SUPPLEMENTAL FIGURES AND TABLE

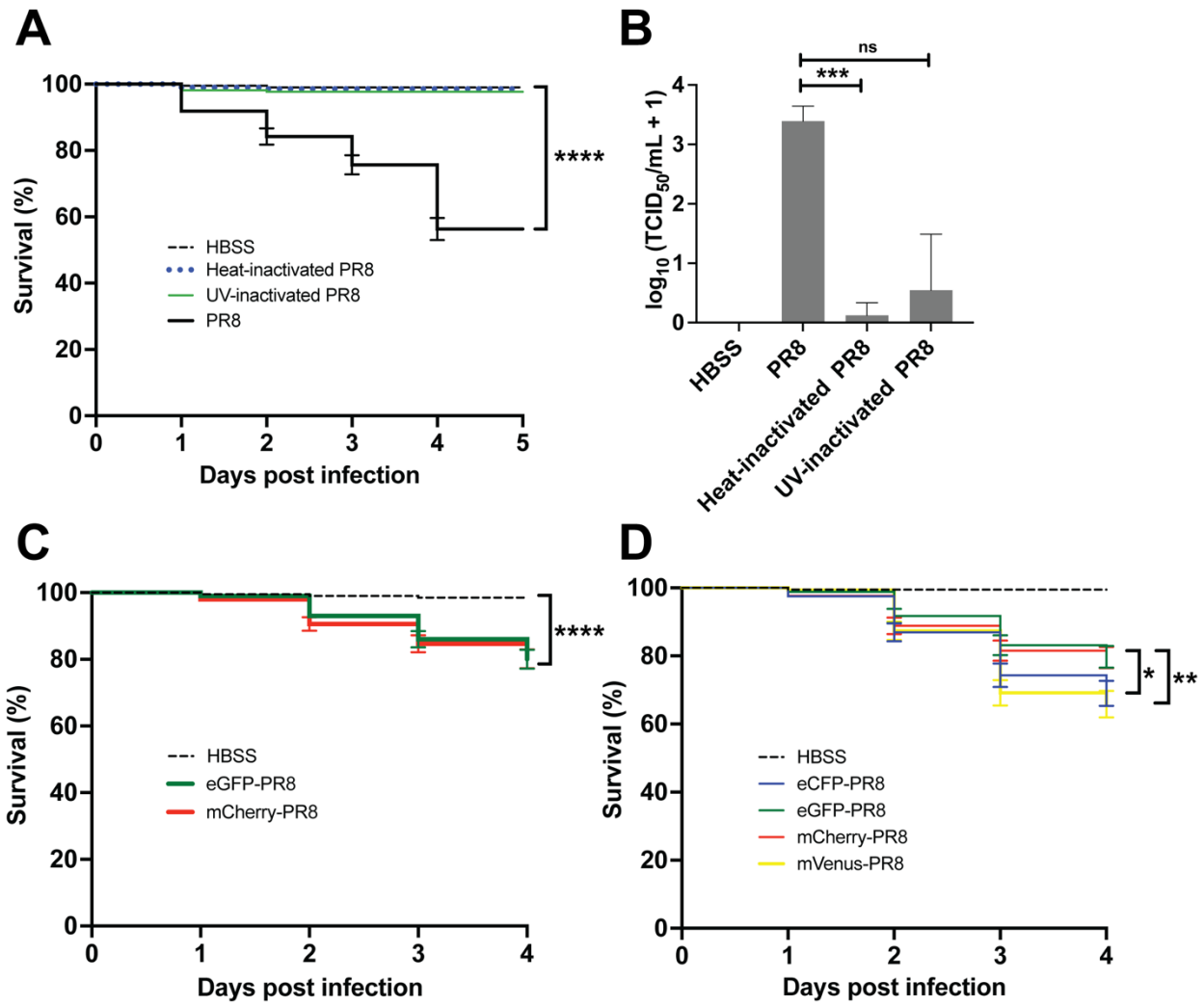

Figure S1: Survival of zebrafish larvae with inactivated PR8 and Color-flu IAV strains. A) Survival of AB larvae injected with live PR8 (8.7 x 102 EID_{50}), heat-inactivated PR8, UV-inactivated PR8 or HBSS (vehicle control) at 2 dpf. Live PR8 infection resulted in significantly lower survival than HBSS, heat-inactivated PR8, or UV-inactivated PR8 ($p < 0.0001$). B) Viral burden of larvae at 24 hpi with live PR8 (8.7 x 102 EID_{50}), heat-inactivated PR8, and UV-inactivated PR8 at 2 dpf. 24 hpi. Viral burden was different between live PR8 and heat-inactivated PR8 ($p = 0.0001$). C) Survival of larvae was reduced with eGFP-PR8 and mCherry-PR8 infection compared to HBSS controls ($p < 0.0001$). D) Survival of Color-flu infected larvae was lower with eCFP-PR8 ($p = 0.0288$) and mVenus-PR8 ($p = 0.0063$) infected larvae than eGFP-PR8. Survival assays were conducted using $n = 4$ and 50 larvae per sample group. $TCID_{50}$ assays were conducted using $n = 3$ and 25 larvae per group. Not significant (ns), $p > 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

