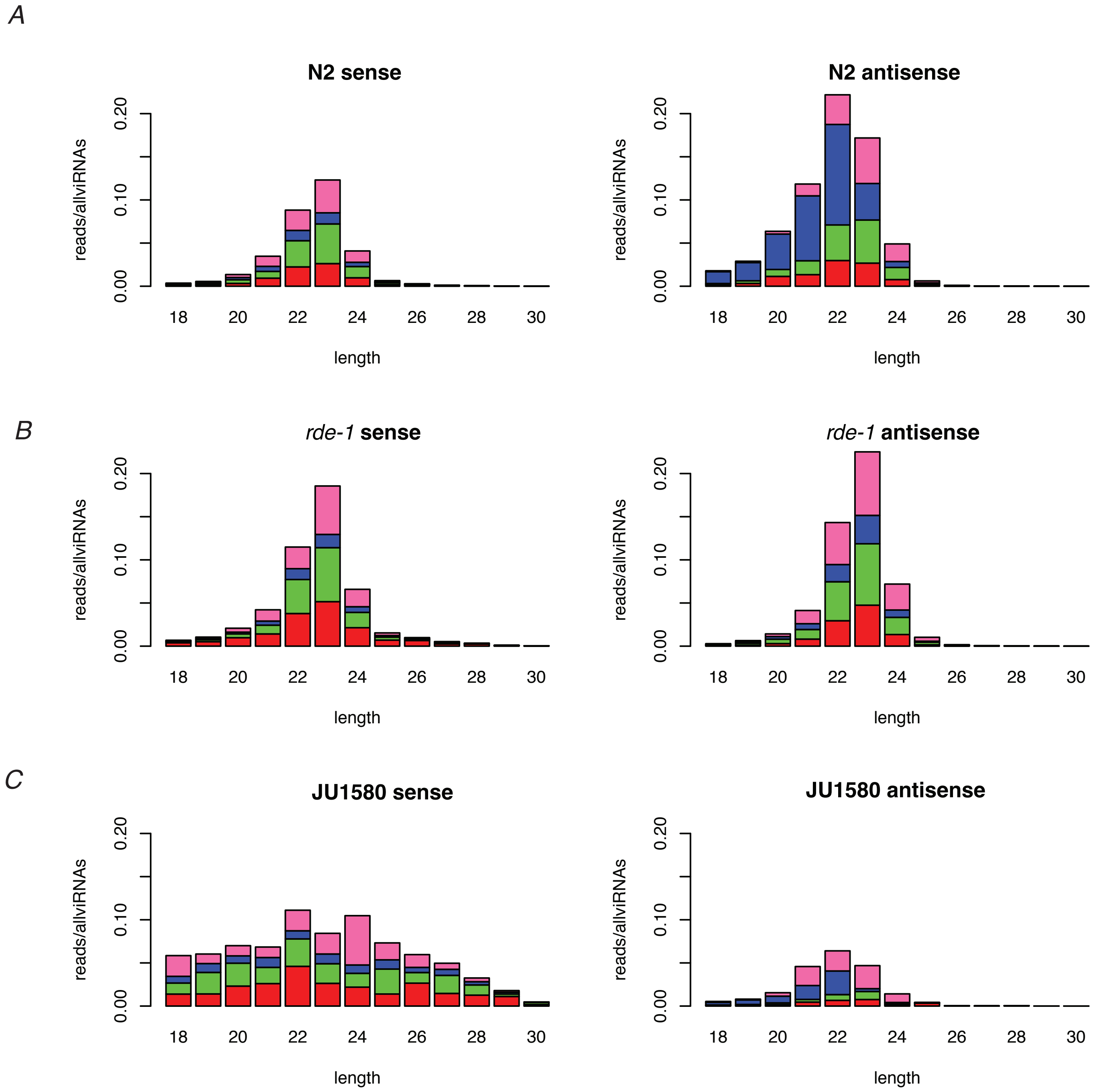
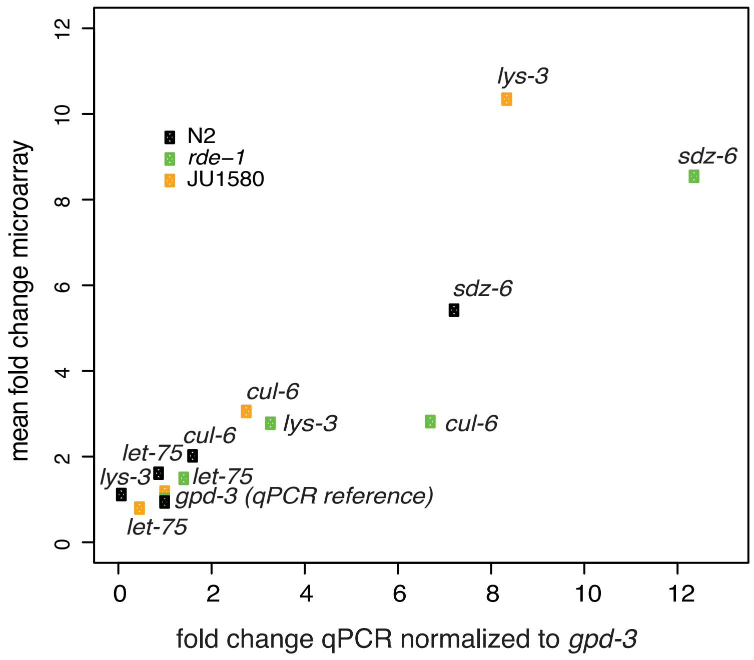
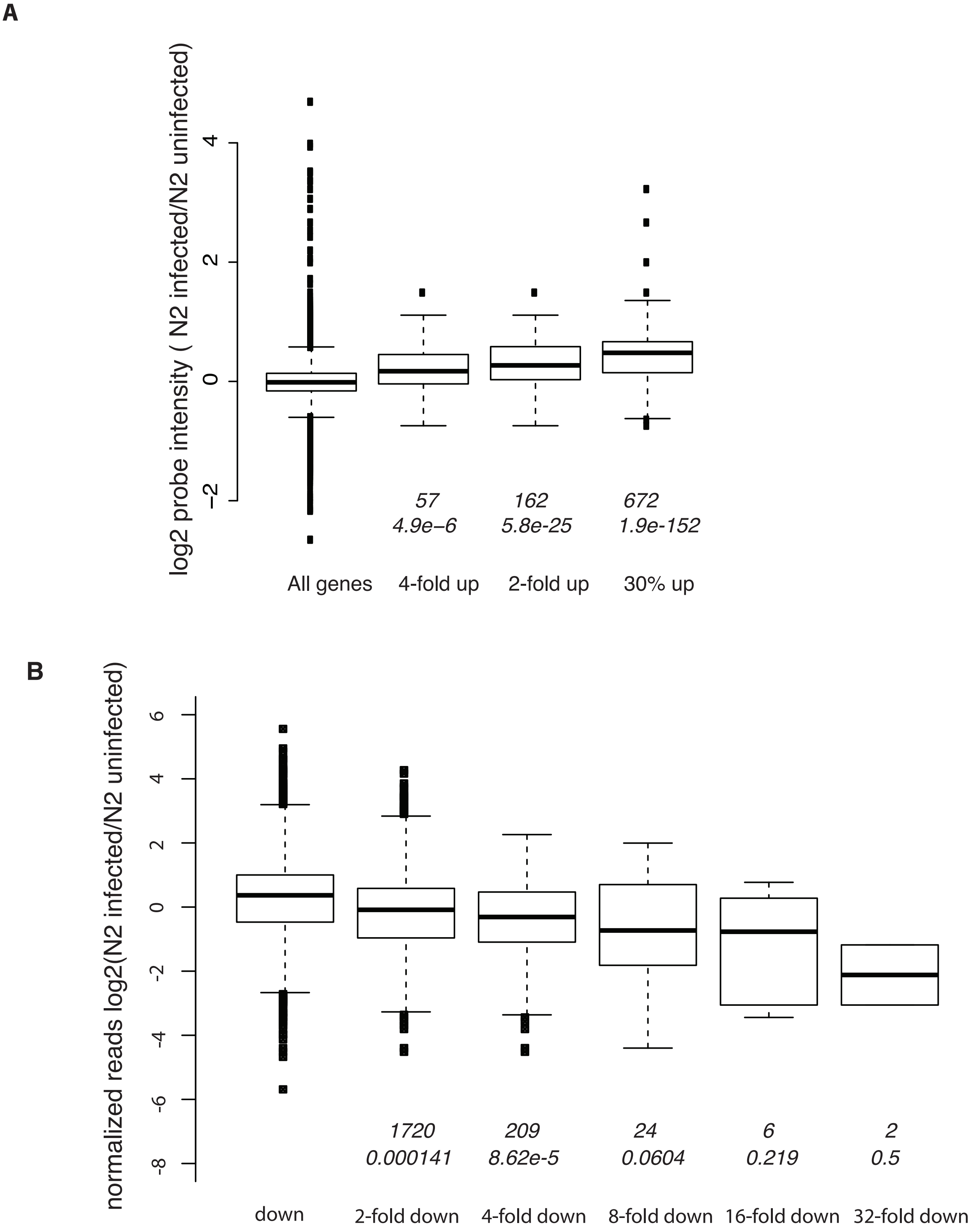


Supplemental Figure 1. Small RNA