

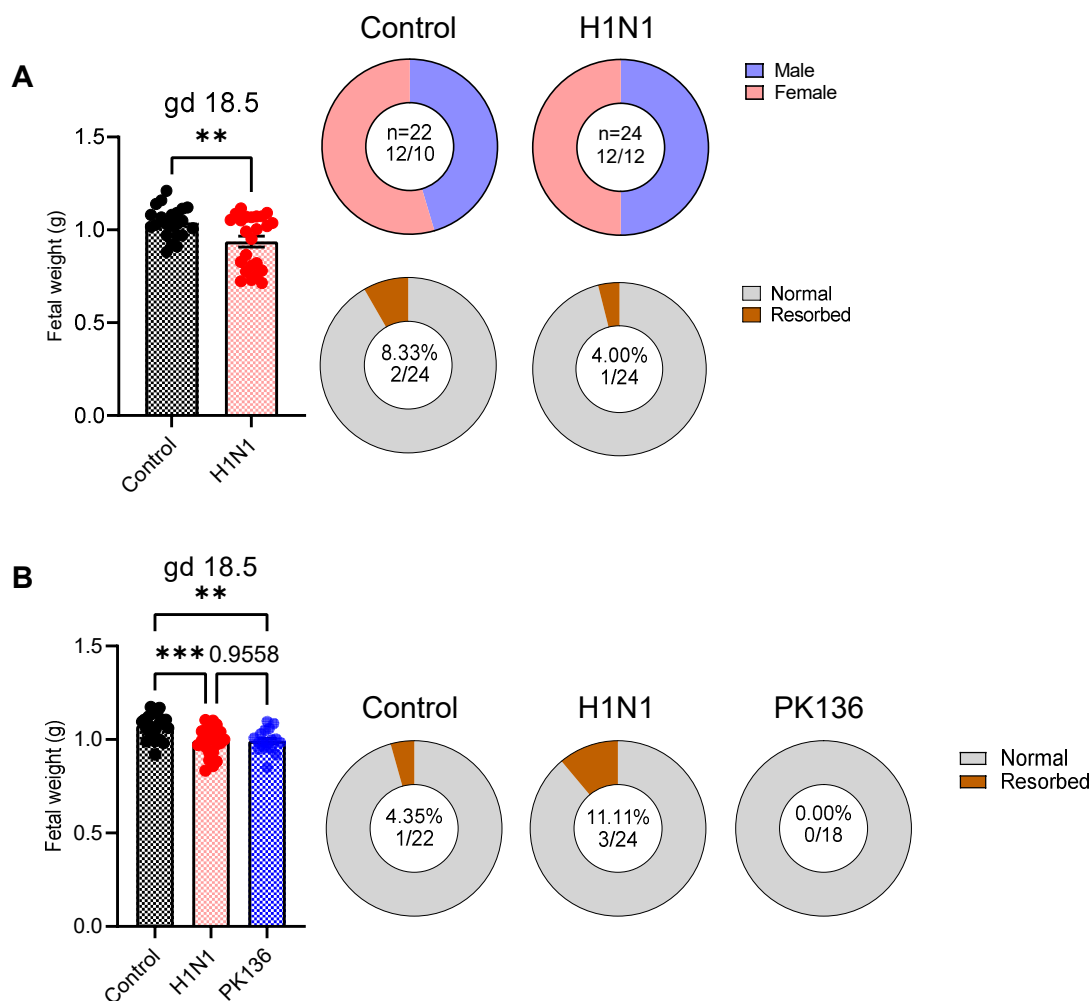


Figure S1. Maternal H1N1 infection induces fetal growth restriction without increasing fetal loss or altering fetal sex ratio.

(A) Fetal weight, fetal resorption rate, and fetal sex ratio at gd 18.5 in control and H1N1-infected dams. Maternal H1N1 infection reduced fetal weight but did not increase fetal resorption rate or alter fetal sex ratio. Fetal numbers per litter were as follows: Control, 8, 7, and 7 fetuses; H1N1, 9, 7, and 8 fetuses.

