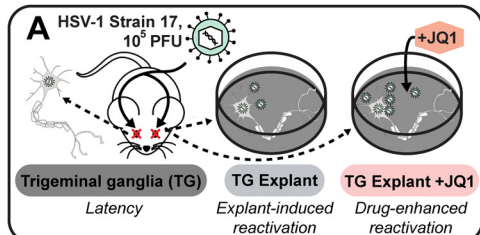


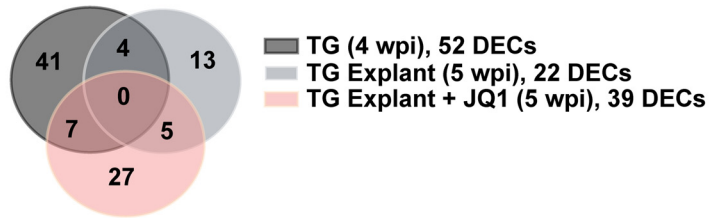
Expanded View Figures

Figure EV1. Murine circRNAs upregulated in HSV-1 infection models.

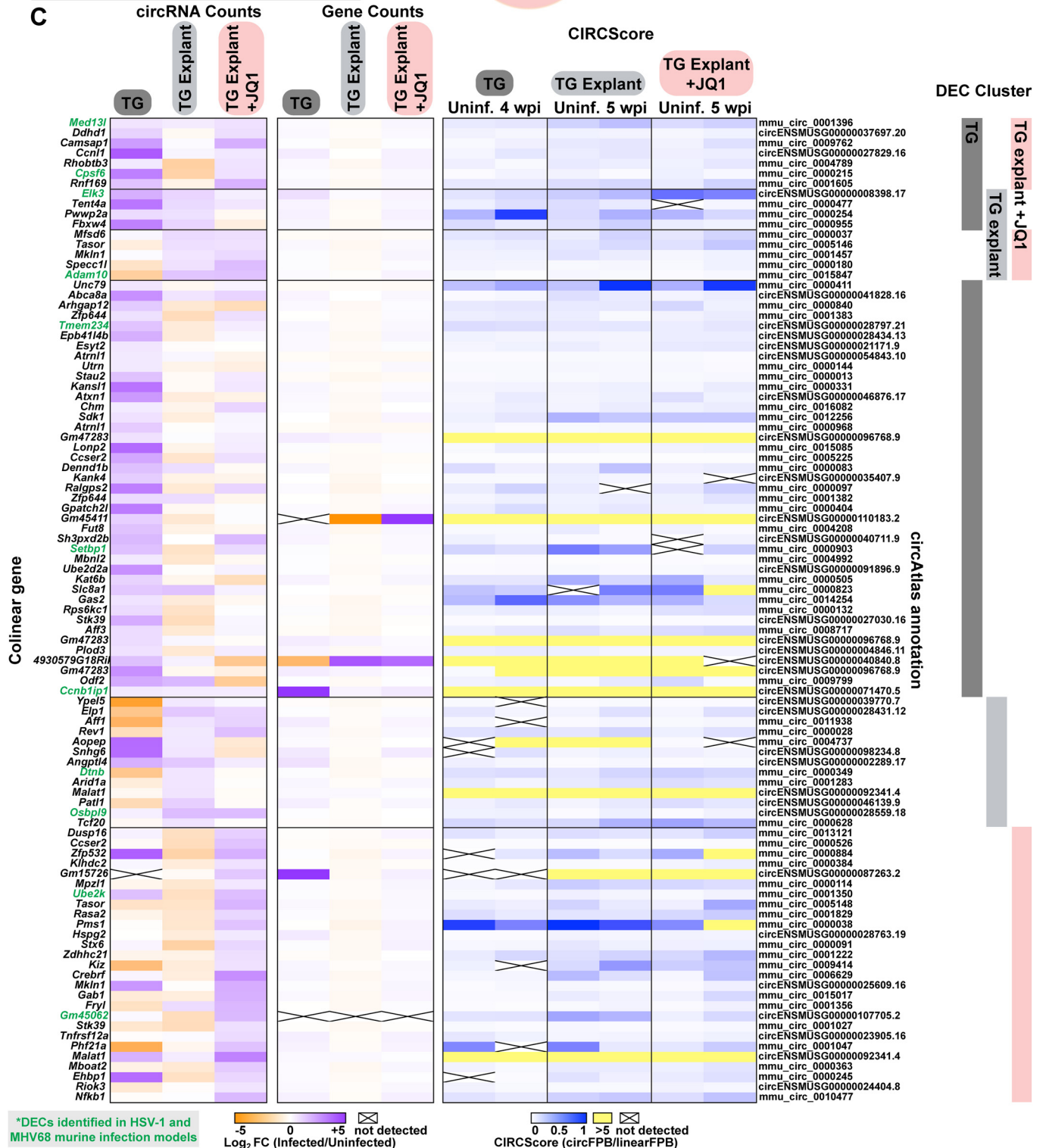
(A) Infographic for murine HSV-1 infection models used in this study. (B) Overlap of upregulated murine circRNA detected by bulk RNA-Seq from HSV-1 latency (TG, $n = 4$), explant-induced reactivation (TG explant, $n = 3$), and drug-enhanced reactivation (TG explant + JQ1, $n = 2$). (C) Heatmaps for upregulated murine circRNAs, plotted as circRNA counts (\log_2FC), Gene counts (\log_2FC), or CIRCscore (circFPB/linearFPB). Data Information: Bulk RNA-Seq data was normalized to ERCC spike-in controls. \log_2FC is relative to a paired uninfected control. Differential expression p -values were calculated using RankProd non-parametric permutation tests. DECs were those with raw back splice junction (BSJ) count across the sample set >10 , $\log_2FC > 0.5$, and p -value < 0.05 . Heatmap values are the average of biological replicates.