sequencing data showing antiviral small RNAs in N2, *rde-1* and JU1580. Length and first nucleotide of all small RNAs aligning to the Orsay virus genome are shown, normalized to all small RNAs aligning to the viral genome.

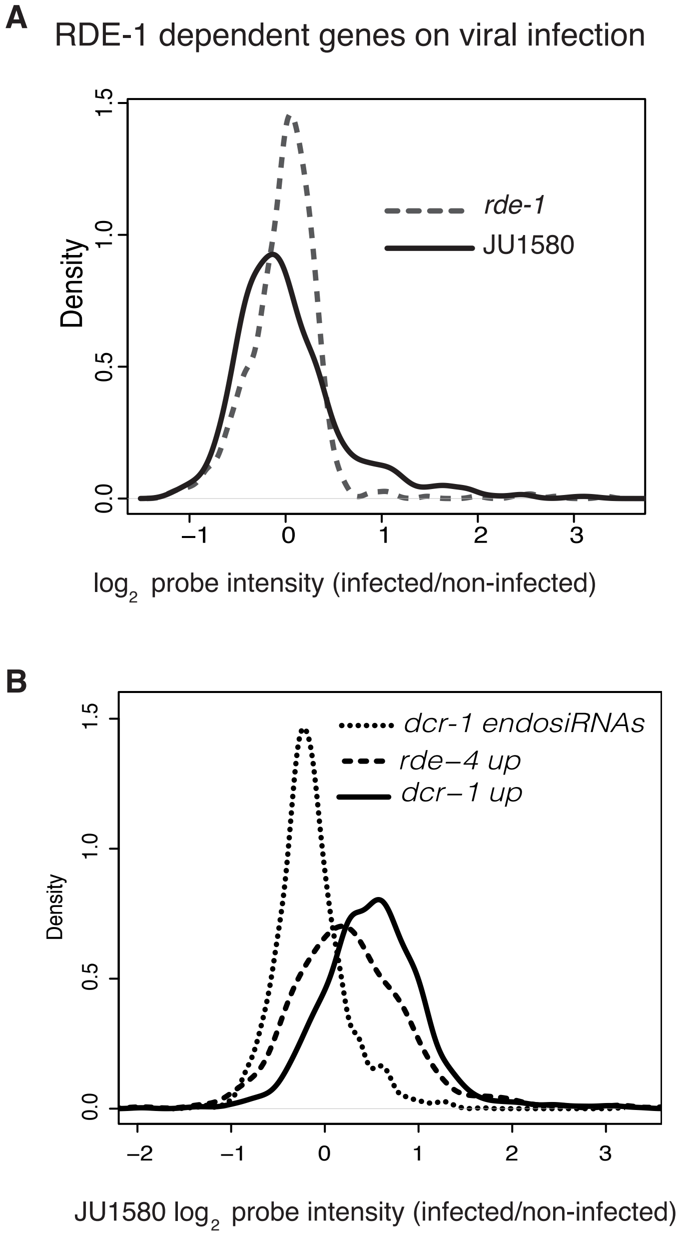


*No data for *sdz-6* in JU1580 due its deletion from the genome.