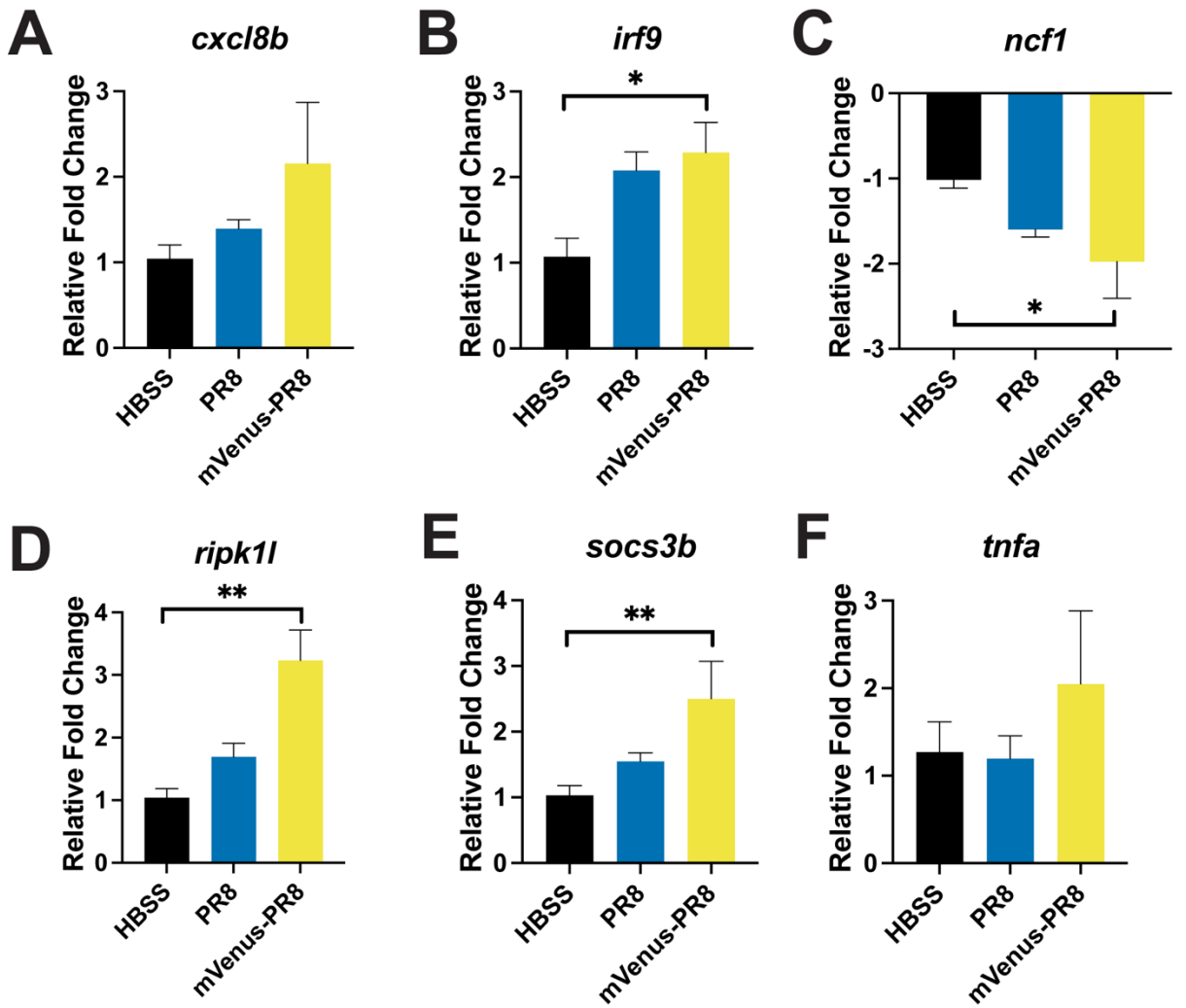

Figure S2: Expression of candidate genes at 24 hpi. Relative fold change of six genes using qRT-PCR ($n = 4$): A) *cxcl8b.1*; B) *irf9* had increased expression with mVenus-PR8 infection (adjusted p-value = 0.0281); (C) *ncf1* had decreased expression with mVenus-PR8 infection (adjusted p-value = 0.0285); (D) *ripk1l* had increased expression with mVenus-PR8 infection (adjusted p-value = 0.0065); (E) *socs3b* had increased expression with mVenus-PR8 infection (adjusted p-value = 0.0088); and (F) *tnfa*. * $p < 0.05$; ** $p < 0.01$.

