Figure S1. Additional hematoxylin- and eosin-stained histopathology images of the C57BL/6 granulomatous response. A. Lungs from a C57BL/6 mouse inoculated with $1 \times 10^6$ WT cells harvested at 7 DPI demonstrated a moderate peribronchiolar neutrophilic and mononuclear inflammatory reaction with vague, early, and poorly formed granulomatous region formation (10X). B. Lungs from a C57BL/6 mouse inoculated with $1 \times 10^6$ WT cells harvested at 14 DPI demonstrated moderate peribronchiolar nodular inflammatory aggregates accompanying a high organism burden (10X). C. A higher power image of (B) showed giant cells present without more discrete granuloma formation (20X). D. Lungs from a C57BL/6 mouse inoculated with $1 \times 10^6 mar1\Delta$ mutant cells harvested at 40 DPI showed a relatively well-circumscribed nodule containing well developed organizing lymphohistiocytic inflammation (4X). E. A medium power image of (D) highlighted compact histiocytic aggregates and peripheral mononuclear cells, characteristic of granuloma formation (10X). F. A higher power image of (E) further highlighted compact histiocytic aggregates and peripheral mononuclear cells, characteristic of granuloma formation (20X). DPI = days post-inoculation.
Figure S2. Movat-stained histopathology images of the C57BL/6 granulomatous response. A. Lungs from a C57BL/6 mouse inoculated with $1 \times 10^5$ mar1Δ mutant cells harvested at 28 DPI demonstrated leukocyte recruitment (dark red), fibrotic tissue formation (light red), and fungal cell (blue) containment within the borders of the granulomatous region (10X). B. A higher power image of (A) (20X). DPI = days post-inoculation.
Figure S3. Recovery of mar1Δ mutant cells from murine lungs at extended timepoints in infection. Lungs from female C57BL/6 mice infected with 1 x 10^5 mar1Δ mutant cells were harvested at 61 and 100 DPI. Single fungal colonies were isolated on YPD agar plates and subsequently incubated in various conditions that allowed for identification of mar1Δ mutant isolates: YPD medium at 30°C, YPD medium at 37°C, YPD medium + nourseothricin (NAT), and YPD medium pH 8.15. The original WT strain (A1) and mar1Δ mutant strain (A2) are included as controls in each condition. DPI = days post-inoculation.
Figure S4. Additional histopathology images of the Csf2rb-/- granulomatous response. A. Lungs from a Csf2rb-/- mouse inoculated with $1 \times 10^5$ WT cells harvested at 7 DPI showed a marked peribronchiolar neutrophilic and mononuclear inflammatory reaction without granulomatous region formation (10X). B. Lungs from a Csf2rb-/- mouse inoculated with $1 \times 10^5$ WT cells harvested at 14 DPI demonstrated an absence of a significant inflammatory reaction (4X). All images are of hematoxylin- and eosin-stained tissue sections. DPI = days post-inoculation.
Figure S5. Murine infections with 1 x 10⁶ CFU inoculum. A-D. Lungs from C57BL/6 mice inoculated with 1 x 10⁶ WT cells harvested at 14 DPI demonstrated moderate inflammatory aggregates accompanying a high organism burden. Low power images (A & C) (4X) and medium power images (B & D) (10X) are included. E-H. Lungs from C57BL/6 mice inoculated with 1 x 10⁶ mar1/2 mutant cells harvested at 21 DPI showed relatively well-circumscribed inflammatory nodules containing well developed organizing lymphohistiocytic inflammation. Low power images (E & G) (4X) and medium power images (F & H) (10X) are included. I. Female C57BL/6 mice (n = 10) were inoculated with 1 x 10⁶ CFU of the WT strain or the mar1/2 mutant strain. Mice were monitored daily for 60 days and sacrificed at predetermined clinical endpoints predictive of mortality. Statistical significance was determined by log-rank test with Bonferroni correction (***, P < 0.0001). DPI = days post-inoculation.
Figure S6. Complete pulmonary cytokine profile throughout infection. Pulmonary cytokine responses of female C57BL/6 mice inoculated with $1 \times 10^4$ cells of the WT strain or the $mar1\Delta$ mutant strain were measured using the Bio-Plex protein array system throughout infection: 1 ($n = 15$), 3 ($n = 15$), 7 ($n = 10$), 14 ($n = 10$), and 21 ($n = 10$) DPI. Error bars represent SEM. Statistical significance between strains at each timepoint was determined using two-way ANOVA (*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$; ns, not significant). DPI = days post-inoculation.
Figure S7. Complete pulmonary leukocyte infiltrate response throughout infection. Pulmonary leukocyte infiltrates of female C57BL/6 mice inoculated with 1 x 10^4 cells of the WT strain or the mar1Δ mutant strain were measured by flow cytometry throughout infection: 1, 3, 7, 14, and 21 DPI. Data shown are the mean ± of absolute cell numbers from three independent experiments (n = 3) performed using five mice per group per timepoint per experiment. Error bars represent the SEM. Statistical significance between strains at each timepoint was determined using two-way ANOVA (*, P < 0.05; **, P < 0.01; ***, P < 0.001; ns, not significant). DPI = days post-inoculation.
Figure S8. Granulomatous response timeline. Chronological summary of important observations about granulomatous region formation and maintenance in the WT strain (top) and mar1Δ mutant strain (bottom) backgrounds. Cartoons adapted from BioRender.com (2021). DPI = days post-inoculation.