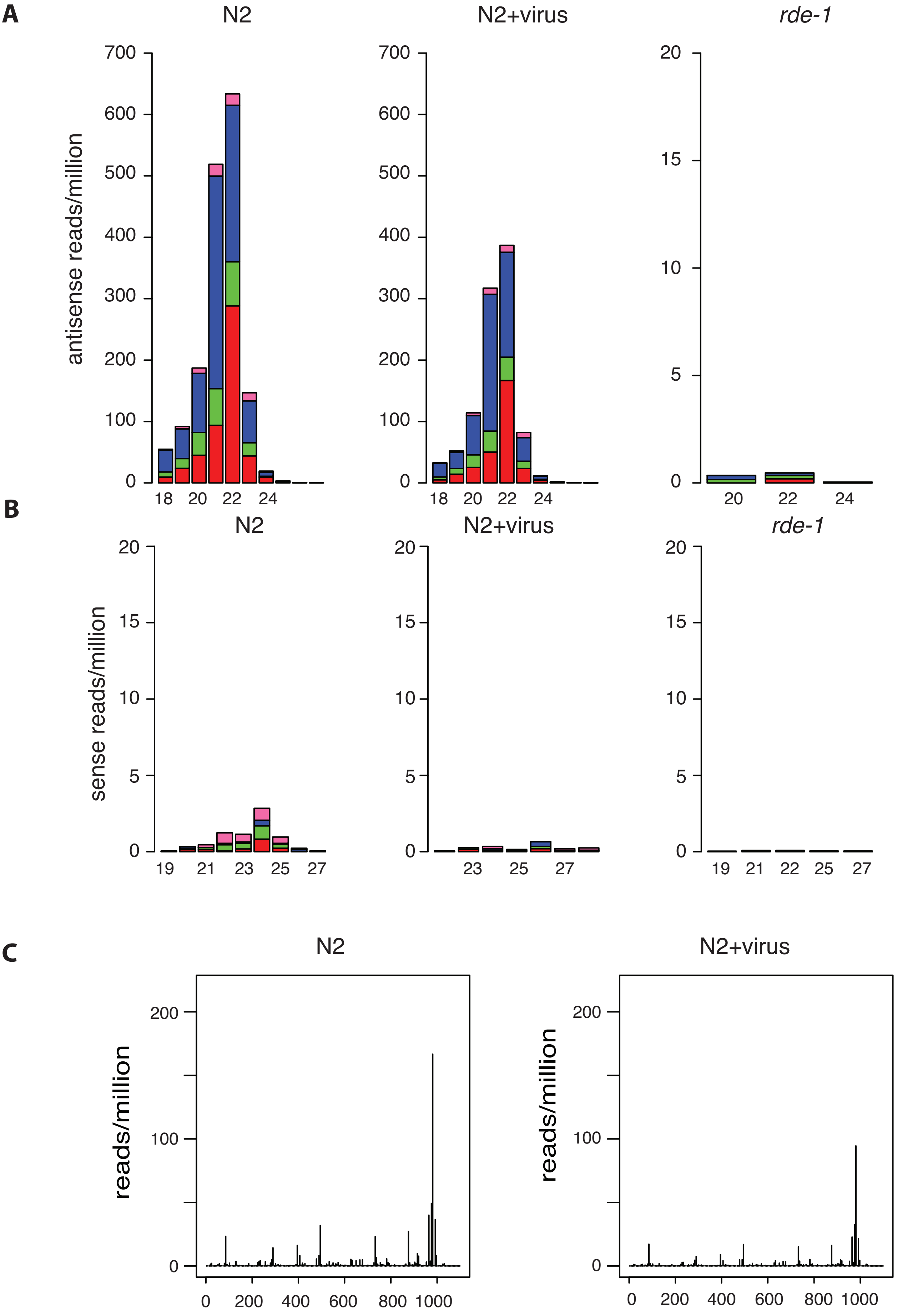
Supplemental Figure 2. Correlation between qPCR data and microarray data. Four genes were chosen, each of which changed statistically significantly in at least one strain according to the microarray data. qRT PCR was performed on RNA generated from a different set of infections to the microarray. Changes of the qPCR reference gene GAPDH according to the microarray data are shown for comparison.