(B) Fetal weight and fetal resorption rate at gd 18.5 in control, H1N1-infected, and PK136-treated H1N1-infected dams. H1N1 infection reduced fetal weight compared with control, and PK136 treatment did not restore fetal weight. Resorption rates were not markedly different among groups. Fetal numbers per litter were as follows: Control, 8, 7, and 7 fetuses; H1N1, 8, 7, and 10 fetuses; PK136, 4, 7, and 7 fetuses. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.

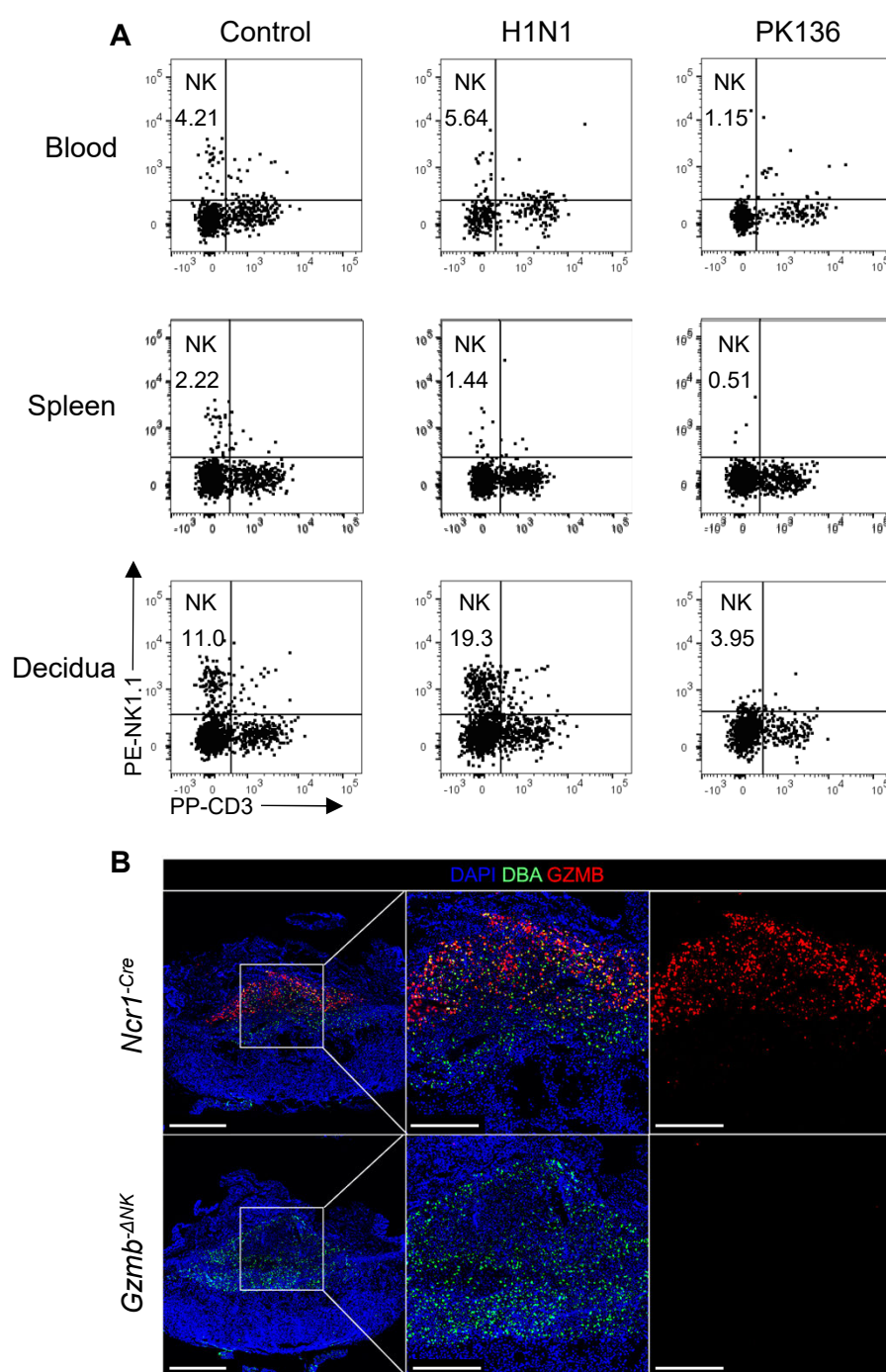


Figure S2. Efficient validation of maternal NK cell *Gzmb* deletion and antibody-mediated NK cell depletion.

