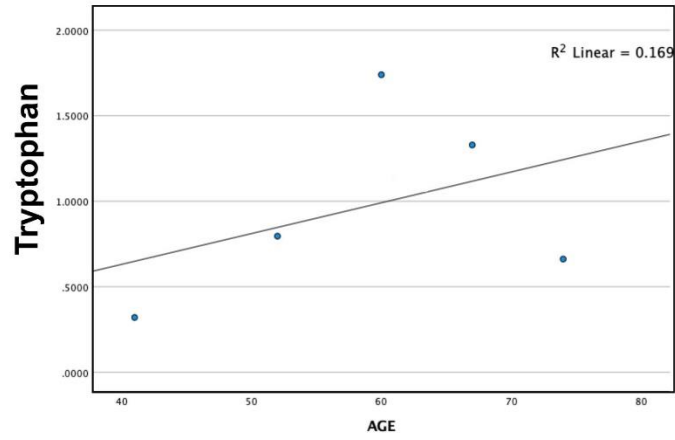
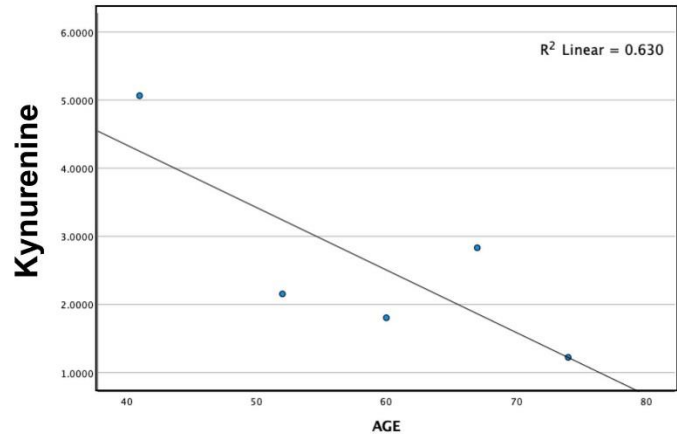
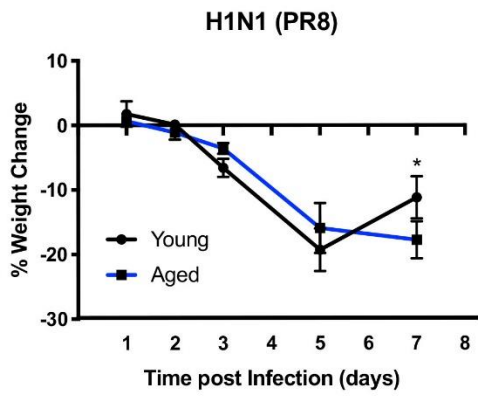