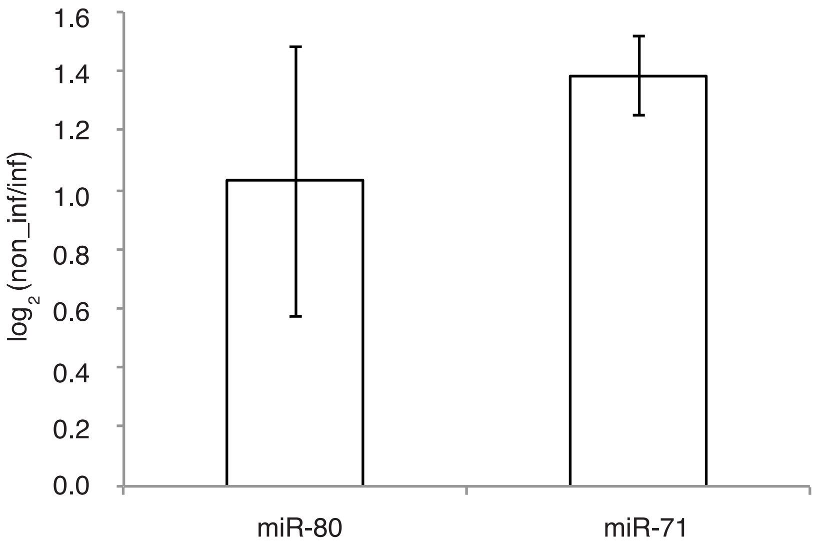
Supplemental Figure 3: *rde-1* regulated genes over a range of cut-offs display similar behaviour on infection of N2 animals. Boxplots show median, interquartile range, with whiskers extending to the most extreme data point which is no more than 1.5 times the interquartile range from the box. The number of genes involved and statistical significance using the two-tailed signed rank test are shown below each bar. (A) gene expression data. (B) small RNA sequencing data.



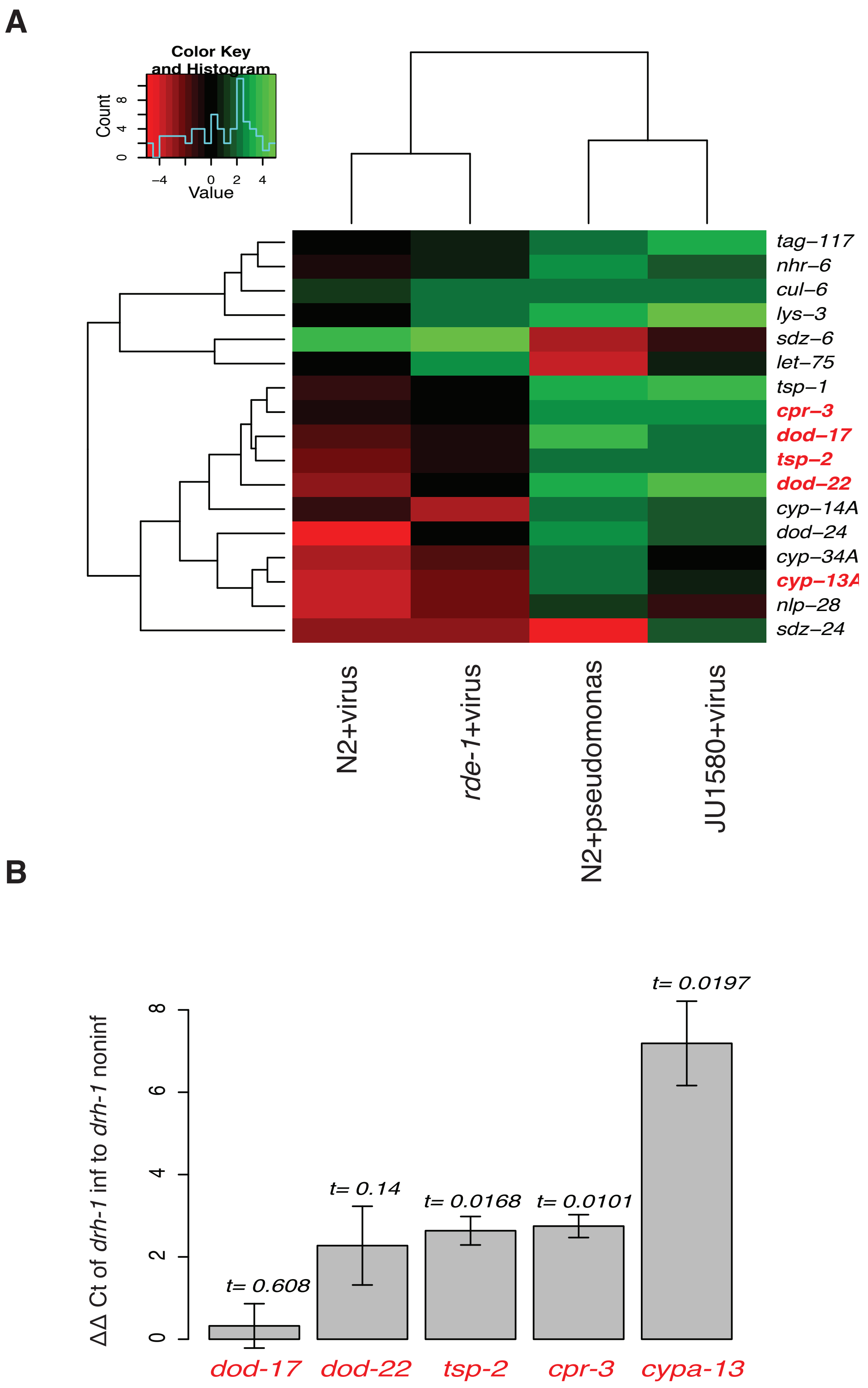
