (p21Cip1)
Fwd 5’-GTCAGGCTGGTCTGCCTCCG-3’
Rev 5’-CGGTCCCGTGACGACGAGCAG-3’

Cdkn2a (p16Ink4a)
5’-CCCAACGCCCCGAACT-3’
Rev 5’-GCAGAAAGAGCTGCTACGTGAA-3’

Cxcl1
Fwd 5’-ACCCGCTCGCTTCTCTGT-3’
Rev 5’-AAGGGAGCTTCAAGGTCAAG-3’

Cxcl2
Fwd 5’-CCTGGTTTCAGAAAATCATCC-3’
Rev 5’-CTTCCGTTGGAGGATCAGC-3’

Cxcl10
Fwd 5’-GCCGTCATTTCTGGTTCAT-3’
Rev 5’-GCTTCCCTATGGCCCTTAT-3’

Gapdh
Fwd 5’-AAGGTCAATCCAGGGCTGAA-3’
Rev 5’-CTGCTTCACCACCTTCTTG-3’

Il1ß
Fwd 5’-CAGCGACGCACATCAACAAG-3’
Rev 5’-GTGCTCATGTCCACATCTTG-3’

Il2
Fwd 5’-CCTGAGCGAGGATGGAGAATTAC-3’
Rev 5’-TCCAGAAACATGCCGAGAAT-3’

Il6
Fwd 5’-CTGGAAATCCTGGGAAT-3’
Rev 5’-CCAGTTTGGTACATCCATC-3’
Il7
Fwd 5’-TCTGCTGCCTGTCACATCATC-3’
Rev 5’-GGACATTGAATTCTTCACTGATATTCA-3’

Il10
Fwd 5’-ATAAATGCACCCACTTCCCA-3’
Rev 5’-GGGCATCACTTCTACCAGGT-3’

Il17
Fwd 5’-TCTCCACCGCAATGAAGACC-3’
Rev 5’-CACACCCACCAGCATCTTCT-3’

Mcp1
Fwd 5’-GCATCCACGTGTTGGCTCA-3’
Rev 5’-CTCCAGCCTACTCATTTGGGATCA-3’

Mip1α
Fwd 5’-CCTTGCATTCTTCTCTGTACC-3’
Rev 5’-GCATTCAGTTCCAGGTCAGTGATG-3’

MHV
Fwd 5’-CAGATCCTTGAGATGCGTAG-3’
Rev 5’-AGAGTGTCCTATCCCGACTTTCT-3’

Pai1
Fwd 5’-GACACCTCAGCATGTTCATC-3’
Rev 5’-AGGGTTGCACTAAACATGTCAG-3’

Pai2
Fwd 5’-ACTTAAATGGGCTTTCTTCC-3’
Rev 5’-TGCGTCTCAATCTCATCG-3’

Tnfa
Fwd 5’-ATGAGAAGGTTCCAAATGGA-3’
Rev 5’-CTCCACTTGAGTGGTGCTA-3’