(A) Flow cytometric validation of NK-cell depletion after anti-NK1.1 antibody (PK136) treatment. Pregnant dams received a single intraperitoneal injection of 500 μg PK136 at E10.5, and NK-cell frequencies in peripheral blood, spleen, and decidua were analyzed at E13.5.

(B) Immunofluorescence of decidual sections from *Ncr1-Cre* and *Gzmb^{-ΔNK}* mice at E13.5, stained for DBA (dNK marker) and GZMB (scale bars: 1000 μm; inset: 500 μm).

Maternal lung

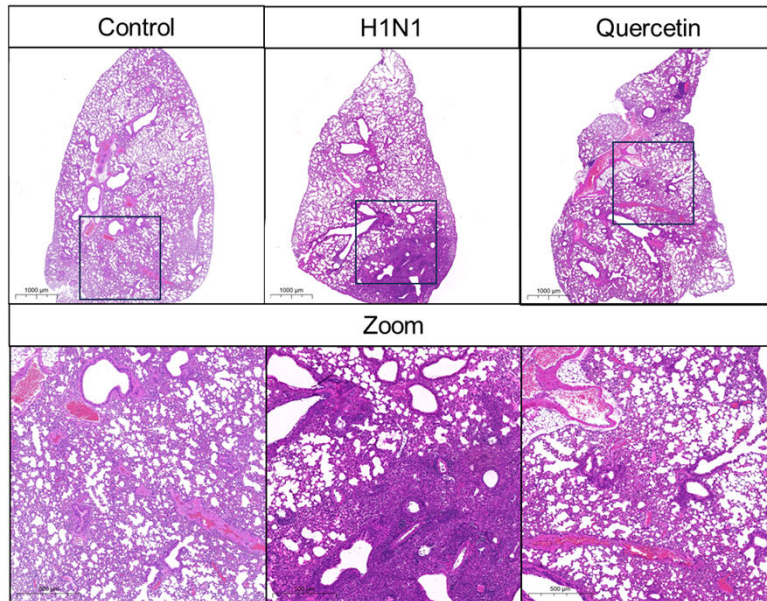
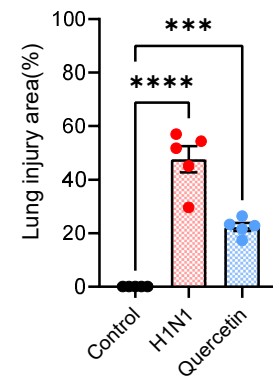


Figure S3. Effects of quercetin on maternal lung pathology following H1N1 infection.

H&E staining of lung sections from pregnant mice post-H1N1 infection with or without quercetin treatment. Scale bars: 1000 μm ; 500 μm (inset). Group sizes: control ($n = 5$), H1N1 ($n = 5$), quercetin ($n = 5$).

Statistical analysis via one-way ANOVA with Tukey's post hoc. Data are mean $\pm$ SEM. $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, $****P < 0.0001$.