B Upregulated murine circRNAs



C



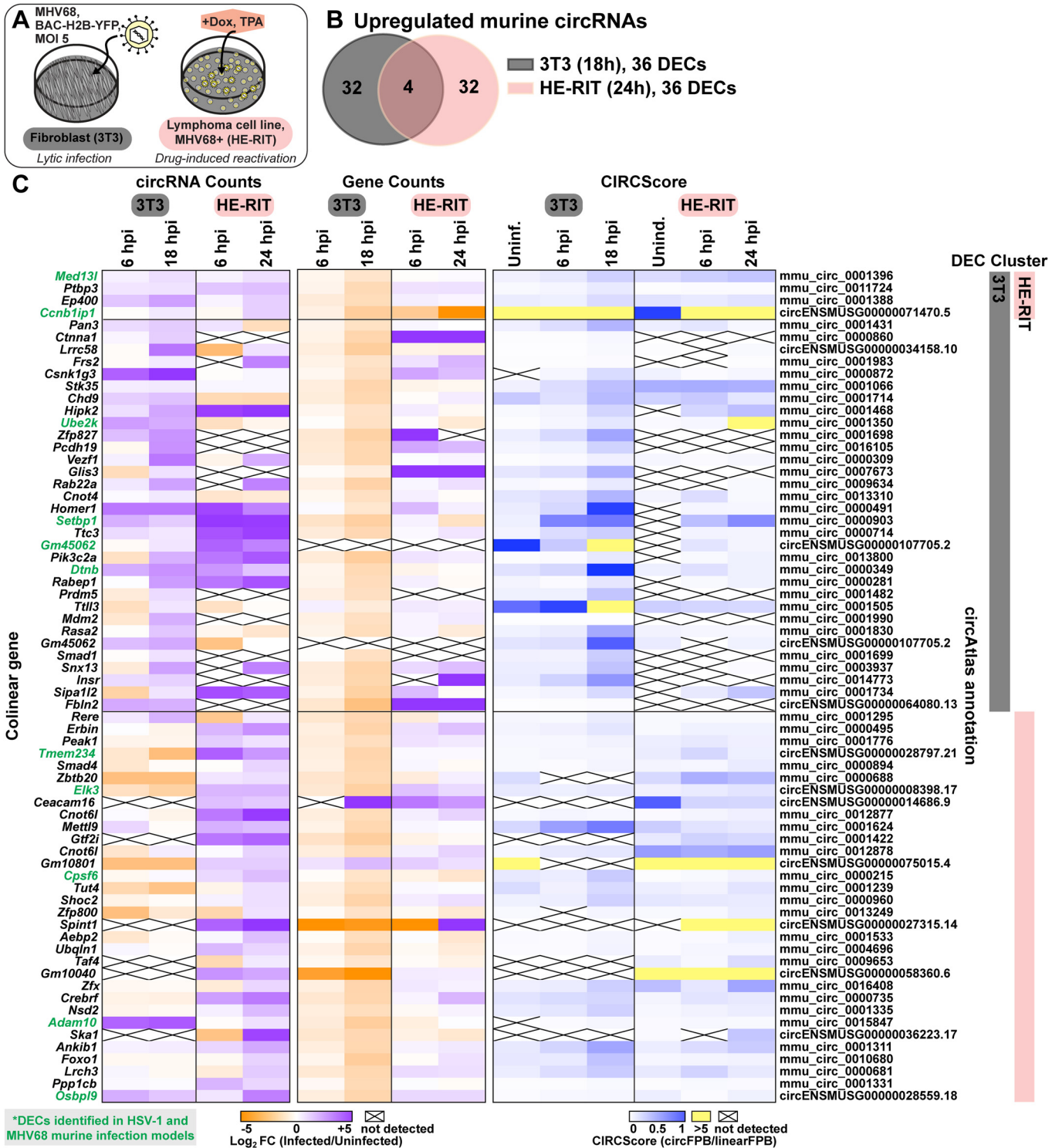
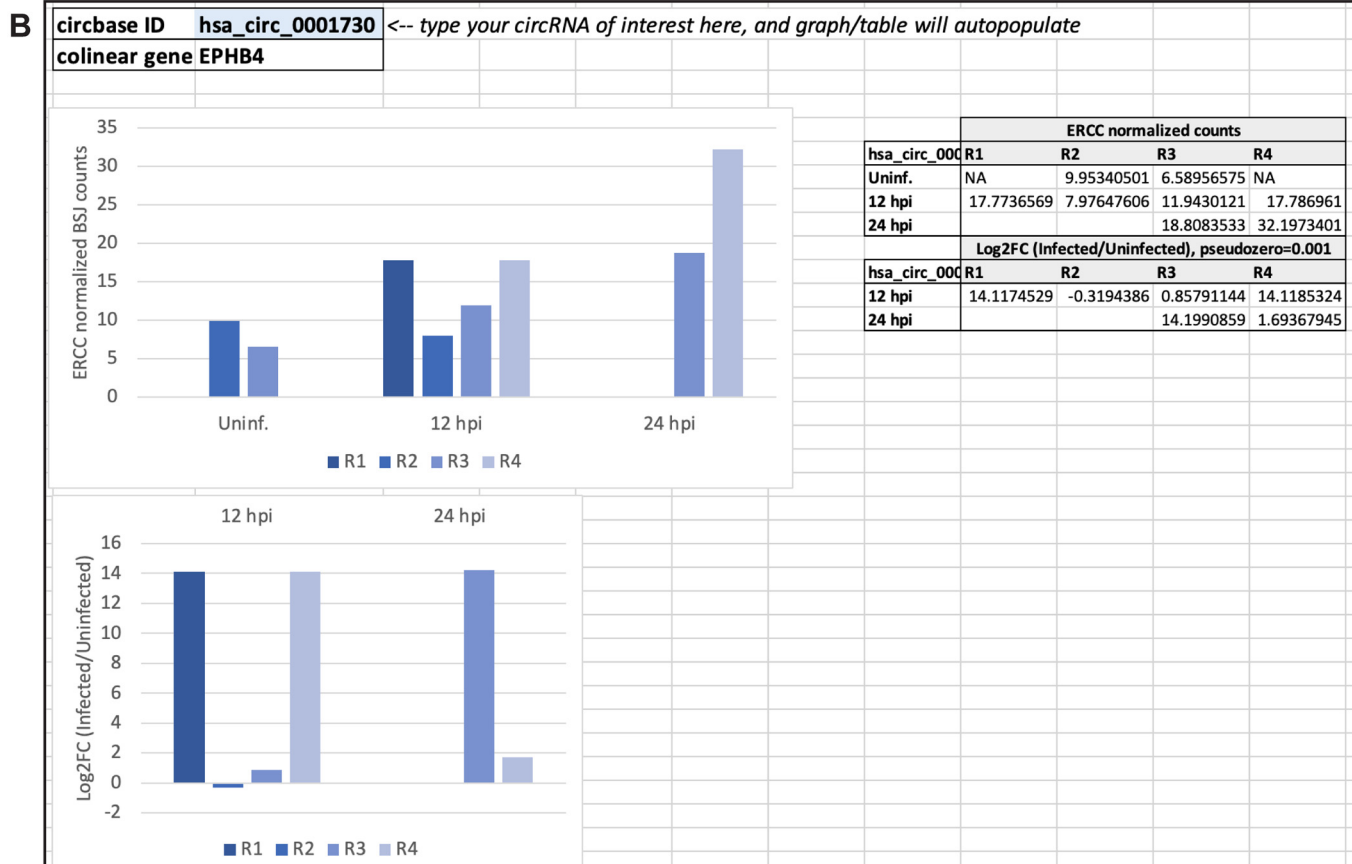