Supplemental Figure 4. Gene expression changes upon viral infection. (A) Changes in expression of RDE-1 dependent genes on infection of *rde-1* mutant and JU1580 animals. (B) Changes in expression of RDE-4-regulated genes and genes regulated by endosiRNA dependent on DCR's helicase domain in JU1580 on infection compared to DCR-regulated genes.



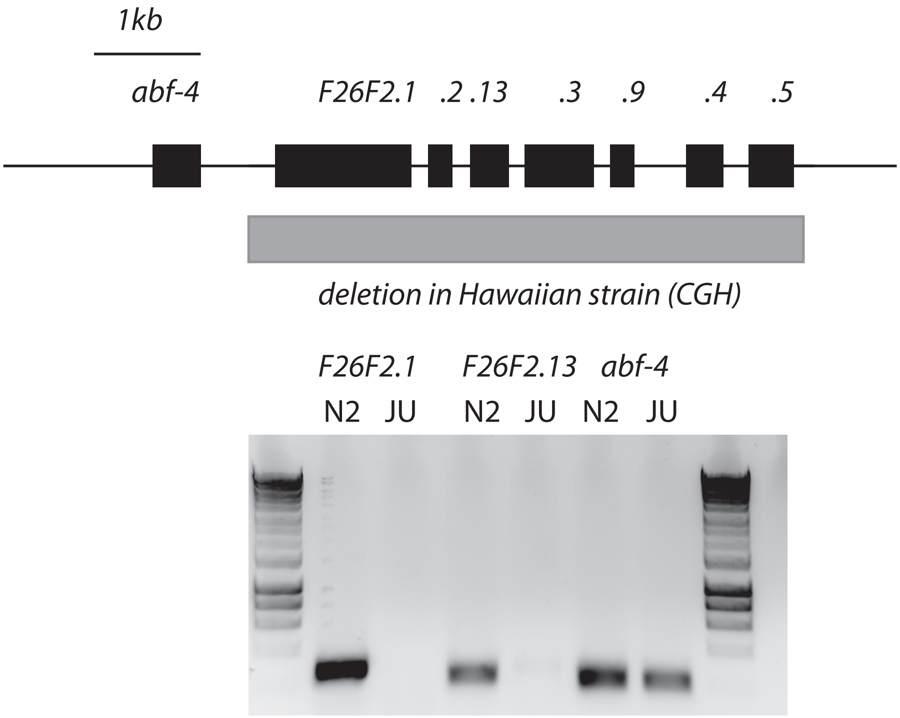
Supplemental Figure 5. Analysis of small RNAs mapping to the Y47H10A.5 locus. (A) shows antisense small RNA reads mapping to the locus, (B) shows sense small RNA reads mapping to the locus and (C) shows the distribution of antisense 22Gs accross the transcript in N2 with and without virus.



