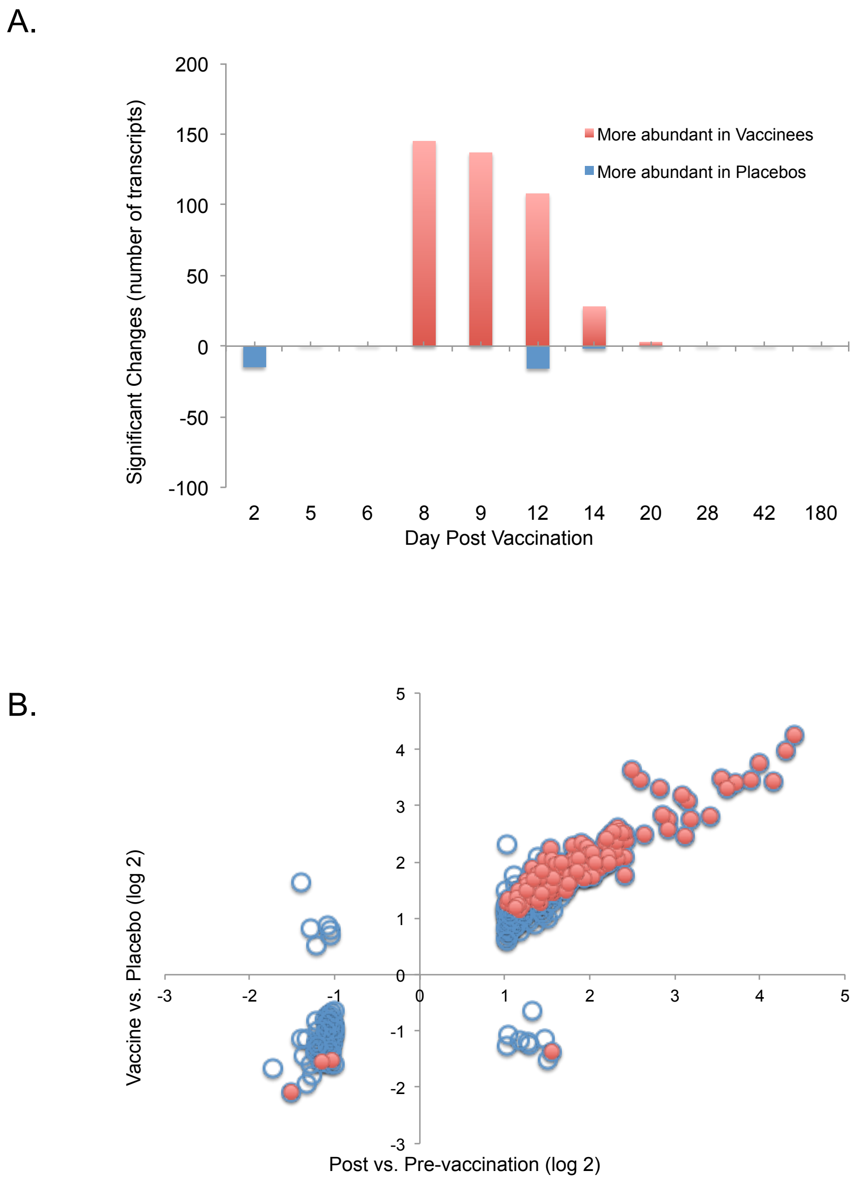
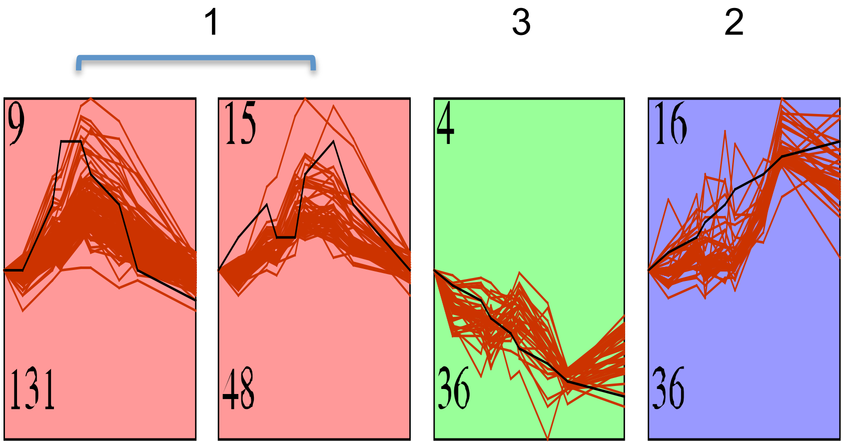
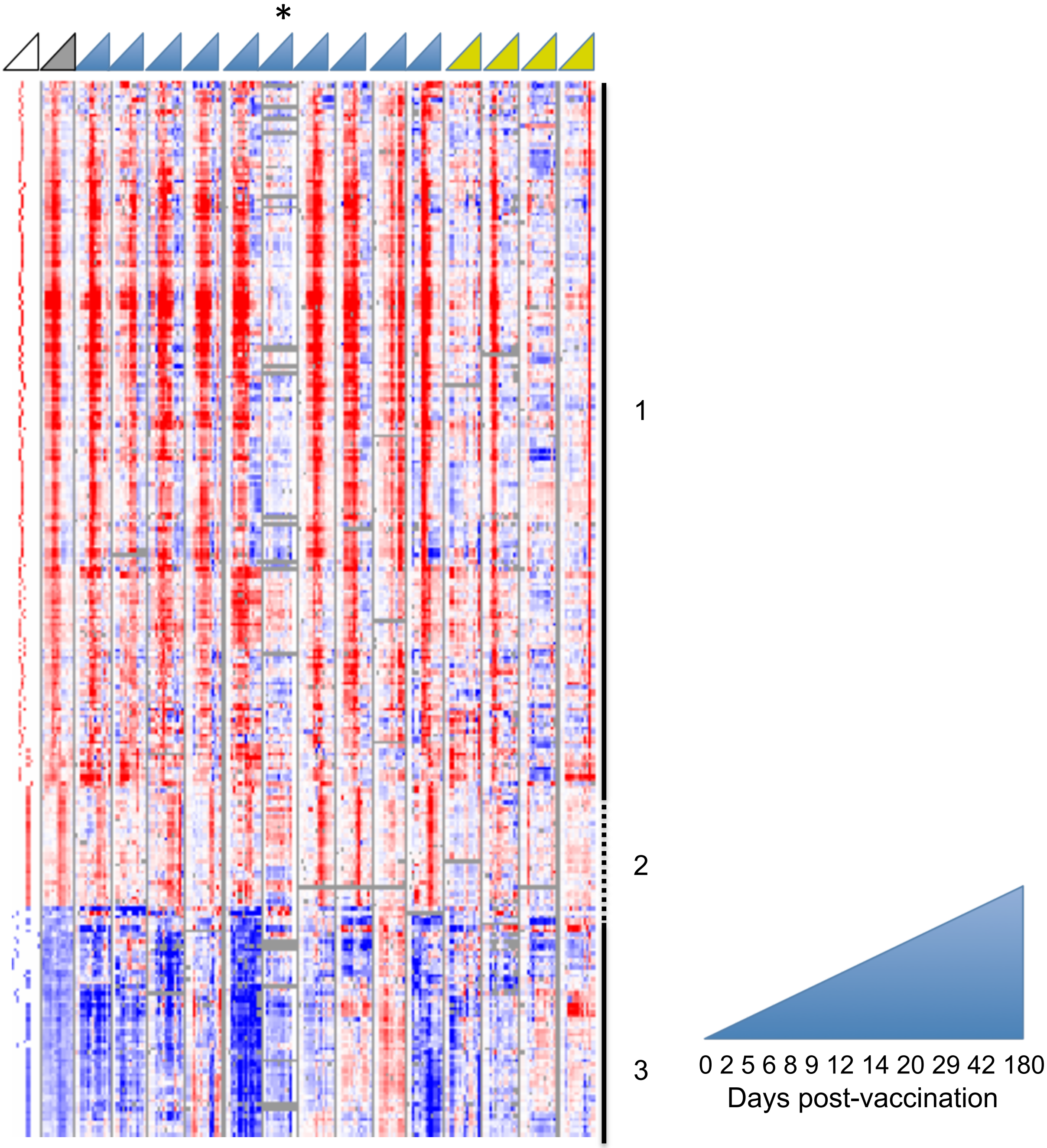


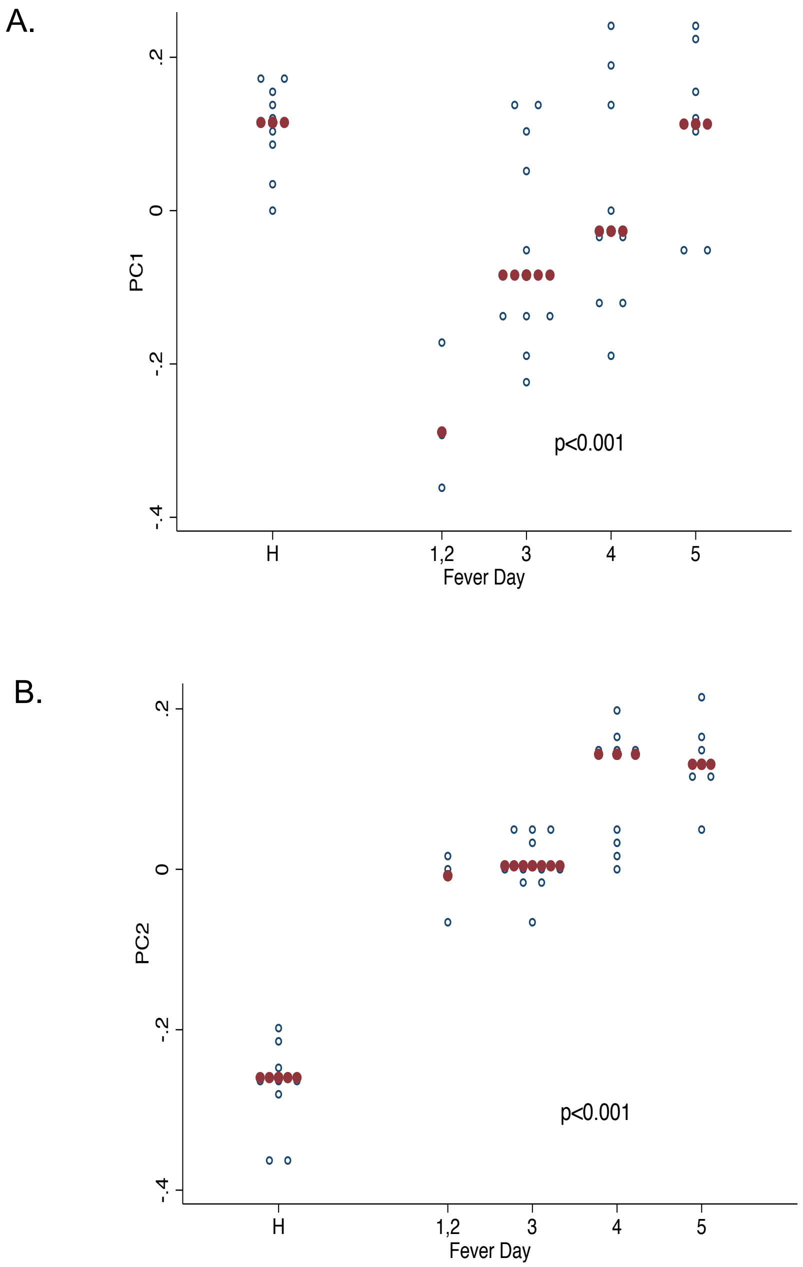
Supplementary Figure 1. Differences in transcript abundance in vaccinees and placebo recipients. A) Post-vaccination changes in transcript abundance in 8 vaccinees were compared to changes in 4 placebo recipients at each time-point following vaccination. Significant changes had a false discovery rate (FDR) of <1%, and a minimum 2-fold average difference in the two comparison groups. B) Maximum fold-change in