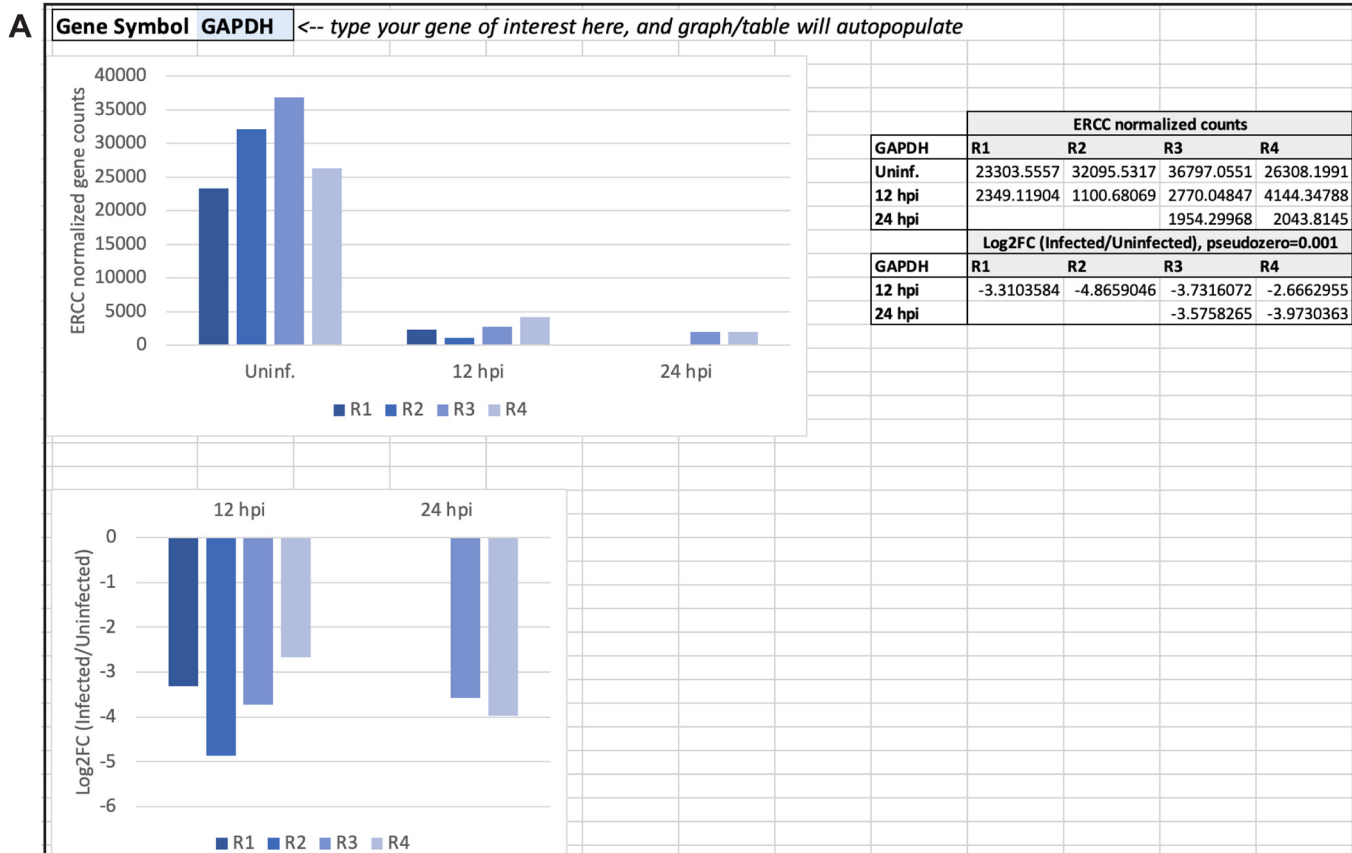


