Supplemental Table 1A: Vaginal shedding of WT and TRAIL-R<sup>+</sup> mice following a primary intravaginal infection with various doses of *C. muridarum* IFU.

| Mouse type | IFU mice | Median number of *C. muridarum* IFU collected post infection days (d) (range) |
|------------|----------|--------------------------------------------------------------------------------|
|            |          | d4 | d7 | d11 | d15 | d18 | d21 | d28 | d35 | d42 |
| TRAIL-R<sup>+</sup> | 1x10<sup>5</sup> | 20 | 106,215<sup>a</sup> (15,392-3,57,006) | 176,540 (31,044-686,760) | 381,096<sup>b</sup> (28,388-1,355,166) | 182,368 (1,184-924,410) | 6,882 (<2) | 488 (<2-466,570) | <2 (<2-465,600) | <2 (<2-2,235) | <2 (<2-11,544) | <2 (<2-<2) |
| WT         | 1x10<sup>5</sup> | 26 | 237,606 (14,762-1,190,418) | 204,771 (52,246-1,307,560) | 1,038,780 (57,312-4,441,680) | 155,545 (222-2,160,190) | 8,577 (<2) | 377 (<2-372,480) | 377 (<2-2,91,000) | <2 (<2-14) | <2 (<2-3,108) | <2 (<2-<2) |
| TRAIL-R<sup>+</sup> | 1x10<sup>4</sup> | 20 | 165,369<sup>b</sup> (<2-464,466) | 73,431<sup>b</sup> (<2-407,154) | 171,339<sup>a</sup> (<2-808,338) | 59,103<sup>b</sup> (<2-776,100) | 692 (<2) | 355 (<2-65,232) | 355 (<2-8,140) | <2 (<2-866) | <2 (<2-2,738) | <2 (<2-<2) |
| WT         | 1x10<sup>4</sup> | 20 | 256,113 (<2-736,698) | 161,190 (<2-592,224) | 450,735 (<2-1,432,800) | 32,163 (<2-146,862) | 1,887 (<2-106,266) | 152 (<2-2,91,000) | <2 (<2-117,012) | <2 (<2-148) | <2 (<2-<2) |
| TRAIL-R<sup>+</sup> | 1x10<sup>3</sup> | 19 | 14,496 (<2-213,726) | 82,386 (<2-705,654) | 111,042 (<2-441,780) | 59,700 (<2-512,226) | 947 (<2) | 614 (<2-296,112) | 614 (<2-139,698) | <2 (<2-139,698) | <2 (<2-151,638) | <2 (<2-151,638) |
| WT         | 1x10<sup>3</sup> | 20 | 48,357 (<2-943,260) | 201,189 (<2-1,322,952) | 223,278 (<2-1,307,430) | 38,807 (<2-132,534) | 3515 (<2-2,770,080) | 344 (<2-146,862) | <2 (<2-132,534) | <2 (<2-437) | <2 (<2-<2) |
| TRAIL-R<sup>+</sup> | 1x10<sup>2</sup> | 22 | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) | <2 (<2-<2) |
| WT         | 1x10<sup>2</sup> | 22 | <2 (<2-290142) | <2-290142 (<2-219,696) | <2-1361160 (<2-171,936) | <2-54924 (<2-25972) | <2-25972 (<2-6142) | <2-6142 (<2-<2) | <2-6142 (<2-<2) |

<sup>a</sup>P<0.05 by the Mann-Whitney U test compared to the WT mice receiving the same number of *C. muridarum* IFU.