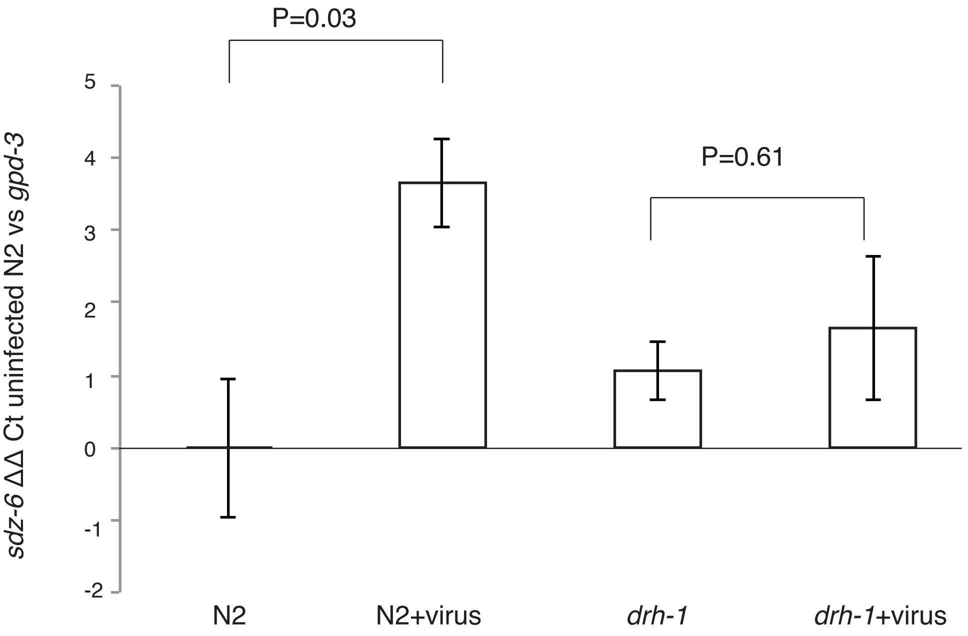
Supplemental Figure 6. qPCR analysis of the miRNAs miR-80 and miR-71 in JU1580 animals upon infection. Error bars represent the standard error of the mean from two biological replicates.



Supplemental Figure 7. Bacterial response genes display similar behaviour on viral infection of both JU1580 and *drh-1*. (A) shows a heatmap showing the behaviour of genes altered on *P. aerigunosa* infection which change by at least 2-fold in one of the lines when infected with virus. Select members of this set were chosen for qRT-PCR analysis of infected *drh-1* mutant animals (names in red). (B) shows the behaviour of these selected genes upon infection of *drh-1* animals. The error bars represent standard deviation of the mean from 3 biological replicates and the p value for a one sample t-test for altered expression relative to GAPDH is shows above the bar.



Supplemental Figure 8 Analysis of deletions in the F26F2 cluster. Top- diagram of the locus taken from Wormbase. .2= F26F.2 etc. Bottom- PCR analysis of F26F2.1 and F26F2.13 as well as the nearby gene *abf-4*. JU= JU1580.



Supplemental Figure 9 qPCR analysis of *sdz-6* expression. *sdz-6* expression measured by qRT-PCR in N2 and *drh-1* mutant animals is shown. Error bars represent standard error of the mean from three biological replicates.