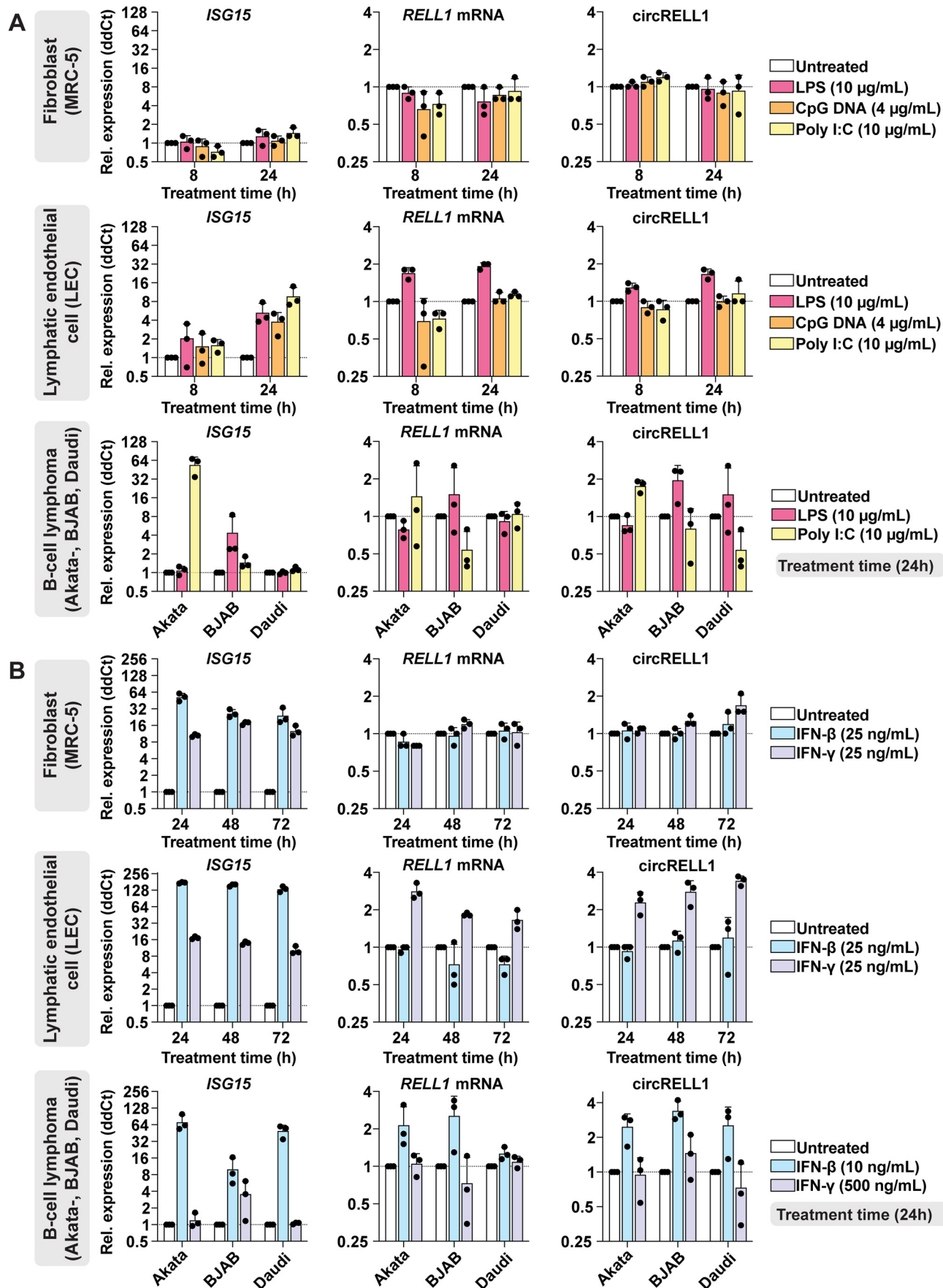
Figure EV2. Murine circRNAs upregulated in MHV68 infection models.