transcript abundance for the 286 transcripts changing post-vaccination. Transcripts that differed significantly in vaccinees and placebo recipients are marked in red.



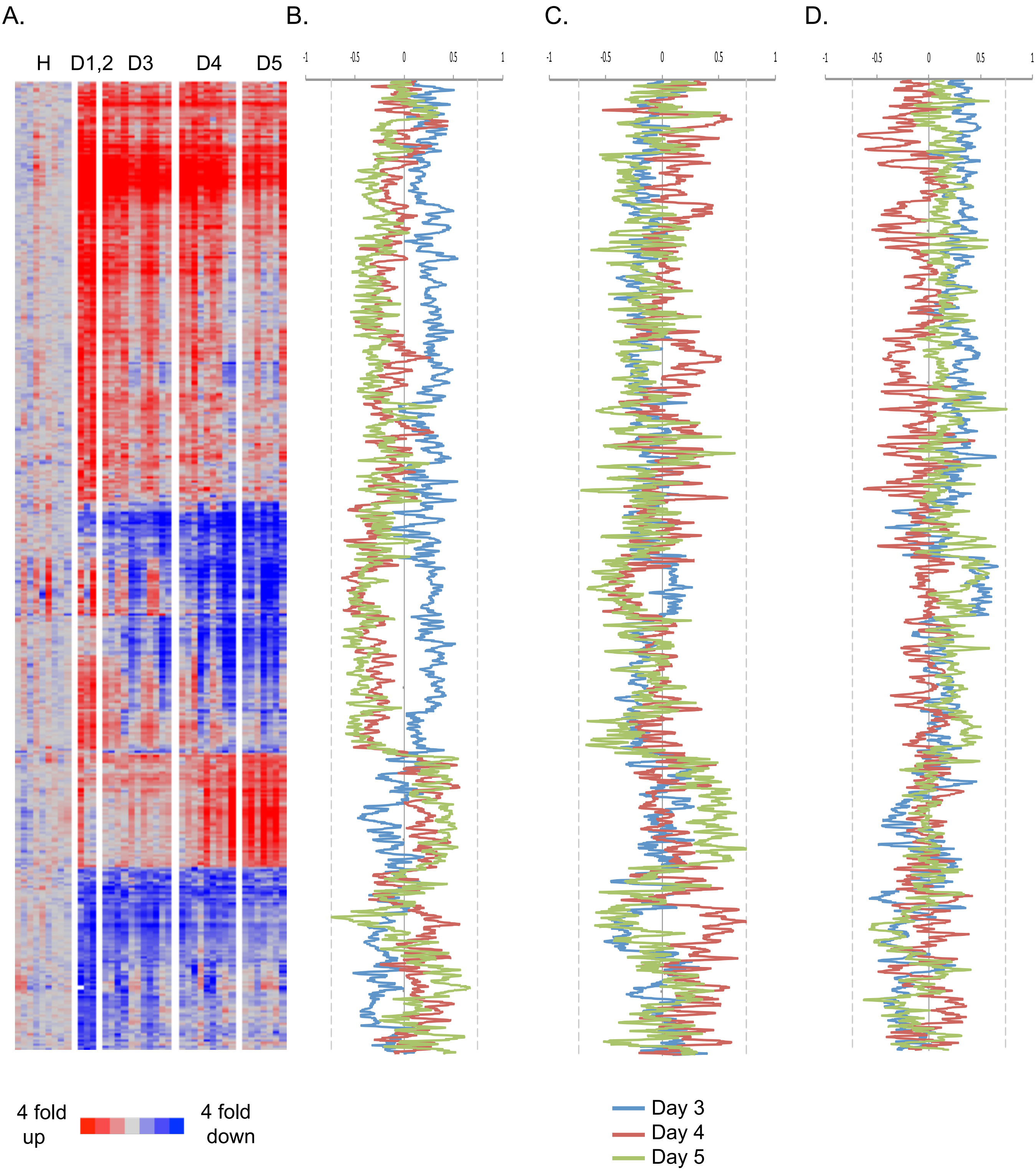
Supplementary Figure 2. Temporal patterns in transcript abundance after vaccination. Transcripts changing significantly in abundance on at least one day post-vaccination were clustered using Short Time Expression Miner; see Methods for details. Models displayed had more transcripts than would be expected if assignment were random; two models with similar temporal