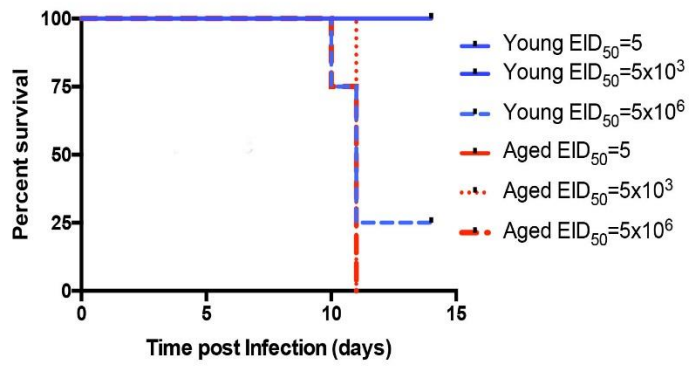
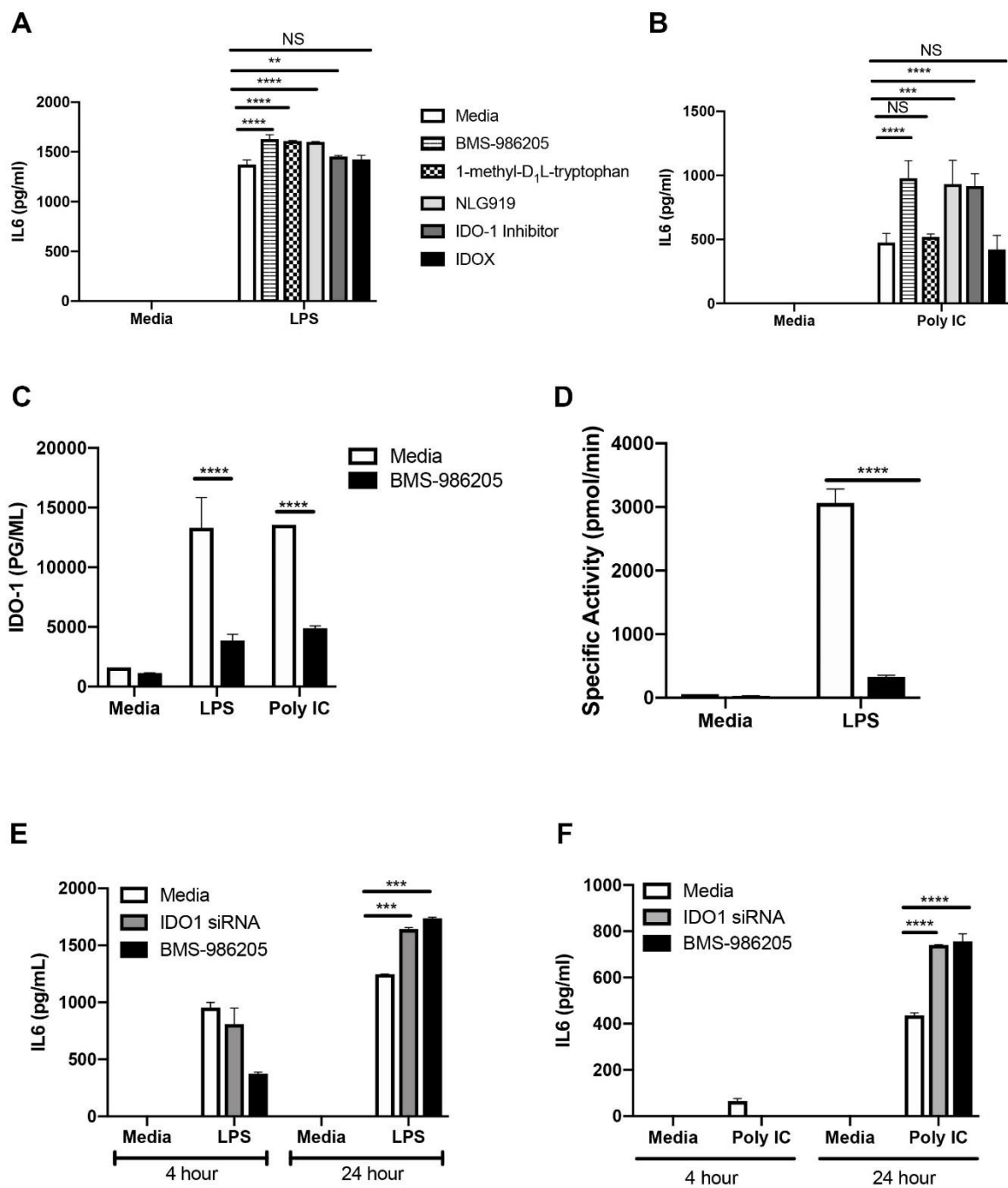