<sup>b</sup>P<0.1 by the Mann-Whitney U test compared to the WT mice receiving the same number of *C. muridarum* IFU.
## Supplemental Table 1B: Vaginal culture and hydrosalpinx formation of WT and TRAIL-R<sup>−/−</sup> mice following a primary intravaginal infection with various doses of C. muridarum IFU.

| Mouse type | #IFU/mouse | Mice with positive cultures/total (%) | Median no. days to negative culture (range) | No. of positive cultures/total (%) | #IFU shed/mouse median (range) | # mice with hydrosalpinx (%) |
|------------|-------------|----------------------------------------|--------------------------------------------|-----------------------------------|-------------------------------|-----------------------------|
| TRAIL-R<sup>−/−</sup> | 1x10<sup>5</sup> | 20/20 (100) | 35 (21-42)<sup>a</sup> | 121/180 (67) | 1,076,484 (308,126-2,666,330)<sup>a</sup> | 15/20 (75) |
| WT | 1x10<sup>5</sup> | 26/26 (100) | 27 (18-42) | 144/220 (65) | 2,005,278 (331,864-5,904,896) | 18/26 (69) |
| TRAIL-R<sup>−/−</sup> | 1x10<sup>4</sup> | 19/20 (95) | 27 (21-42)<sup>a</sup> | 120/180 (67) | 541,581 (<2-2,008,018)<sup>a</sup> | 18/20 (90) |
| WT | 1x10<sup>4</sup> | 19/20 (95) | 27 (4-35) | 108/180 (60) | 1,223,424 (<2-2,071,590) | 14/20 (70) |
| TRAIL-R<sup>−/−</sup> | 1x10<sup>3</sup> | 15/19 (79) | 27 (4-42) | 101/171 (59) | 478,024 (<2-2,014,416)<sup>b</sup> | 8/19 (42)<sup>d</sup> |
| WT | 1x10<sup>3</sup> | 16/20 (80) | 27 (4-42) | 104/180 (58) | 957,606 (<2-2,963,142) | 15/20 (75) |
| TRAIL-R<sup>−/−</sup> | 1x10<sup>2</sup> | 0/22 (0) | 4 (4-42) | 2/198 (1)<sup>c</sup> | <2 (<2-2) | 0/22 (0) |
| WT | 1x10<sup>2</sup> | 3/22 (14) | 4 (4-35) | 27/198 (14) | <2 (<2-1,522,930) | 2/22 (9) |

<sup>a</sup>P<0.05 by the Mann-Whitney U test compared to the WT mice receiving the same number of C. muridarum IFU.

<sup>b</sup>P<0.1 by the Mann-Whitney U test compared to the WT mice receiving the same number of C. muridarum IFU.

<sup>c</sup>P<0.05 by the Fisher's Exact test compared to the WT mice receiving the same number of C. muridarum IFU.

<sup>d</sup>P<0.1 by the Fisher's Exact test compared to the WT mice receiving the same number of C. muridarum IFU.
### Supplemental Table 2A: Vaginal shedding of WT and TRAIL-R<sup>+</sup> mice following a primary and a secondary intravaginal infection with *C. muridarum* IFU.

| Mouse type | Infection   | Median # *C. muridarum* IFU shed from vagina post infection days (range) |
|------------|-------------|--------------------------------------------------------------------------|
|            |             | d4  | d7  | d11 | d15 | d18 | d21 | d28 | d35 | d42 |
| TRAIL-R<sup>+</sup> | Primary     | <2  | <2  | <2  | <2  | <2  | <2  | <2  | <2  | <2  |
|            |             | (<2-118,206) | (<2-248,352) | (<2-331,932) | (<2-101,490) | (<2-410,736) | (<2-152,832) | (<2-161,190) | (<2-<2) | (<2-<2) |
| WT        | Primary     | <2  | <2  | <2  | <2  | <2  | <2  | <2  | <2  | <2  |
|            |             | (<2-643,566) | (<2-199,398) | (<2-442,974) | (<2-463,272) | (<2-319,992) | (<2-403,572) | (<2-2,220) | (<2-<2) | (<2-<2) |
| TRAIL-R<sup>+</sup> | Secondary  | <2a | <2a | <2a | <2a | <2a | <2a | <2  | <2  | <2  |
|            |             | (<2-2,778) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) |
| WT        | Secondary   | <2a | <2a | <2a | <2a | <2a | <2a | <2  | <2  | <2  |
|            |             | (<2-866) | (<2-2,295) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) | (<2-<2) |