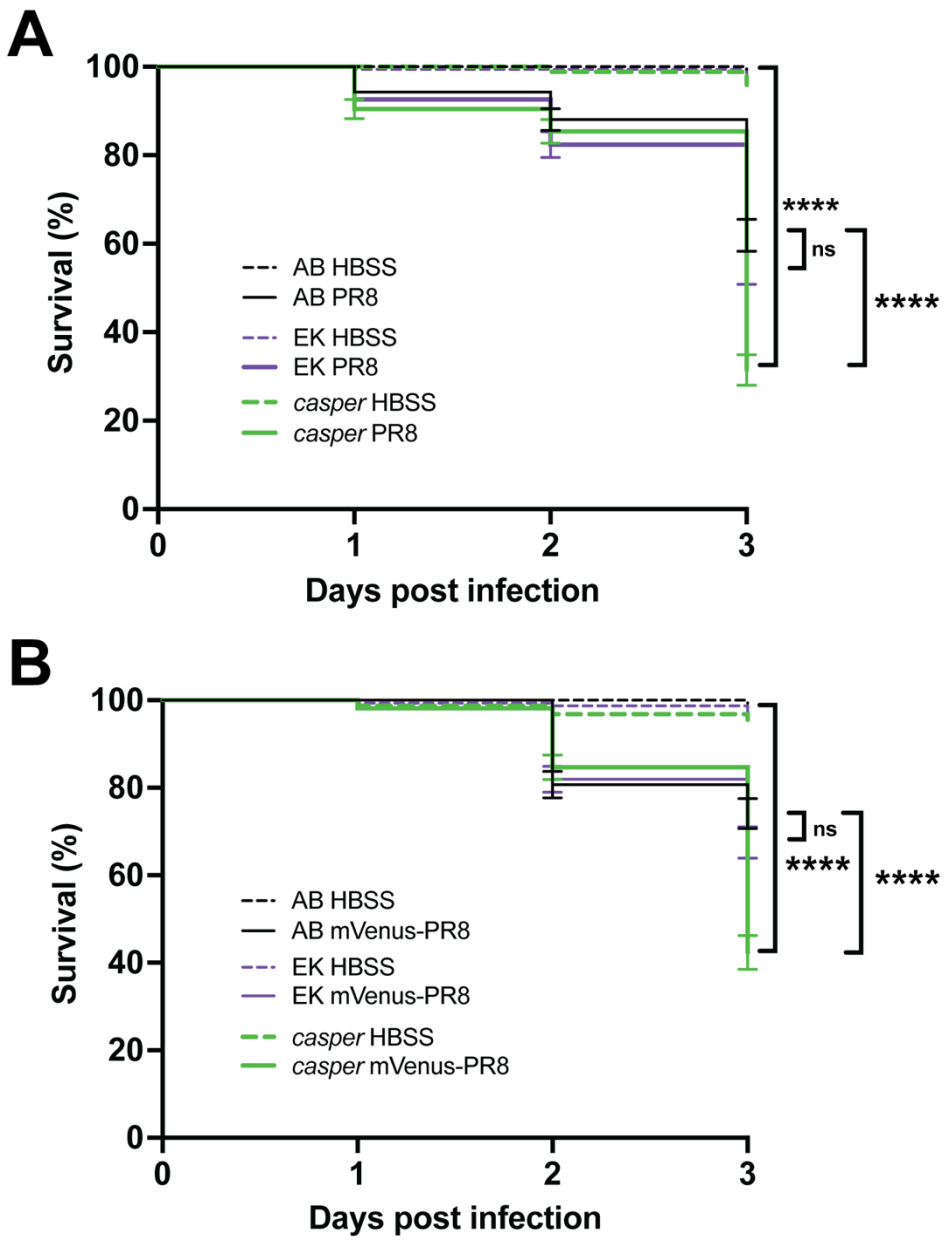

Figure S3: Survival of AB, EK and *casper* zebrafish larvae with swimbladder infections. A) Survival of AB, EK and *casper* larvae infected with PR8 in the swimbladder at 4 dpf. Survival was lower in casper larvae infected with PR8 than HBSS controls ($p < 0.0001$). Survival of PR8-infected *casper* lavae was also lower than AB PR8-infected larvae ($p < 0.0001$). B) Survival of AB, EK and *casper* larvae infected with mVenus-PR8 in the swimbladder at 4 dpf. Survival was lower in *casper* larvae infected with mVenus-PR8 than HBSS controls ($p < 0.0001$). Survival of mVenus-PR8 -infected *casper* lavae was also lower than AB PR8-infected larvae ($p < 0.0001$). Survival assays were conducted using $n = 4$ and 50 larvae per sample group. Not significant (ns), $p > 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