(A) Infographic for murine MHV68 infection models used in this study. (B) Overlap of upregulated murine circRNA detected by bulk RNA-Seq from MHV68 de novo infection (NIH 3T3, $n = 2$) and drug-induced reactivation (HE-RIT, $n = 2$). (C) Heatmaps for upregulated murine circRNAs, plotted as circRNA counts (\log_2FC), Gene counts (\log_2FC), or CIRCScore (circFPB/linearFPB). Bulk RNA-Seq data was normalized to ERCC spike-in controls. \log_2FC is relative a paired uninfected or uninduced control. Differential expression p -values were calculated using RankProd non-parametric permutation tests. DECs were those with raw back splice junction (BSJ) count across the sample set >10 , $\log_2FC > 0.5$, and p -value < 0.05 . Heatmap values are the average of biological replicates.



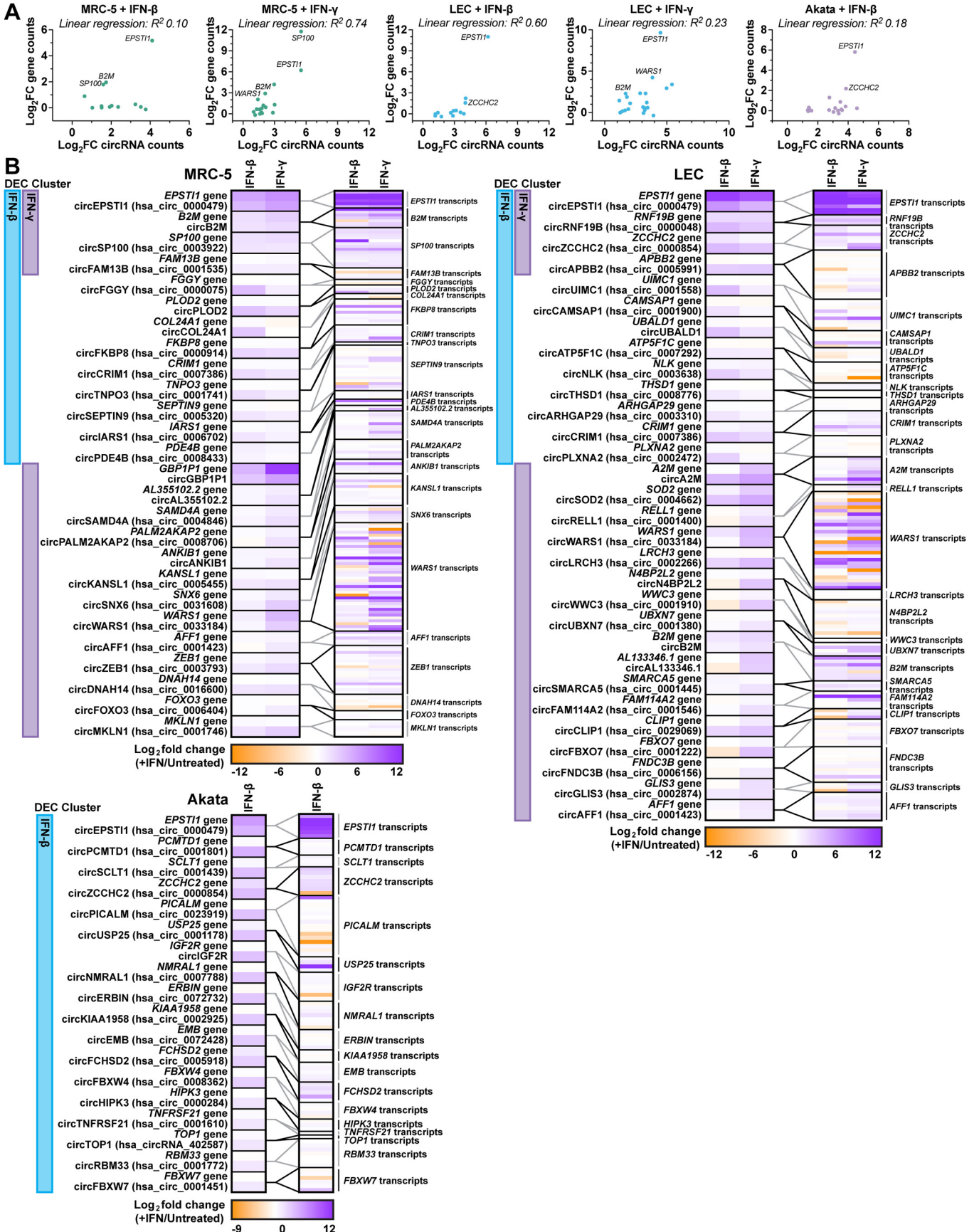
◀ Figure EV3. Screenshot of interactive resource table for transcriptomic data.