<sup>a</sup>P<0.05 by the Mann-Whitney U test compared to the primary infection of the same type of mice.
### Supplemental Table 2B: Vaginal shedding and hydrosalpinx formation of WT and TRAIL-R<sup>+</sup> mice following a primary (2×10<sup>5</sup>) and a secondary (10<sup>3</sup> IFU) intravaginal inoculation with *C. muridarum*.

| Mouse type  | Infection  | Mice with positive cultures/total (%<sup>+</sup>) | Median no. days to negative culture (range) | No. of positive cultures/total (%<sup>+</sup>) | IFU shed/mouse median (range) | # mice with hydrosalpinx (%<sup>+</sup>) |
|------------|------------|-------------------------------------------------|---------------------------------------------|---------------------------------------------|-------------------------------|-----------------------------------|
| TRAIL-R<sup>+</sup> | Primary | 13/20 (65) | 25 (4-36) | 56/180 (31.1) | 12 (<2-759,687) | ND |
| WT         | Primary  | 9/20 (45)  | 4 (4-36)  | 49/180 (27.2) | <2 (<2-1,792,544) | ND |
| TRAIL-R<sup>-</sup> | Secondary | 2/20 (10)<sup>a</sup> | 4 (4-11)<sup>b</sup> | 3/180 (1.7)<sup>a</sup> | <2 (<2-2,818)<sup>b</sup> | 7/20 (35) |
| WT         | Secondary | 1/20 (5)<sup>a</sup> | 4 (4-11)<sup>b</sup> | 2/180 (1.1)<sup>a</sup> | <2 (<2-3,161)<sup>b</sup> | 5/20 (25) |

ND= Not done as the same mice were reinfected vaginally.

<sup>a</sup> P < 0.05 by the Fisher’s Exact test compared to the primary infection of the same type of mice.

<sup>b</sup> P < 0.05 by the Mann-Whitney U test compared to the primary infection of the same type of mice.
Supplemental Table 3: Serum antibody titers to *C. muridarum* EB 42 days following a primary vaginal infection.

| Mouse strain | Inoculation dose (Cm IFU/mouse) | Geometric mean titer (range) | IgG2c/IgG1 |
|--------------|----------------------------------|-----------------------------|------------|
|              |                                  | IgG                        | IgG1       | IgG2c    |                     |
| TRAIL-R^−/−  | 10⁵                              | 40,637 (25,600-51,200)      | 200 (100-800) | 12,800 (6,400-25,600) | 64       |
| WT           | 10⁶                              | 32,254 (25,600-51,200)      | 400 (100-1,600) | 8,063 (6,400-12,800) | 20       |
| TRAIL-R^−/−  | 10⁴                              | 51,200 (51,200-51,200)      | 159 (100-200) | 12,800 (12,800-12,800) | 81       |
| WT           | 10⁴                              | 51,200 (25,600-102,400)     | 126 (100-200) | 10,159 (3,200-25,600) | 81       |
| TRAIL-R^−/−  | 10³                              | 25,600 (25,600-25,600)      | 283 (100-800) | 8,063 (6,400-12,800) | 28       |
| WT           | 10³                              | 40,637 (25,600-51,200)      | 141 (100-200) | 12,800 (12,800-12,800) | 91       |
| TRAIL-R^−/−  | 10²                              | 112 (100-200)^a             | <100^a      | <100^a   | -         |
| WT           | 10²                              | 3,592 (100-25,600)          | 238 (<100-400) | 3,676 (200-12,800) | 15       |
| TRAIL-R^−/−  | 0                                | <100                       | <100        | <100     | -         |
| WT           | 0                                | <100                       | <100        | <100     | -         |

^a P < 0.05 by the Mann-Whitney U test compared to the WT mice.
Supplemental Table 4: Serum antibody titers to *C. muridarum* EB following primary and secondary vaginal infections.