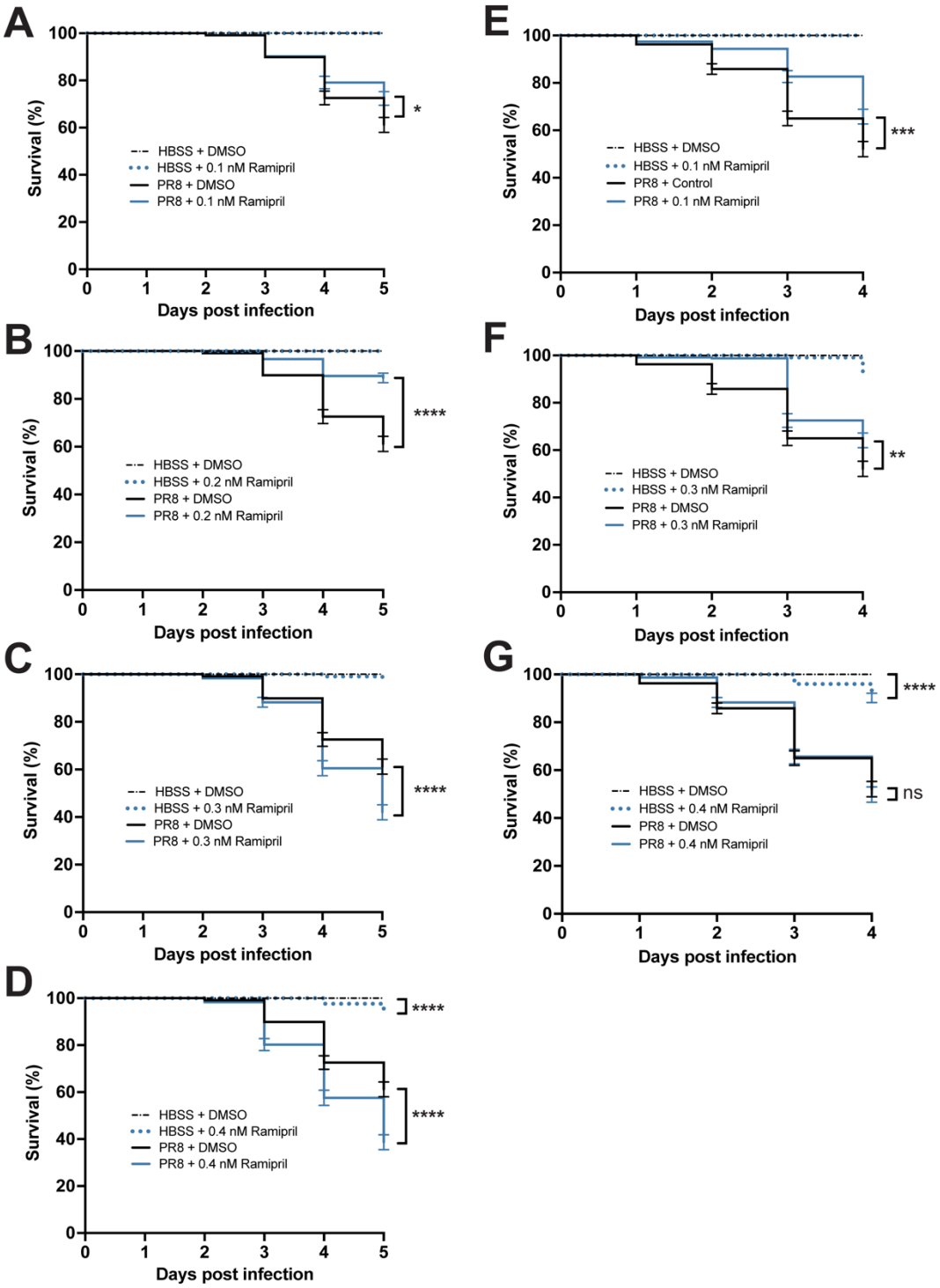

Figure S4: Survival of AB larvae infected with PR8 and treated with DMSO (control) or ramipril. A-D) Survival of larvae infected at 2 dpf and the treated with 0.1, 0.2, 0.3 or 0.4 nM MDIVI-1. Survival was higher in PR8-infected larvae with ramipril exposure at 0.1 nM ($p = 0.0157$), 0.2 nM, 0.3 nM and 0.4 nM ($p < 0.0001$) than DMSO controls. Survival was lowered with 0.4 nM ramipril exposure in HBSS controls ($p < 0.0001$). E-G) Survival of larvae infected at 3 dpf with ramipril exposure at 0.1 nM ($p = 0.0005$), 0.3 nM ($p = 0.0017$). Survival was lowered with 0.4 nM ramipril exposure in HBSS controls ($p < 0.0001$). Survival assays were conducted using $n = 4$ and 50 larvae per sample group. Not significant (ns), $p > 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