patterns (r>0.7) have the same background color. Red lines indicate individual transcripts; black lines represent the original model. Each model was assigned an identifying number, upper left. The number of transcripts assigned to each model is indicated at bottom left. Numbers above the colored models refer to gene clusters identified using hierarchical clustering as shown in Figure 2.



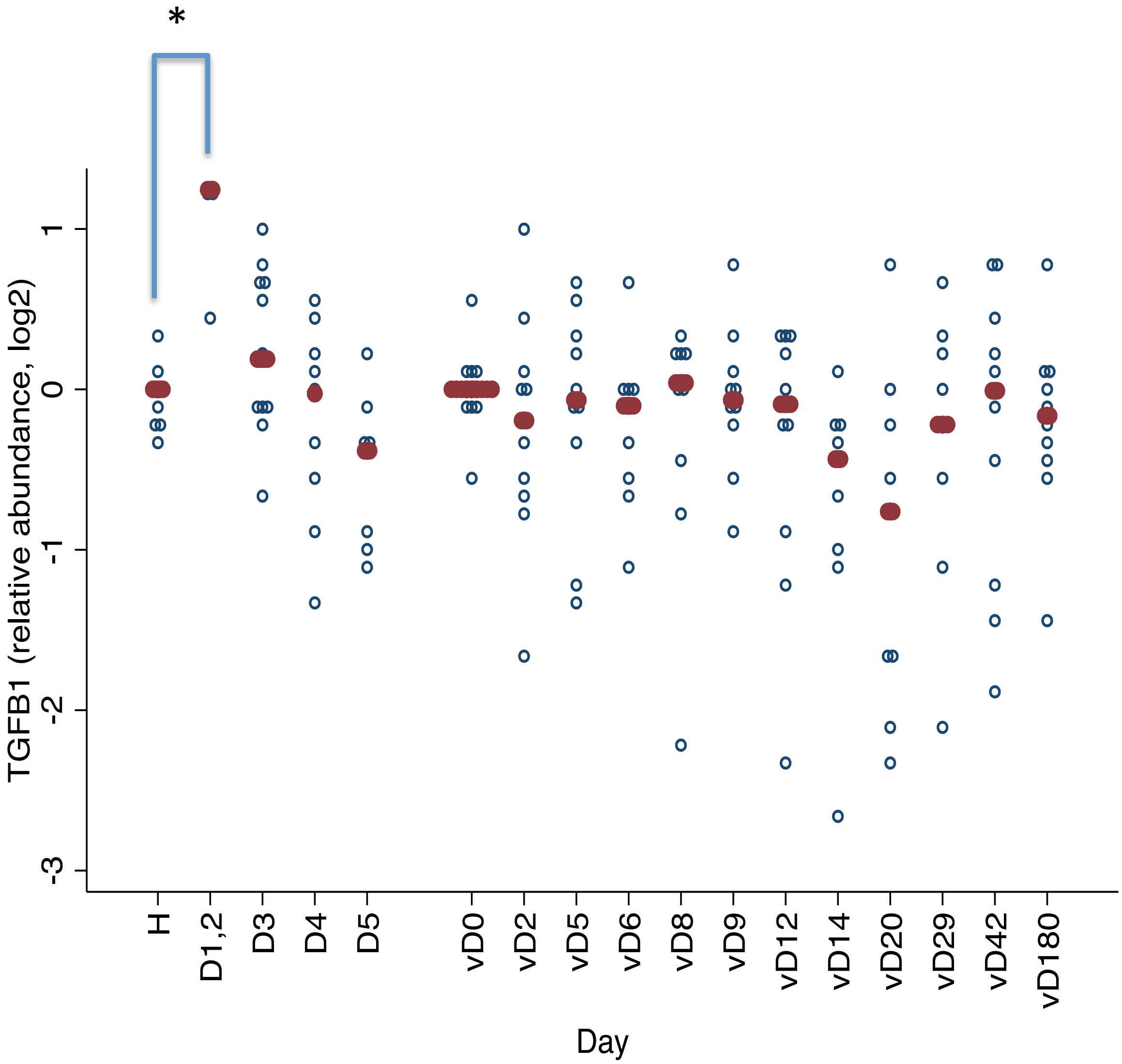
Supplementary Figure 3. Patterns of gene expression in dengue vaccinees, by subject. Hierarchical clustering of the 286 transcripts that changed