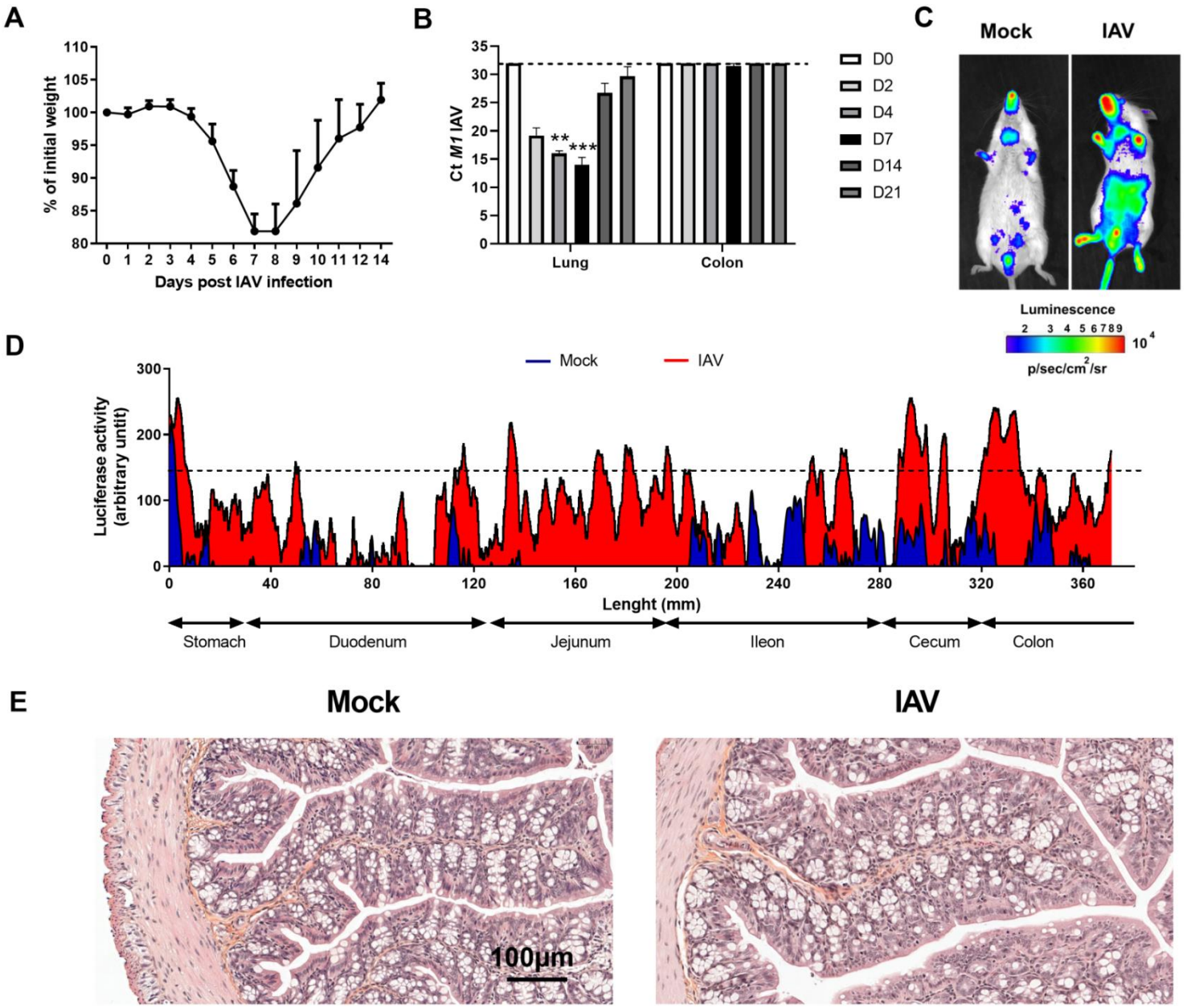

FIG S1 Assessment of weight loss and of NF-kB activity, viral load and pathological scores in the intestine of IAV-infected mice. (A) Mice were infected or not (mock) with IAV (H3N2). The weight curve is shown (n = 8). (B) IAV *M1* mRNA levels were measured in the whole lungs and in the colon by quantitative RT-PCR. Data are expressed as Ct values. The dashed line represents the detection threshold (n = 6). Significant differences were determined using the Kruskal–Wallis ANOVA test (**p < 0.01; ***p < 0.001). (C) Mock-treated and IAV-infected NF-kB luciferase transgenic mice were analyzed *ex vivo* by bioluminescence imaging. Mice were anesthetized at 7 dpi and luciferin was intra-nasally instilled (0.75 $mg.kg^{-1}$). Bioluminescence was then measured using the IVIS system. The scale