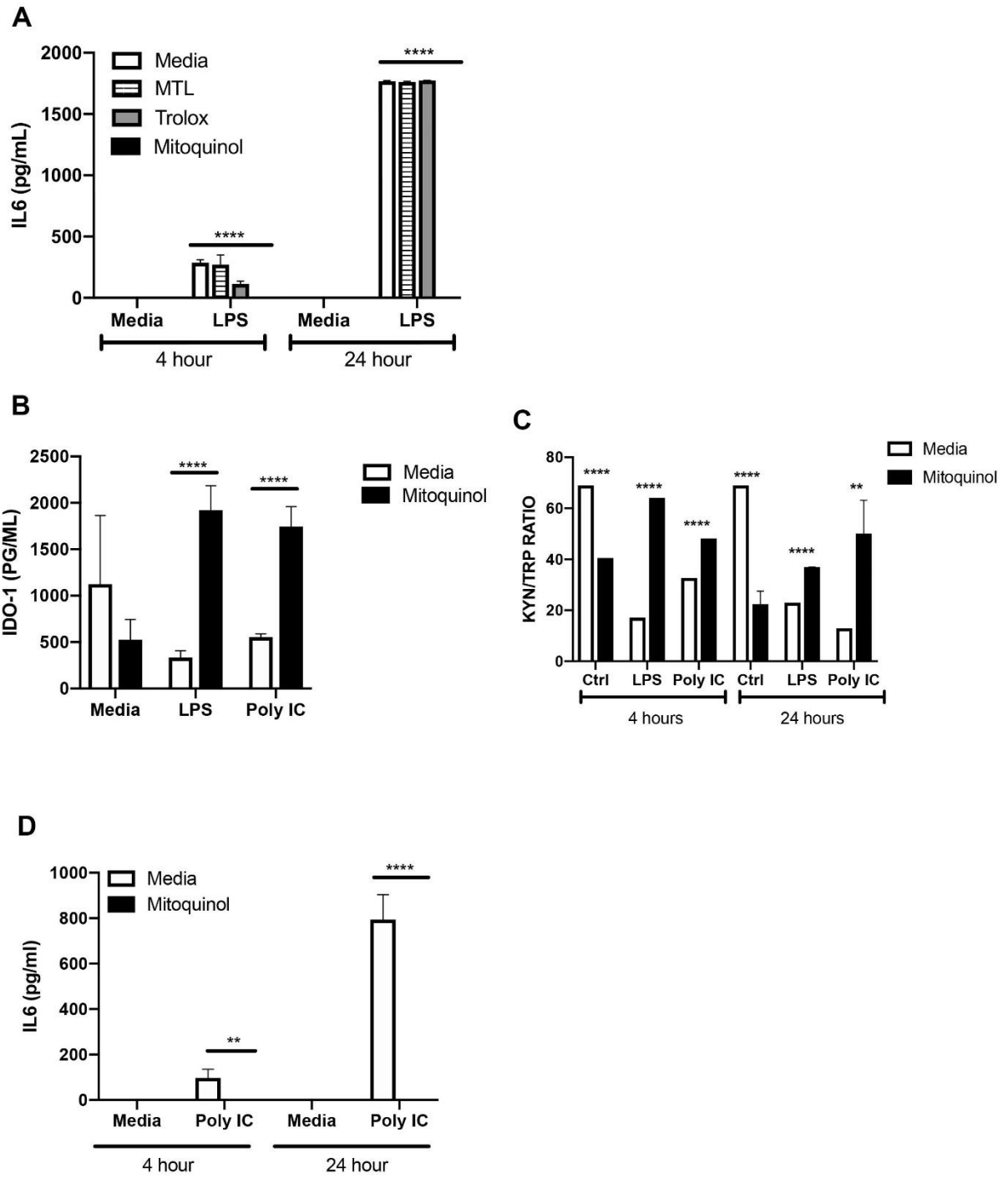
**A****B****C****Supplemental Figure 1**