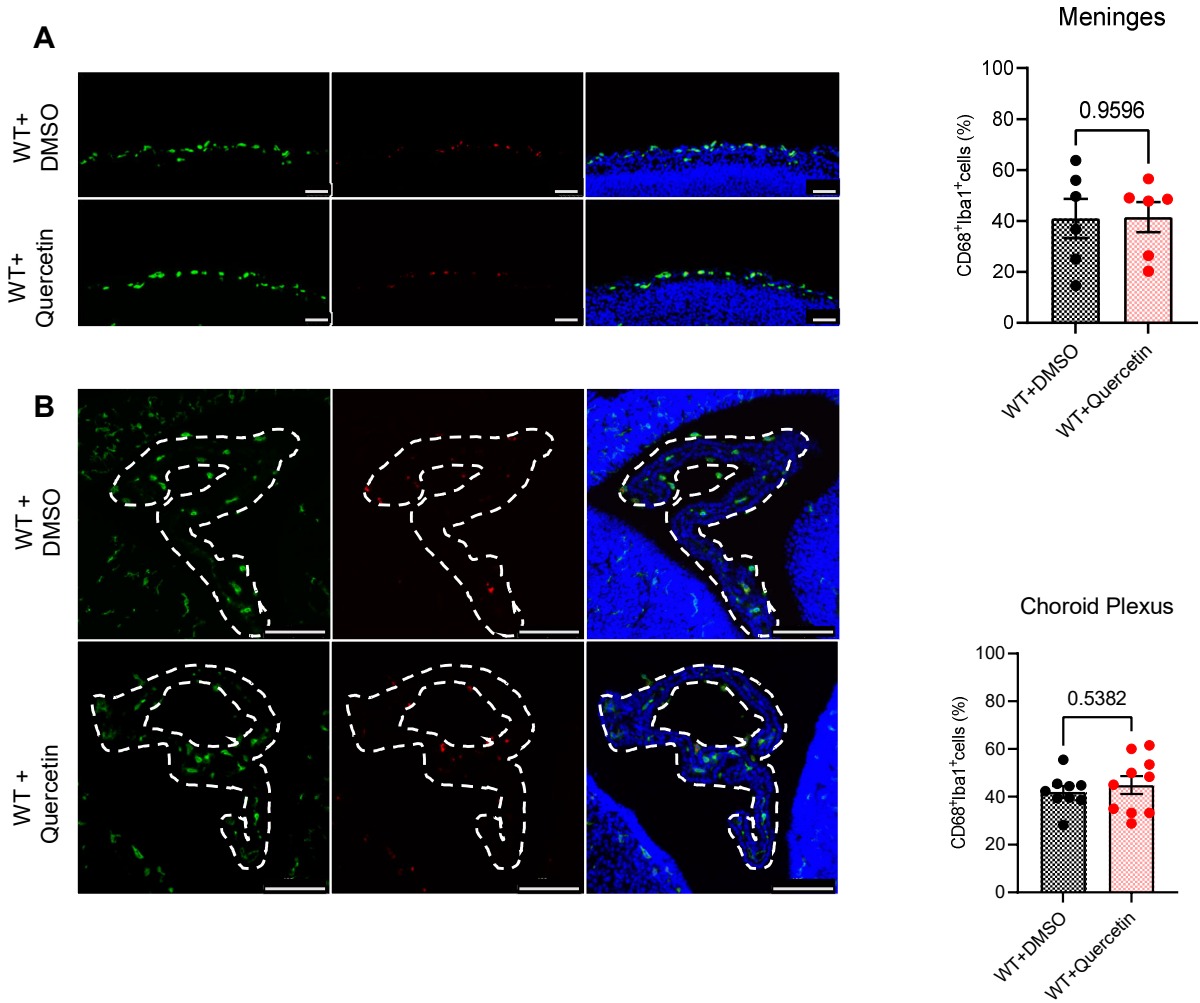


Figure S4. Quercetin alone does not alter baseline fetal brain Iba1⁺CD68⁺ macrophage proportions.

(A-B) Immunofluorescence and quantification of meningeal macrophages from non-infected WT dams treated with DMSO or quercetin (A; scale bar: 50 μ m; WT + DMSO: n = 6, WT + Quercetin : n = 6), and choroid plexus macrophages (B; scale bar: 100 μ m; Vehicle: n = 9, Quercetin: n = 10). Statistical analysis was performed using an unpaired two-tailed Student's t-test. Data are shown as mean $\pm$ SEM. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001.