indicates the average radiance : the sum of the photons per second from each pixel inside the ROI/number of pixels ($photons/sec/cm^2/sr$). One representative mouse of at least ten mice is shown. (D) Bioluminescence values of the whole intestine (arbitrary units, 7 dpi) (n = 3). (E) Histological analysis of intestinal (proximal colon) sections in mock-treated mice and IAV-infected mice (7 dpi). Sections were colored with hematoxylin and eosin. No major changes were observed in duodenum (not shown).

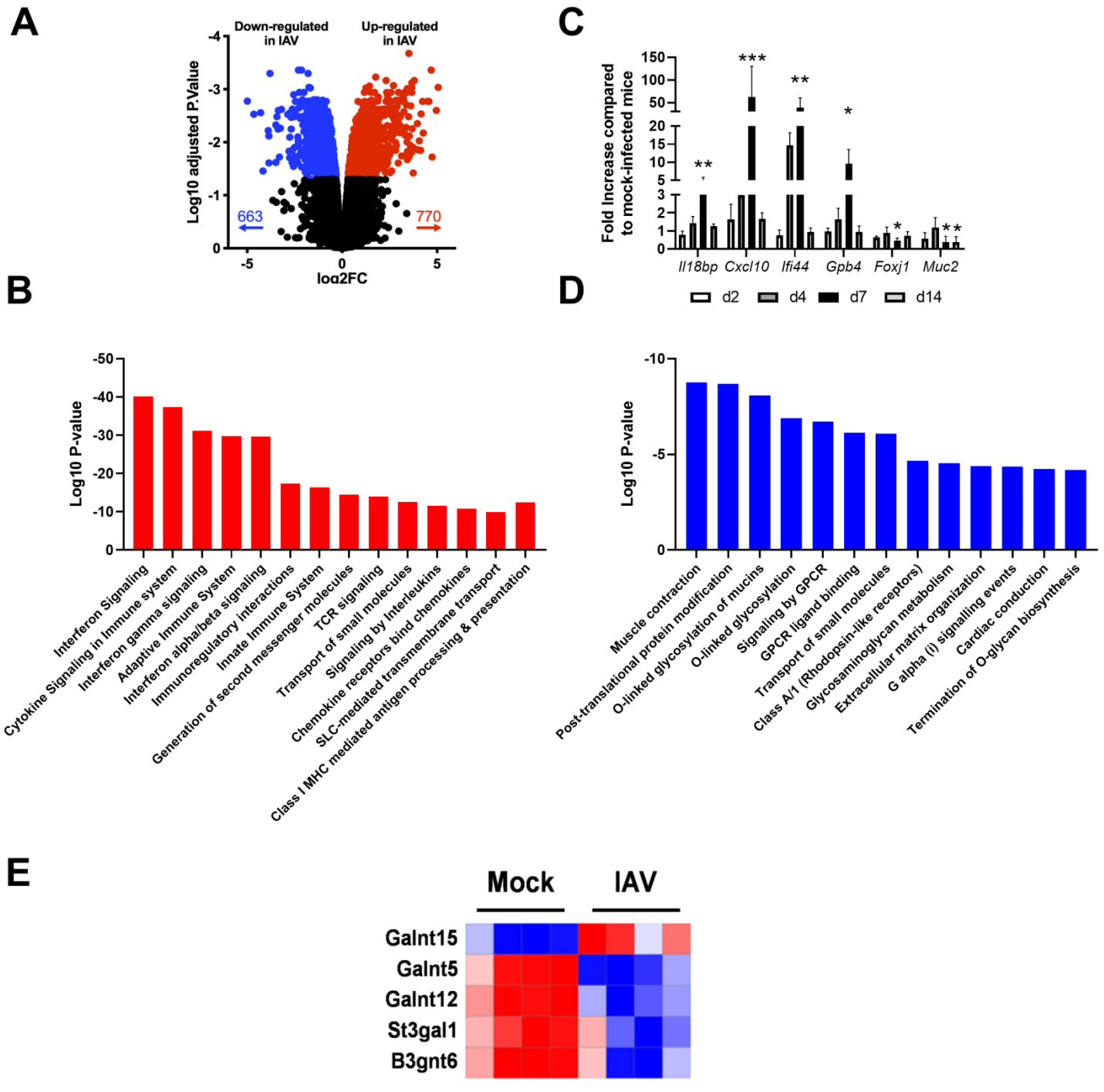

FIG S2 Transcriptomic analysis of the colon collected from mock-treated and IAV-infected mice. (A) Total RNA from mock-treated mice or IAV-infected mice (7 dpi) were extracted from colons and used to quantify gene expression. IAV-induced (red) and IAV-repressed (blue) genes are represented