(A) Representative screenshot of the GenePlotter tab where users can query any gene of interest. Supporting datasets were generated for all bulk RNA-Seq data analyzed in this study. Datasets include raw and normalized gene counts. (B) Representative screenshot of the CircPlotter tab where users can query any circRNA of interest. Supporting datasets were generated for all bulk RNA-Seq data analyzed in this study. Datasets include raw and normalized BSJ counts.



◀ Figure EV4. CircRELL1 expression changes in response to immune stimuli.

(A) Transcript quantitation for RNA collected from fibroblasts (MRC-5), lymphatic endothelial cells (LEC), or B-cell lymphoma cells (Akata-, BJAB, Daudi) treated with lipopolysaccharide (LPS), poly I:C, or CpG DNA ($n = 3$). (B) Transcript quantitation for RNA collected from MRC-5, LEC, or B-cell lymphoma cells treated with IFN- β and - γ ($n = 3$). Data Information: qPCR data is plotted as relative expression (ddCt) using 18S rRNA as the reference gene, and relative to a paired untreated sample. Data points are biological replicates, column bars are the average, and error bars are standard deviation.



◀ Figure EV5. Transcript isoform analysis of interferon-stimulated cells.

(A) Bulk RNA-Seq data from Fig. 4 plotting \log_2FC (+IFN/untreated) for DECs relative to their colinear gene reads. Genes with similar levels of upregulation for circRNA and colinear gene species are labeled. (B) Bulk RNA-Seq data from Fig. 4 plotted as heatmaps showing \log_2FC (+IFN/untreated) for circRNA species and their colinear gene or transcript isoforms. Gene and transcript quantitation was performed using Salmon and a reference transcriptome fasta. The sample (+IFN- β or +IFN- γ) where a differentially expressed circRNA (DEC) was identified are labeled on the left of each heatmaps as "DEC cluster". Data Information: Bulk RNA-Seq data was normalized to ERCC spike-in control and \log_2FC was determined relative to a paired untreated sample. All data plotted is the average of biological replicates ($n = 3$). The relationship between circRNA and colinear gene expression changes was assessed by linear regression analysis, R^2 values are given.