| Mouse strain | Inoculation dose (Cm IFU/mouse) | Days p.i. | Geometric mean titer (range) | IgG2c/IgG1 |
|--------------|---------------------------------|-----------|-----------------------------|------------|
| TRAIL-R<sup>-/-</sup> | 1<sup>°</sup> infection 2x10<sup>2</sup> | 63 | 12,800 (12,800-12,800) | 18,102 (12,800-25,600) | 23 |
| WT | 1<sup>°</sup> infection 2x10<sup>2</sup> | 63 | 25,600 (25,600-25,600) | 12,800 (12,800-12,800) | 16 |
| TRAIL-R<sup>-/-</sup> | 2<sup>°</sup> infection 1x10<sup>3</sup> | 122 | 12,800 (12,800-12,800) | 25,600 (25,600-25,600) | 16 |
| WT | 2<sup>°</sup> infection 1x10<sup>3</sup> | 122 | 36,204 (25,600-51,200) | 18,102 (12,800-25,600) | 23 |
**Supplemental Table 5: Vaginal antibody titers to *C. muridarum* EB following primary and secondary vaginal infections.**

| Mouse strain | Inoculation dose (Cm IFU/mouse) | Days p.i. | Vaginal wash titer | IgG | IgA |
|--------------|---------------------------------|-----------|--------------------|-----|-----|
| TRAIL-R⁻/⁻   | 1° infection $2 \times 10^2$     | 63        |                    | 160 | 160 |
| WT           | 1° infection $2 \times 10^2$     | 63        |                    | 320 | 320 |
| TRAIL-R⁻/⁻   | 2° infection $10^3$             | 122       |                    | 320 | 320 |
| WT           | 2° infection $10^3$             | 122       |                    | 160 | 320 |
Supplemental Table 6: Disease burden and yields of *C. muridarum* IFU following a primary i.n. infection of WT and TRAIL-R−/− mice.

| Mouse strain | Cm #IFU | % Body weight change mean±SE | Lung weight (g) mean±SD | # of *C. muridarum* IFU in the lungs Median min max |
|--------------|---------|------------------------------|-------------------------|---------------------------------------------------|
| TRAIL-R−/−   | 10^5    | -29.0±0.6                    | 0.62±0.06               | 5,696,825,000 423,325,000 11,918,500,000          |
| WT           | 10^5    | -28.5±1.5                    | 0.46±1.0                | 7,990,000,000 5369 21,165,000,000                  |
| TRAIL-R−/−   | 10^4    | -18.4±1.6                   | 0.45±0.07              | 4,162,500,000 8,510,000 21,624,500,000            |
| WT           | 10^4    | -13.3±2.0                    | 0.38±0.08               | 2,250,850,000 8,325,000 7,310,100,000             |
| TRAIL-R−/−   | 10^2    | 1.8±1.0                     | 0.23±0.03              | 187,550 41,745 10,285,000                          |
| WT           | 10^2    | 2.7±0.7                     | 0.20±0.01              | 91,355 250 1,712,150                               |

\( ^a \) P<0.05 by the Student’s *t* test compared to the WT mice receiving the same number of *C. muridarum* IFU.

\( ^b \) P<0.1 by the Student’s *t* test compared to the WT mice receiving the same number of *C. muridarum* IFU.

\( ^c \) P<0.1 by the Mann-Whitney U test compared to the WT mice receiving the same number of *C. muridarum* IFU.
Supplemental Table 7: Disease burden and yields of *C. muridarum* IFU of WT and TRAIL-R⁻/⁻ mice following a secondary (10⁴ IFU) i.n. infection.

| Mouse strain | Infection | % Body weight change Mean ± SE | Lung weight Mean ± SD | # of *C. muridarum* IFU recovered |
|--------------|-----------|-------------------------------|----------------------|---------------------------------|
| TRAIL-R⁻/⁻   | Secondary | -1.0±0.5                      | 0.31±0.04            | <50                             |
| WT           | Secondary | 0.4±0.4                       | 0.31±0.02            | <50                             |