in a volcano plot. Compared to mock-infected mice, 770 genes were up-regulated and 663 were down-regulated genes in the colon of IAV-infected mice (fold change >2, adjusted p-value < 0.05). (B) Gene Set Enrichment Analysis was run on IAV-induced genes (fold change >2, adjusted p-value < 0.05) using the Reactome database. (C) Gene expression in colon after 2, 4, 7 and 14 days of infection was analyzed by RTqPCR (n = 6). Significant differences were determined using the Kruskal–Wallis ANOVA test (* P<0.05, ** P<0.01; *** P<0.001). (D) IAV-repressed pathways (fold change >2, adjusted p-value < 0.05). (E) Heatmap showing significantly modulated genes (fold change >2, adjusted p-value < 0.05) belonging to the KEGG mmu00512 (pathway mucin-type O glycan biosynthesis) in mock-infected and IAV-infected mice.

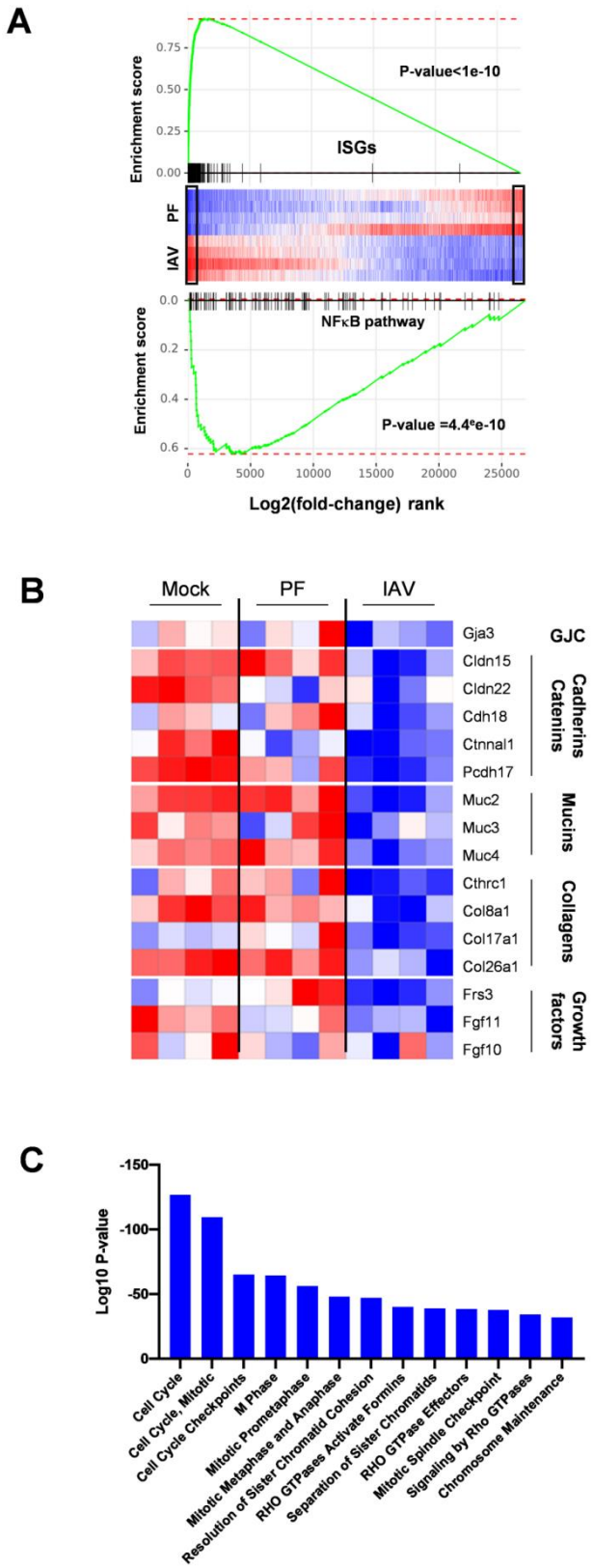

FIG S3 (A) GSEA plot showing enrichment of ISGs and genes involved in the NF-kB signaling pathway (KEGG mmu04064) in pair-fed and IAV-infected mice. Black rectangles indicate statistically significant differences (fold change >2, adjusted p-value < 0.05) in the ”IAV vs pair-feeding (PF)” comparison. Both gene sets appear IAV-specific. (B) Comparison of transcriptional expression of components involved in barrier functions and epithelial integrity in the colon of pair-fed mice and IAV-infected mice (GJC: gap junction components)**.** (C) Gene Set Enrichment Analysis was run on pair-feeding (PF)-repressed genes in comparison to Mock condition (fold change >2, adjusted p-value < 0.05) using the Reactome database.

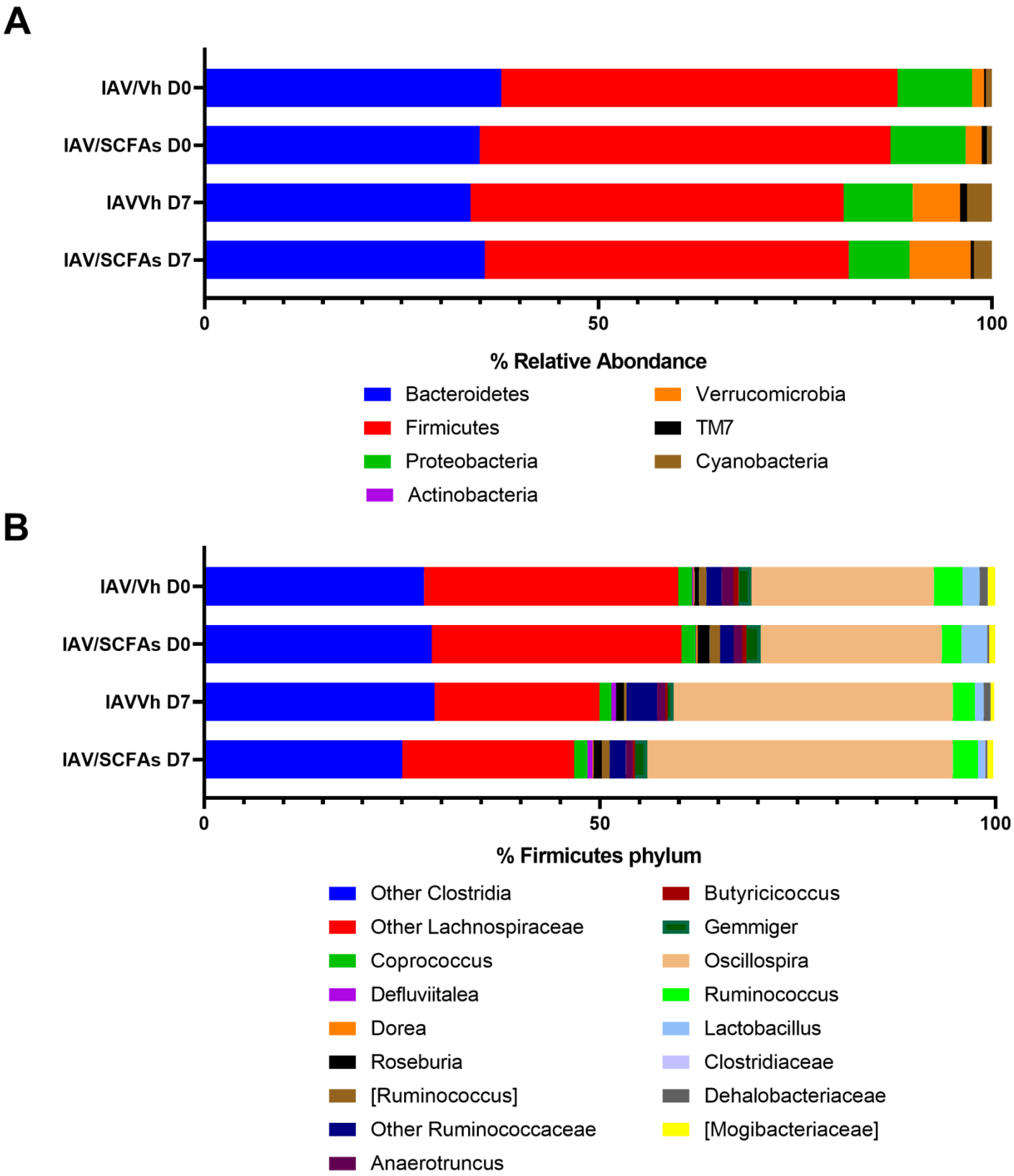