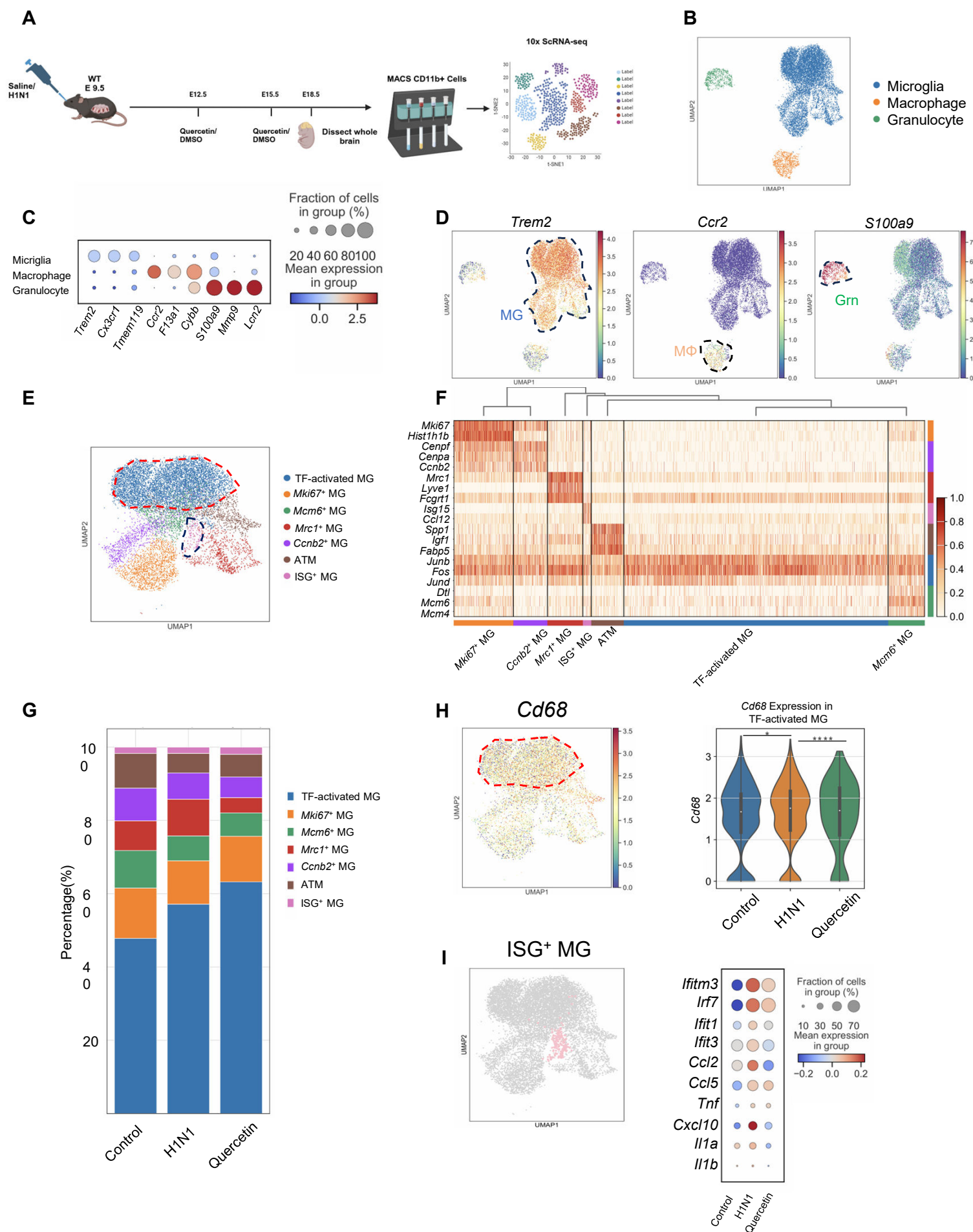


Figure S5. Quercetin reverses fetal brain microglial inflammation induced by maternal H1N1 infection.

(A) Schematic of single-cell isolation from E18.5 male fetal brains of control, H1N1, and quercetin-treated dams (300 µg/dose, i.g. at E12.5 and E15.5) for scRNA-seq.

(B-D) CD11b⁺ cell subclustering revealed three subtypes: color-coded UMAP (B), subtype-defining marker genes in DotPlot (C), and UMAP visualization (D).

(E-G) Further subclustering of microglia identified seven subtypes: UMAP with color-coded clusters (E), subtype-specific marker genes in heatmap (F), and distribution of microglial subtypes across groups (G). MG:microglia; TF: transcription factors; ATM: axon tract-associated microglia.

(H) UMAP plot and violin plots show Cd68 expression and activation in TF-activated microglia across groups.

(I) UMAP and dot plots showing ISG⁺ microglia and expression of ISGs across control, H1N1, and quercetin groups.