significantly on at least one day. Triangles represent time-courses: white triangle indicates the days on which transcript abundance showed a significant change; grey triangle shows average fold change in transcript abundance for responders; blue triangles show fold change in transcript abundance for each vaccinee; yellow triangles show fold change in transcript abundance for each placebo recipient. Lines and numbers on right mark clusters of co-expressed genes described in text and Figure 2. Asterisk marks the one vaccinee who did not develop neutralizing antibodies.



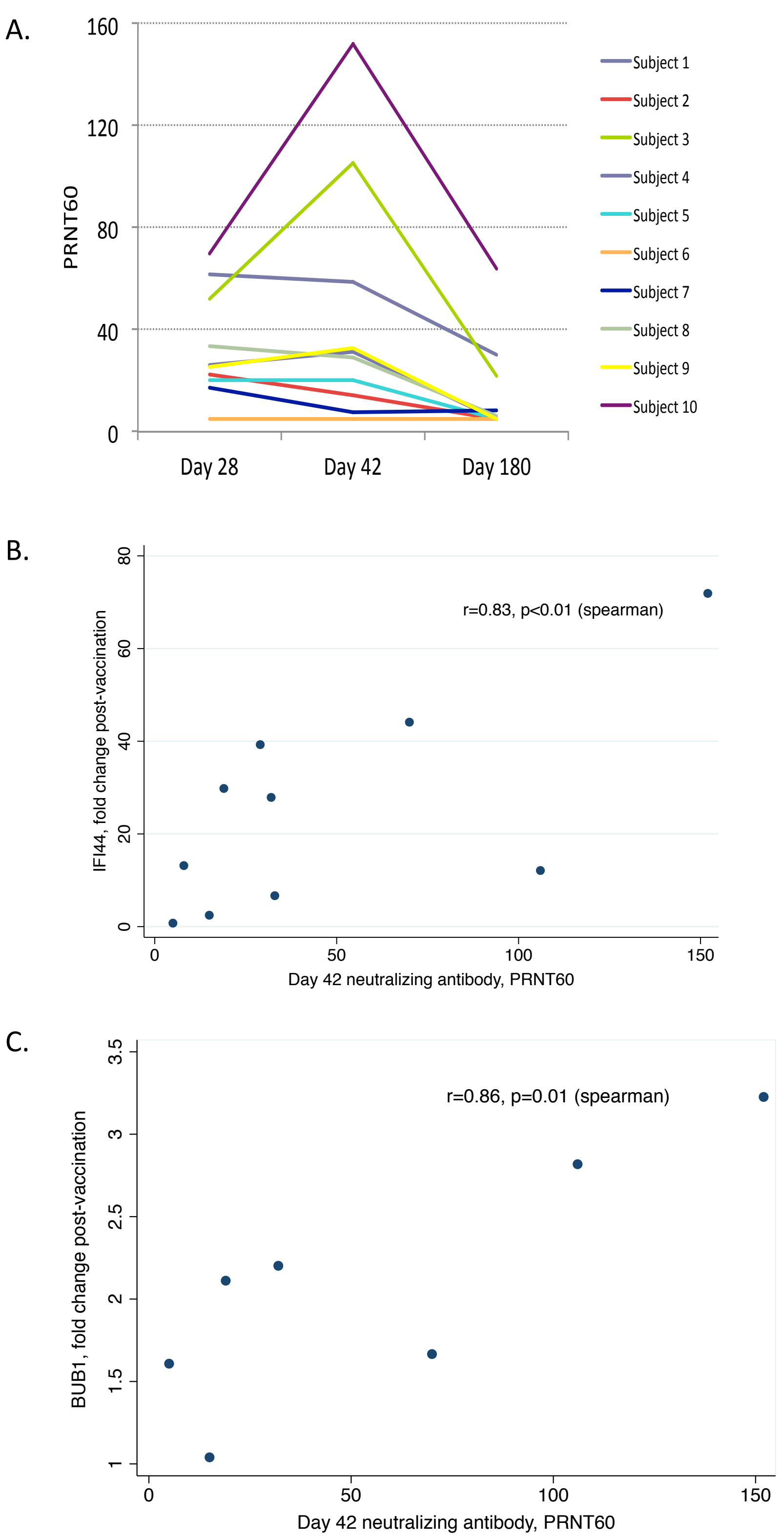
Supplementary Figure 4. Day of fever is associated with variation in the transcriptional response to DENV infection. Principal components analysis of the transcripts with the highest variance in the dataset (top 10%). A) Principal Component 1. B) Principal Component 2. Red dots mark median level by day. P-value indicates significant trend across days. Trend significance calculated using an extension of the Wilcoxon rank-sum test; healthy samples (H) included only for reference.



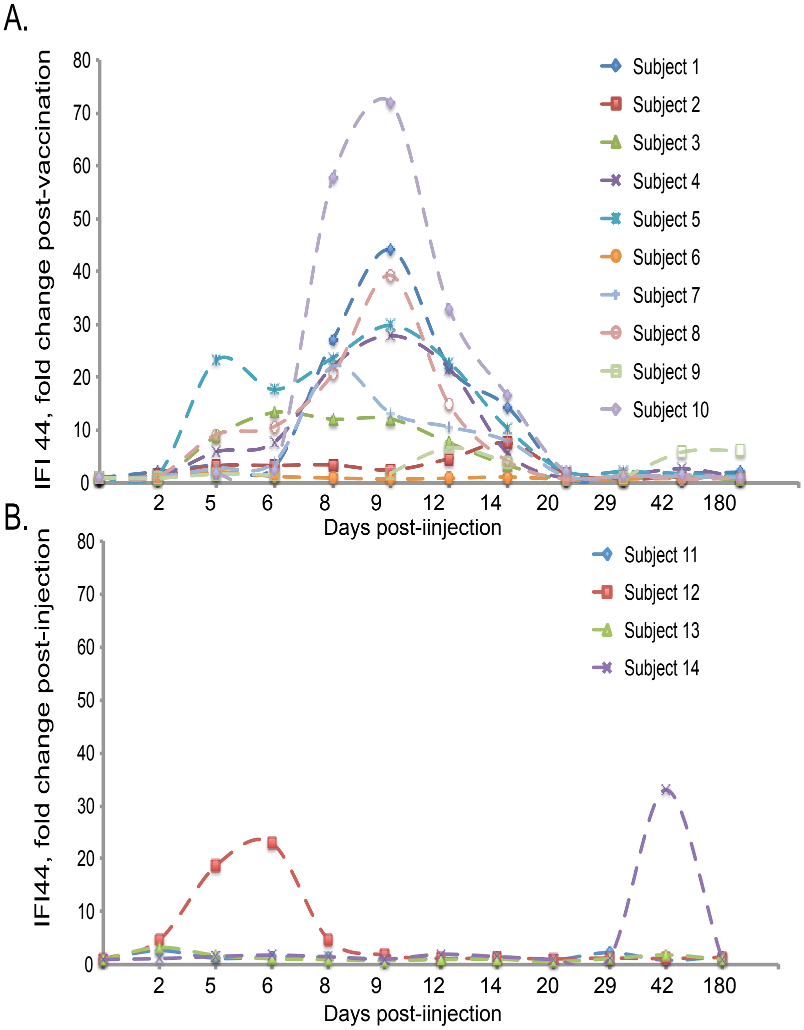
Supplementary Figure 5. Transcript abundance during natural infection. A) Relative abundance of the 3,210 transcripts (rows, hierarchically clustered by similarity in temporal patterns) that differed significantly from healthy controls on at least one day of fever. Samples from dengue patients (columns) are sorted by day of fever. B,C) Spearman correlation with convalescent and 3 month neutralizing antibody titer, respectively. D) Spearman correlation with viral load measured on the same day as gene expression. Correlations use a moving window of size 9. Dotted lines mark $p<0.01$.