FIG S4 Composition of the gut microbiota after SCFA treatment in mock-infected and IAV-infected mice. (A and B), Microbiota composition at the phylum level (A) and within the Firmicutes phylum (B). Colored blocks indicate taxa with an average relative abundance (n = 4-5).

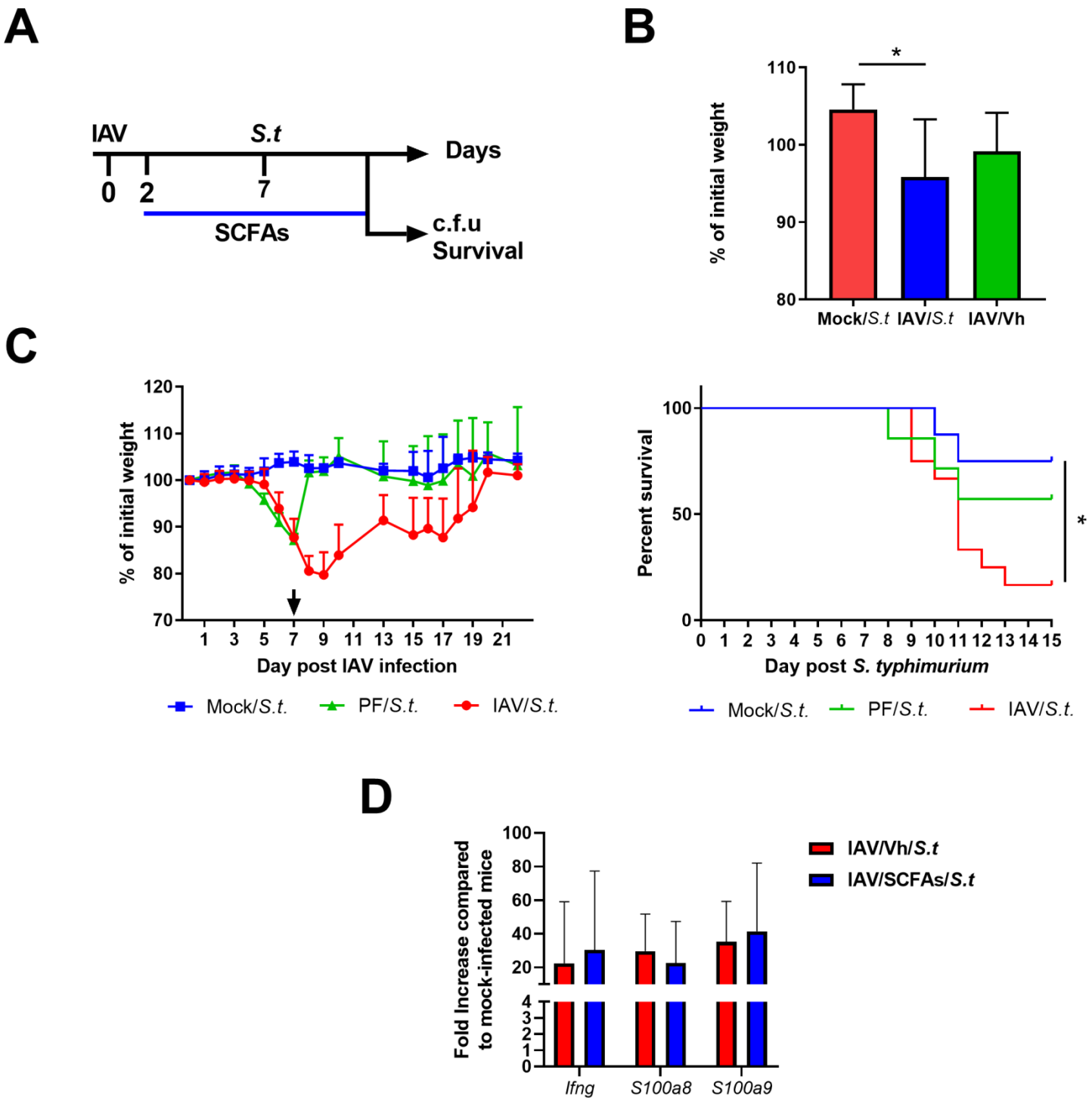

FIG S5 Weight loss during *S.* Thyphimurium enteric infection of IAV-infected mice and pair-fed mice and assessment of gene expression in the colon of doubly infected mice treated or not with SCFAs. (A) Schematic representation of the double infection system. Naïve mice and IAV-infected mice (7 dpi) were infected with *S.* Thyphimurium ($1x10^4$ c.f.u.). IAV-infected mice were treated or not with SCFAS at 2 dpi. (B) Body weight after 7 days of *S.* Thyphimurium infection (in % initial body weight). (C) The food access was restricted in order to mimic weight loss of IAV-infected mice (~15% of body mass). Mice were infected with *S.* Thyphimurium. As a control, IAV-infected mice were (super)infected with *S.* Thyphimurium. *Left panel*, Body weight evolution (in % initial body weight). *Right panel*, The survival of singly infected and doubly infected animals was monitored. n = 8 (one representative experiment out of two). Mice survival was compared using Kaplan-Meier analysis and the log-rank test (* $P<0.05$). (D) Gene expression in colon collected from double-infected mice, either treated or not with SCFAs analyzed by RTqPCR. (B) and (D), n = 6-8, one out of two independent experiments. Significant differences were determined using the Kruskal–Wallis ANOVA test (B and D) (* $P < 0.05$). Mice survival was compared using Kaplan-Meier analysis and the log-rank test (C) (* $P<0.05$).