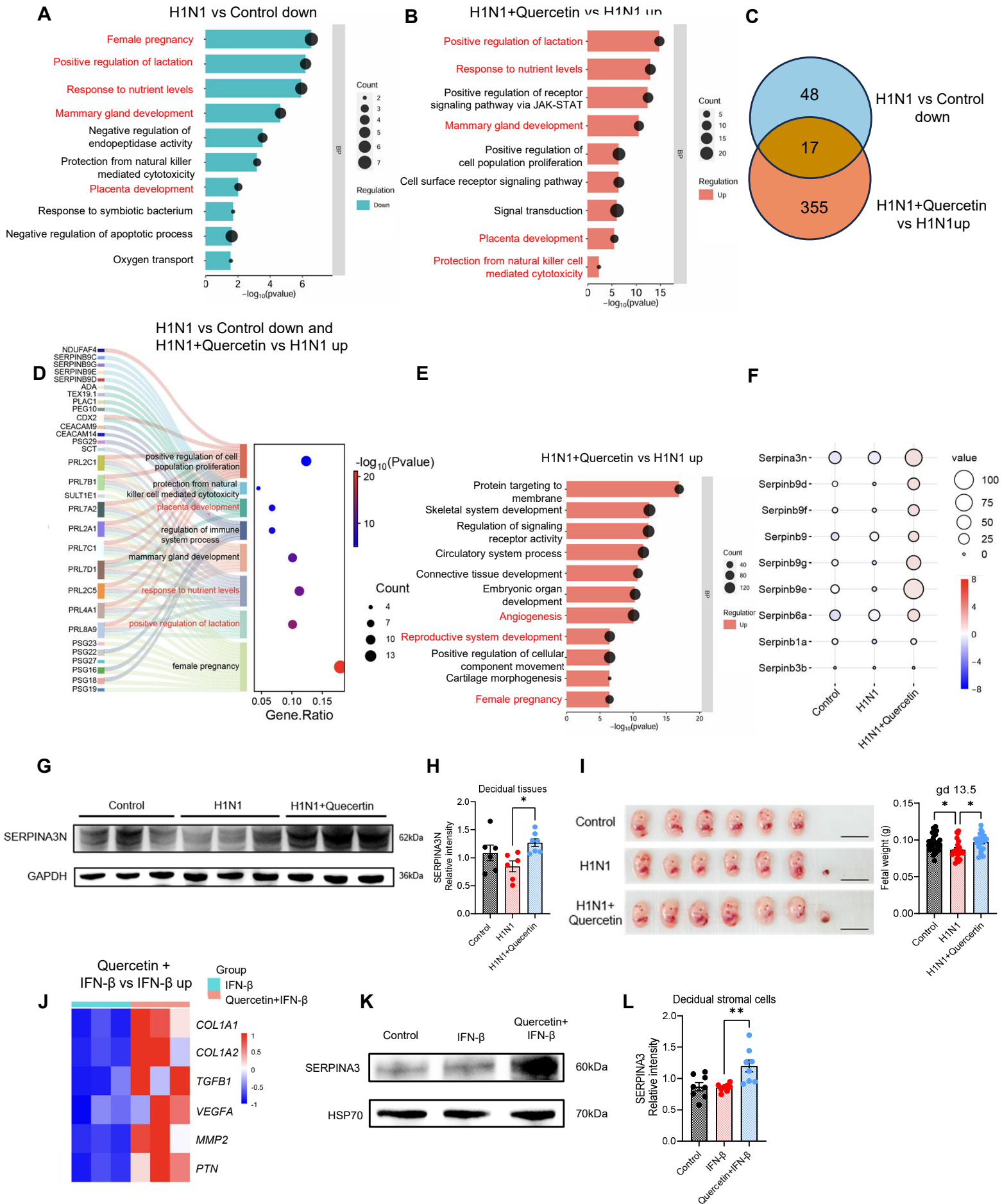


Figure S6. Quercetin restores decidual homeostasis and promotes protective programs following maternal H1N1 infection.

(A–I) Mouse in vivo analyses of decidual transcriptional programs, SERPINA3N expression, and fetal growth following maternal H1N1 infection and quercetin treatment. (J–L) Human in vitro validation of quercetin-induced pregnancy-supportive and SERPINA3-associated responses in decidual cells.

(A–D) Enriched pathways associated with genes downregulated by H1N1 (A) and those upregulated by quercetin treatment (B). Venn diagram showing overlapping genes downregulated by H1N1 and restored by quercetin (C). Sankey and dot plots display corresponding DEGs and their GO term enrichment (D).