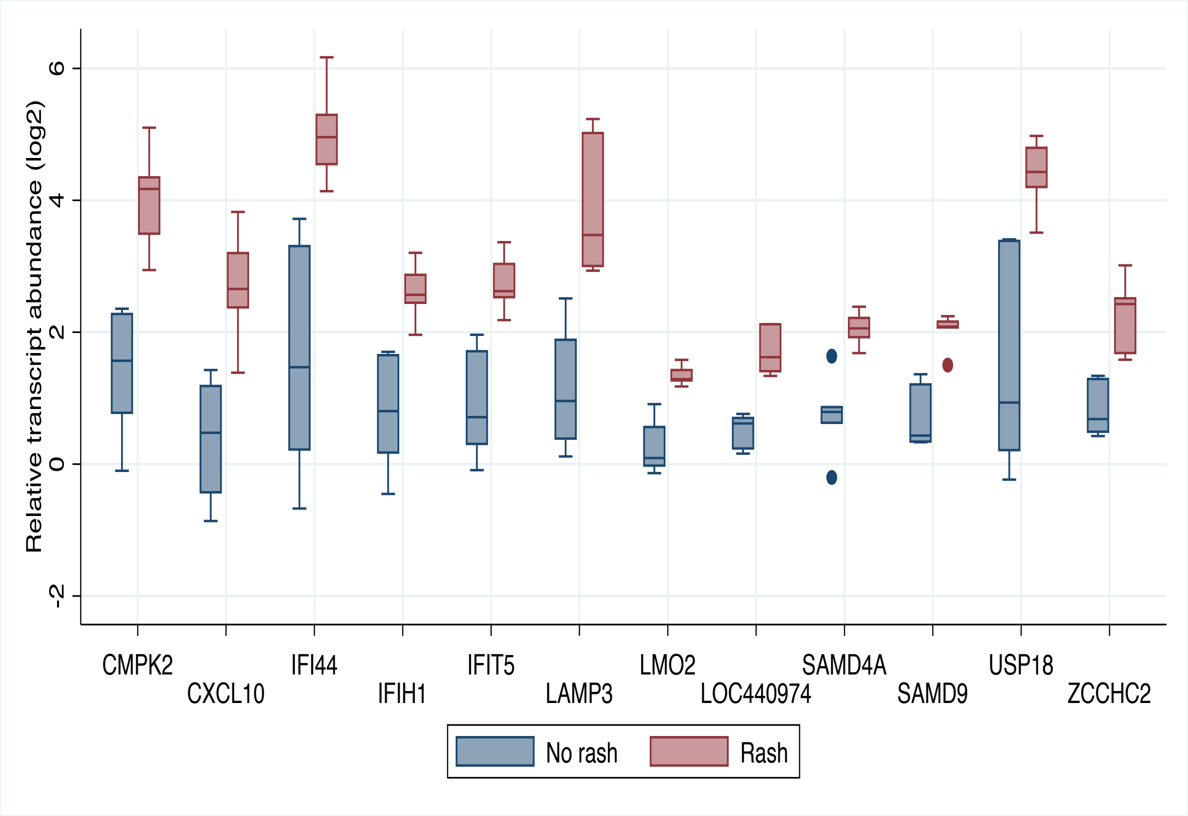
Supplementary Figure 6. TGFB1 transcript abundance in natural infection and vaccination. Blue circles represent individual samples; red dots represent median levels by day. H, healthy controls; "D" indicates day of fever for infected individuals; "vD" indicates days post-vaccination. Asterisk (*), p<0.01.