**Supplemental Figure S1 (related to Figure 2):** (A) Correlation of kynurenine and tryptophan levels in severe influenza patients by age. (B) Weight change and (C) survival during influenza infection.



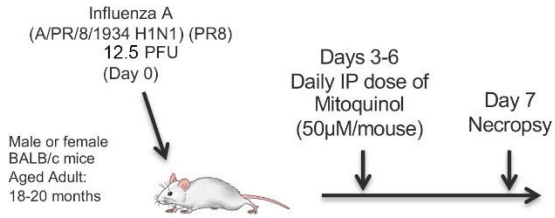
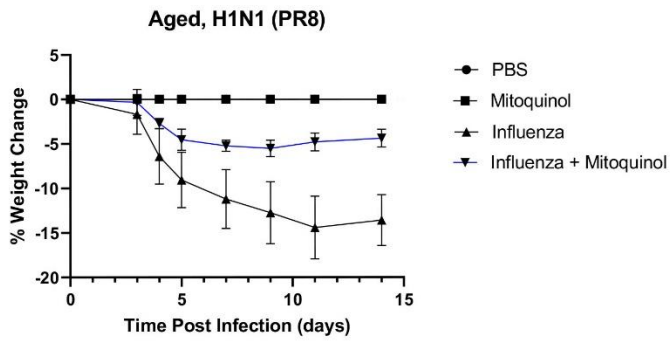
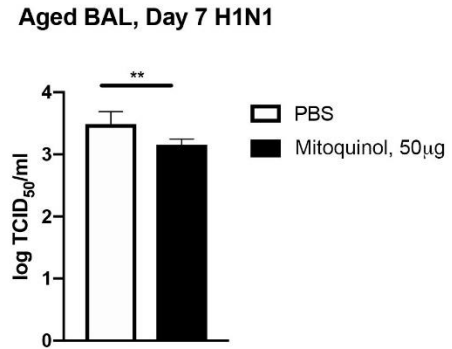
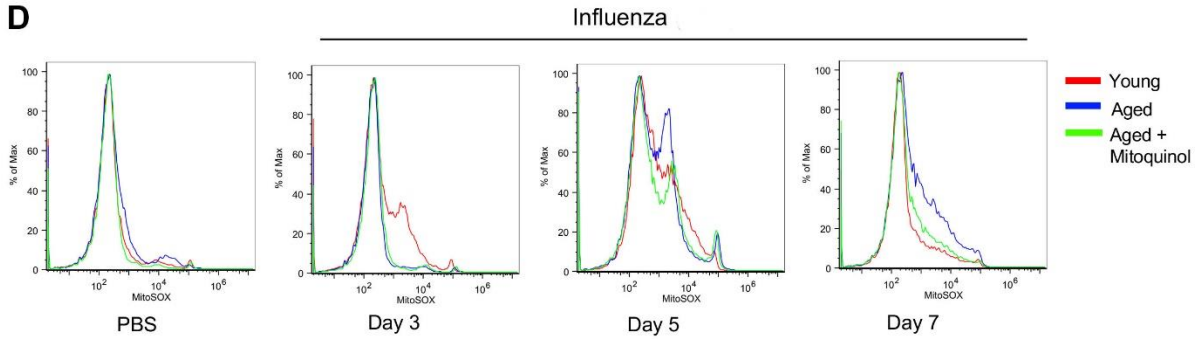
Supplemental Figure 2

**Supplemental Figure S2 (related to Figure 5):** IL6 production by young bone marrow derived macrophages in response to IDO1 modulators and co-stimulation with (A) LPS or (B) poly I:C. (C) IDO1 expression and (D) specific activity was assessed in young macrophages post treatment with IDO1 inhibitor BMS-986205. Comparison of IL6 production post (E) LPS or (F) poly I:C stimulation of untreated or IDO1 inhibited young macrophages. Student's t-test: \*\*P<0.01, \*\*\*P<0.001, and \*\*\*\*P<0.0001. Similar results were obtained from at least three independent experiments with N=10 per group. Data are expressed as the mean  $\pm$  SD.



Supplemental Figure 3

**Supplemental Figure S3 (related to Figure 6):** Aged bone marrow derived macrophages were pre-treated with antioxidants prior to stimulation with LPS. (A) IL6 production was measured at 4- and 24-hours post stimulation. (B) Impact of mitoquinol (50 $\mu$ M) on IDO1 expression was assessed in response to 24-hour stimulation with LPS or poly I:C. (C) Ratio of kynurenine to tryptophan in response to mitoquinol was measured in aged macrophages at 4- and 24-hours post stimulation. Student's t-test: \*\*\*P<0.001 and \*\*\*\*P<0.0001. Similar results were obtained from at least three independent experiments with N=10 per group. Data are expressed as the mean  $\pm$  SD.

**A****B****C****D****Supplemental Figure 4**

**Supplemental Figure S4 (related to Figure 7):** (A) Schematic overview of mitoquinol administration in aged mice. (B) Weight change was assessed in PBS or mitoquinol controls (solid circle and square, respectively) and compared to influenza infected treated with PBS (solid up triangle, black line) or mitoquinol (solid down triangle, blue line). (C) Viral titers were measured in BAL collected on day 7 (Q50: mitoquinol, 50 $\mu$ M). (D) BAL cells were collected from young, aged, and aged + mitoquinol (50 $\mu$ M) treated mice during the course of influenza infection and strained with mitoSOX. Fluorescence was assessed by flow cytometry. Student's t-test: \*\*\*P<0.001 and \*\*\*\*P<0.0001. Similar results were obtained from at least three independent experiments with N=10 per group. Data are expressed as the mean  $\pm$  SD.