(E) Pathway enrichment analysis showing quercetin-induced upregulation of genes associated with angiogenesis and reproductive system development in mouse decidual NK cells.

(F) Bubble plot showing FPKM-based expression of Serpin family genes in mouse decidual tissues.

(G) In vivo Western blot analysis of SERPINA3N protein expression in mouse decidual tissues from control, H1N1-infected, and H1N1 + quercetin-treated pregnant dams (Control: n = 6; H1N1: n = 6; H1N1 + Quercetin: n = 7). Uncropped blots are provided in the Supplementary Files.

(H) Quantification of SERPINA3N protein expression in mouse decidual tissues, normalized to GAPDH.

(I) Fetal growth analysis. Measurement of body weight of E13.5 embryos (Control (Saline + DMSO), n = 27; H1N1 (H1N1 + DMSO), n = 22; Quercetin (H1N1 + Quercetin), n = 22).

(J) Expression analysis of pregnancy-supportive factors, including *VEGFA* and *PTN*, in human decidual NK cells following quercetin treatment.

(K) In vitro Western blot analysis of SERPINA3 protein expression in human decidual stromal cells treated with IFN- β in the presence or absence of quercetin (Control: n = 8; IFN- β : n = 8; IFN- β + Quercetin: n = 8). Uncropped blots are provided in the Supplementary Files.

(L) Quantification of SERPINA3 protein expression in human decidual stromal cells, normalized to HSP70.

(H, I and L) One-way ANOVA with Tukey's post hoc. Results shown as mean $\pm$ SEM. * P < 0.05, ** P < 0.01, *** P < 0.001, **** P < 0.0001.

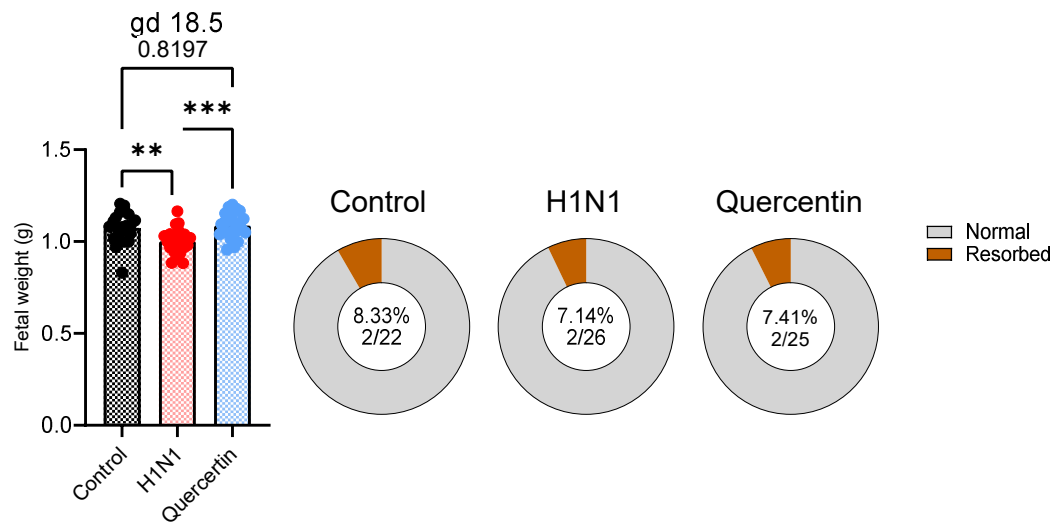


Figure S7. Quercetin ameliorates H1N1-induced fetal growth restriction without increasing fetal resorption.

Fetal weight and fetal resorption rate at gd 18.5 in control, H1N1-infected, and quercetin-treated H1N1-infected dams. Quercetin treatment ameliorated H1N1-induced fetal growth restriction, whereas resorption rates were not markedly different among groups. Fetal numbers per litter were as follows: Control, 8, 6, and 8 fetuses; H1N1, 9, 7, and 10 fetuses; Quercetin, 9, 9, and 7 fetuses.

Data are shown as mean $\pm$ SEM. Statistical analysis in (A) was performed using an unpaired two-tailed Student's t-test. Statistical analyses in (B) and (C) were performed using one-way ANOVA followed by Tukey's post hoc test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$.