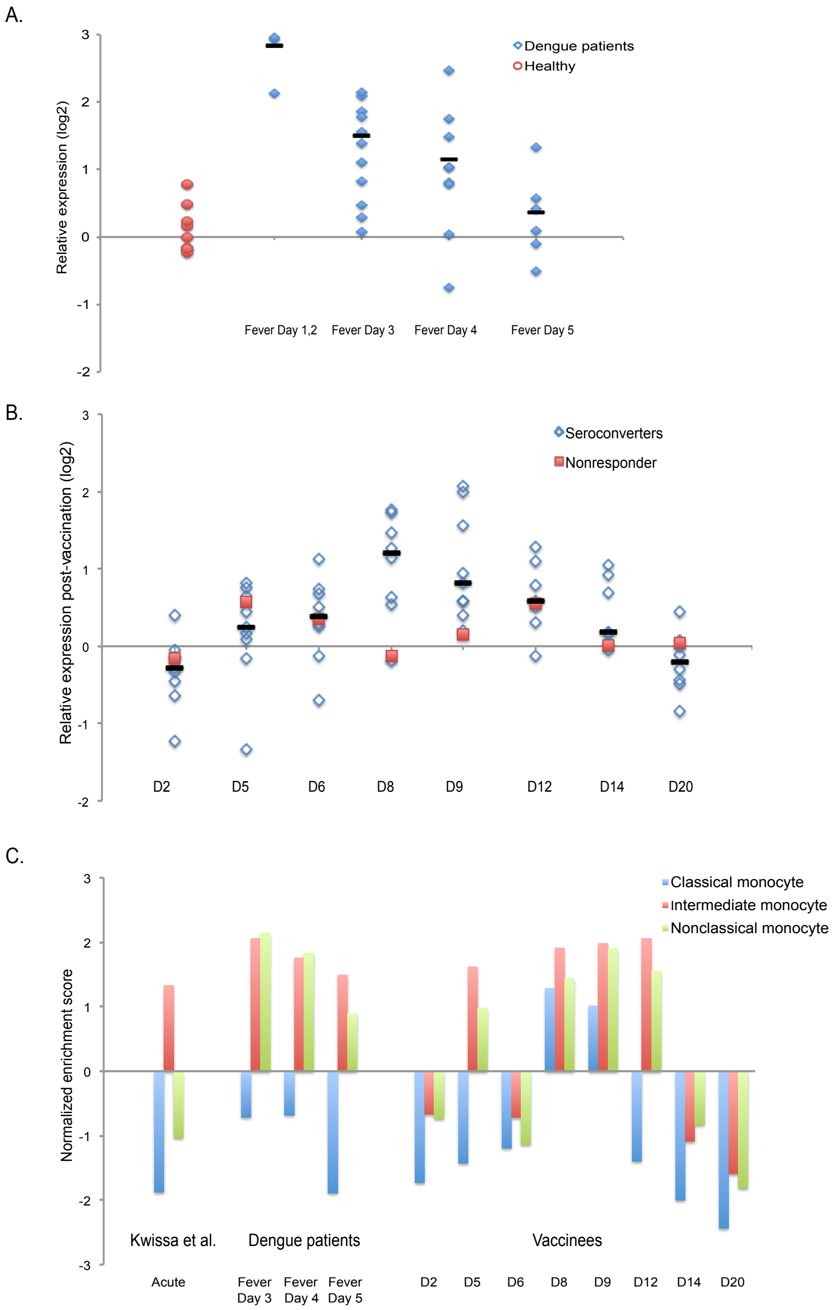
Supplementary Figure 7. Correlation of DENV-3 neutralizing antibody titer and transcript abundance. A) Neutralizing antibody titers post-vaccination. PRNT60, (60%) plaque reduction neutralizing titer. B) IFI44 transcript abundance on day 9 post-vaccination vs. Day 42 NAb titer C) BUB1 transcript abundance on day 14 post-vaccination vs Day 42 NAb titer



Supplementary Figure 8. IFI44 transcript levels in A) vaccinees and B) placebo recipients, by post-vaccination day. Y-axis indicates fold-change in transcript abundance relative to pre-vaccination.



Supplementary Figure 9. Transcripts in vaccinees associated with subsequent development of a maculopapular rash. Boxes define interquartile range (IQR); whiskers are set at 1.5x the IQR; dots indicate outlying values.



Supplementary Figure 10. Monocyte-associated gene expression after DENV infection and vaccination. A) Change in TNFSF13B (aka BAFF) transcript abundance post-vaccination. B) TNFSF13B transcript abundance in dengue patients and healthy controls. Black bars mark median level on each day. C) Normalized enrichment score for gene-sets associated with three monocyte subsets as defined by Wong et al. (36). Data for Kwissa et al. (19) were obtained at NCBI (GEO dataset GDS5093). GEO2R was used to compare samples from acute dengue patients with healthy controls, and the resulting ordered list of genes was downloaded for GSEA analysis.