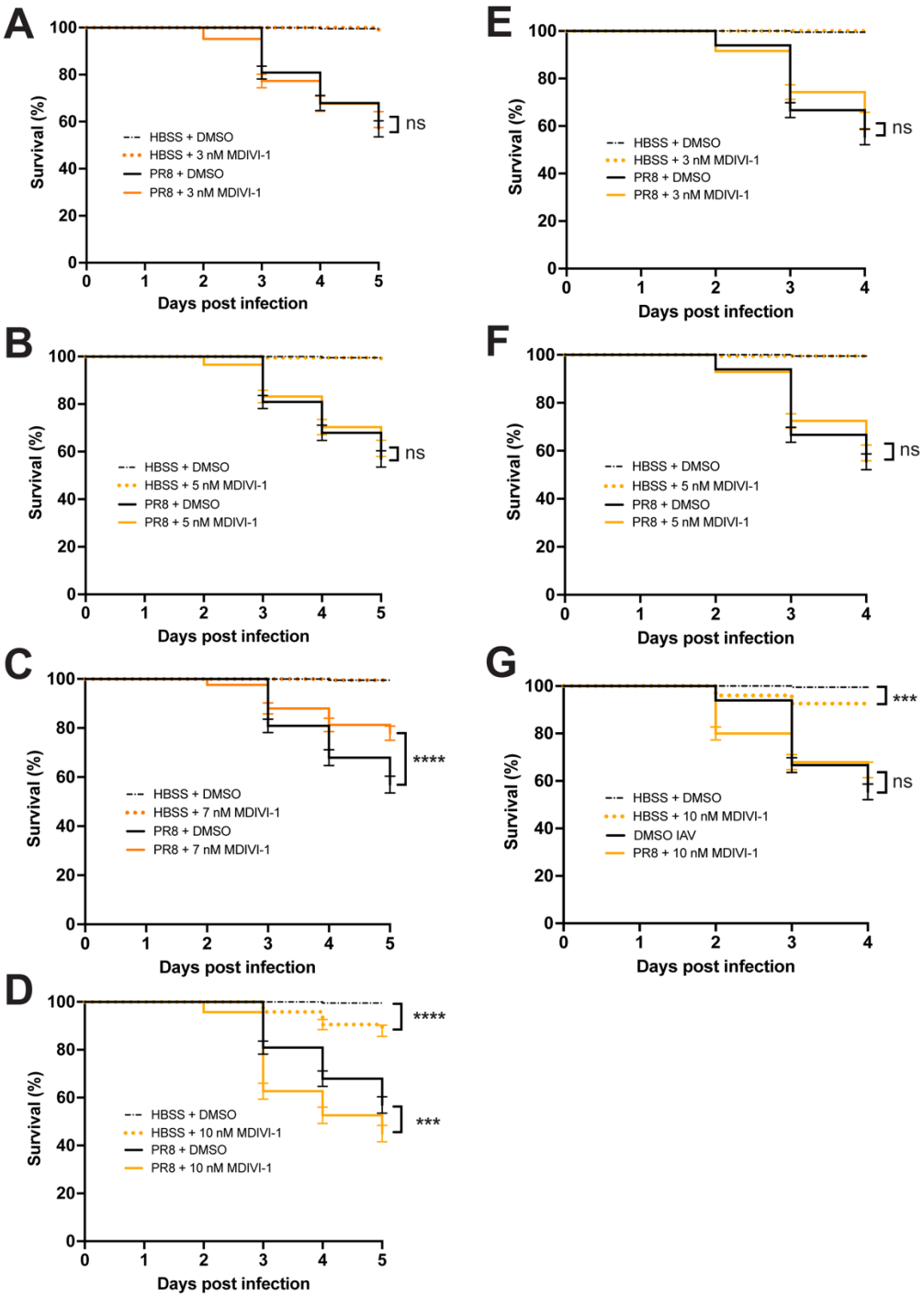

Figure S5: Survival of AB larvae infected with PR8 and treated with DMSO (control) or MDIVI-1. A-D) Survival of larvae infected at 2 dpf and the treated with 3, 5, 7 or 10 nM MDIVI-1. Survival was higher in PR8-infected larvae with 7 nM MDIVI-1 than DMSO controls ($p < 0.0001$). Survival was lowered with 10 nM MDIVI-1 exposure in HBSS controls ($p < 0.0001$) and PR8-infected larvae ($p = 0.0004$). E-G)) Survival of larvae infected at 3 dpf and the treated with 3, 5, or 10 nM MDIVI-1. Survival was lowered with 10 nM MDIVI-1 exposure in HBSS controls ($p = 0.0003$). Survival assays were conducted using $n = 4$ and 50 larvae per sample group. Not significant (ns), $p > 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

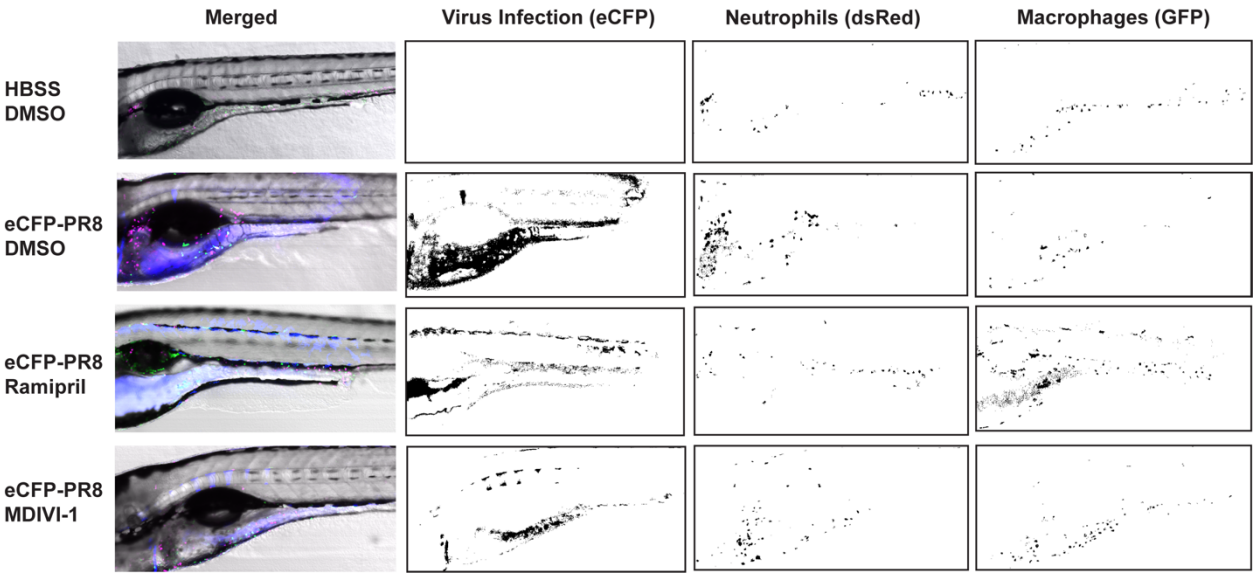

Figure S6: Quantification of virus infected cells, neutrophils and macrophages by fluorescent confocal imaging of Tg(*mpeg1*:eGFP;*lyz*:dsRed) larvae at 48 hours post injection by eCFP-PR8 or HBSS following treatment by DMSO, ramipril and MDIVI-1. Representative images and masks used to quantitate the level of eCFP-PR8 virus infection by pixel intensities in the cyan (emission at 476 nm) channel, number of neutrophils estimated from pixel intensities in the red channel (emission at 583 nm), and number of macrophages estimated from pixel intensities in the green (emission at 510 nm) channel.

Target	**Forward Oligo**	**Reverse Oligo**
actb1	TTC ACC ACC ACA GCC GAA AGA	TAC CGC AAG ATT CCA TAC CCA
cxcl8b.1	GAT GAT GAA GTT GAG CGT TTC AG	GTC TCG GTA GGA TTG AGA CAA AT
irf9	AAA TCC CTG CTA CCC TTC ATG	CGT GCC TGA TCT TTC CAT TTT AC
ncf1	CAG CTC ATT CGG GAC TTC TT	GTT CTC TCT GTT TGT CCT CCT C
ripk1l	CAA ACT GGA GCA GGA GTA CAA	TTC GGG CCT GTG TAA ACT ATC
socs3b	AGT ATG GGA GTT AAG TGT GGC	GAA GCA GTG GAA ATG TGT ACG
tnfa	GGA GAG TTG CCT TTA CCG CT	TTG CCC TGG GTC TTA TGG AG

Table S1: qRT-PCR primers.