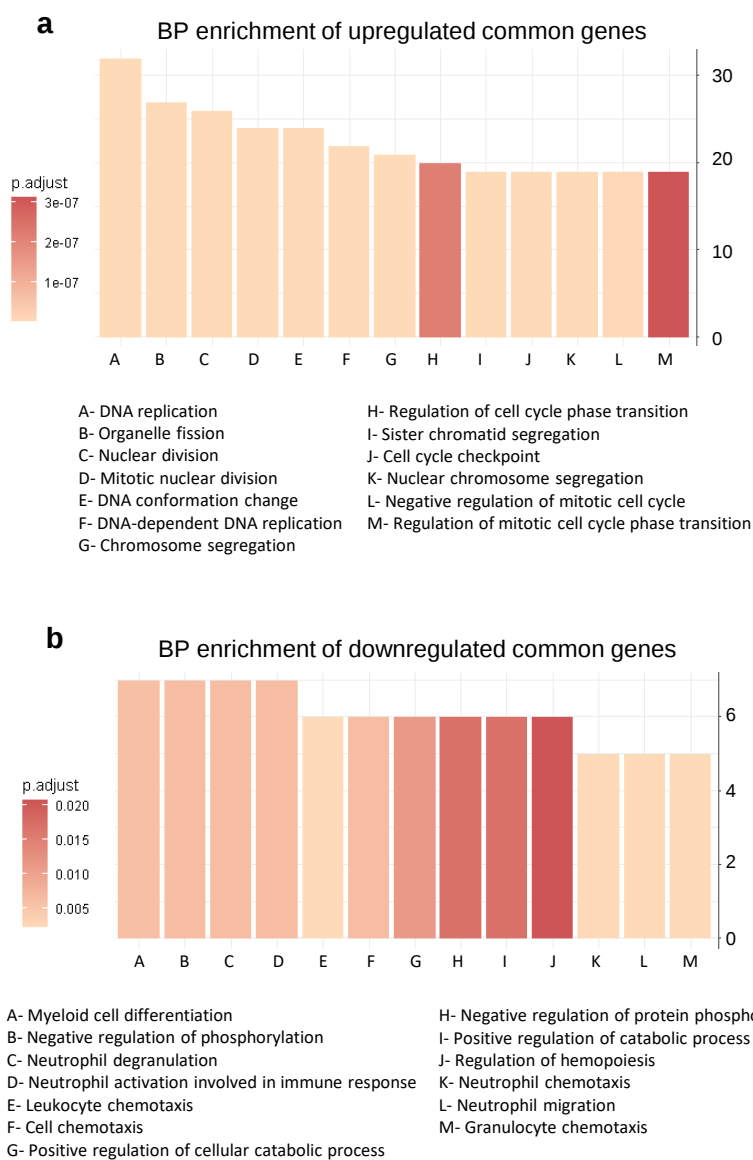
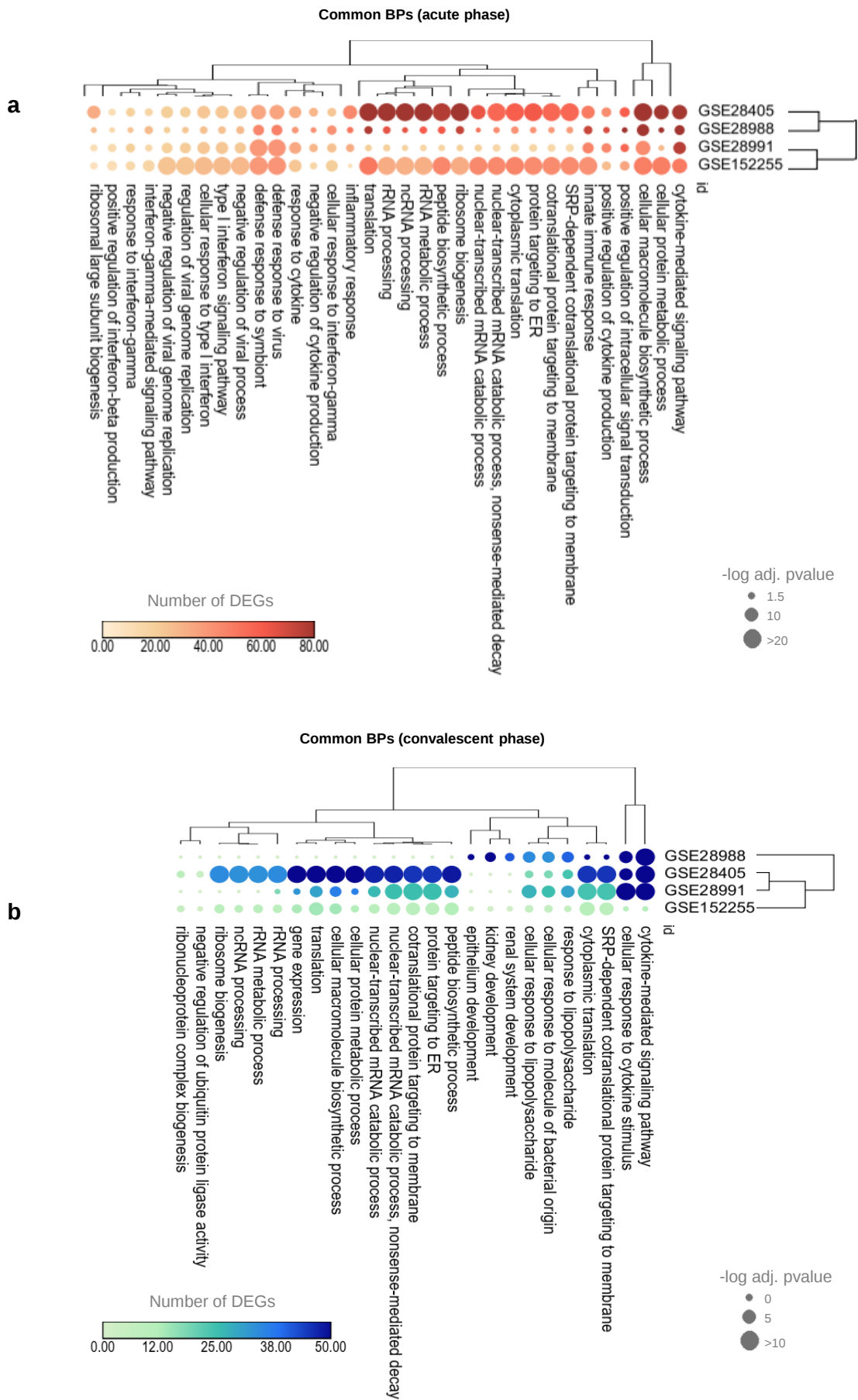
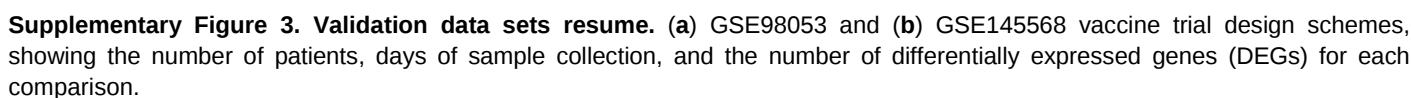


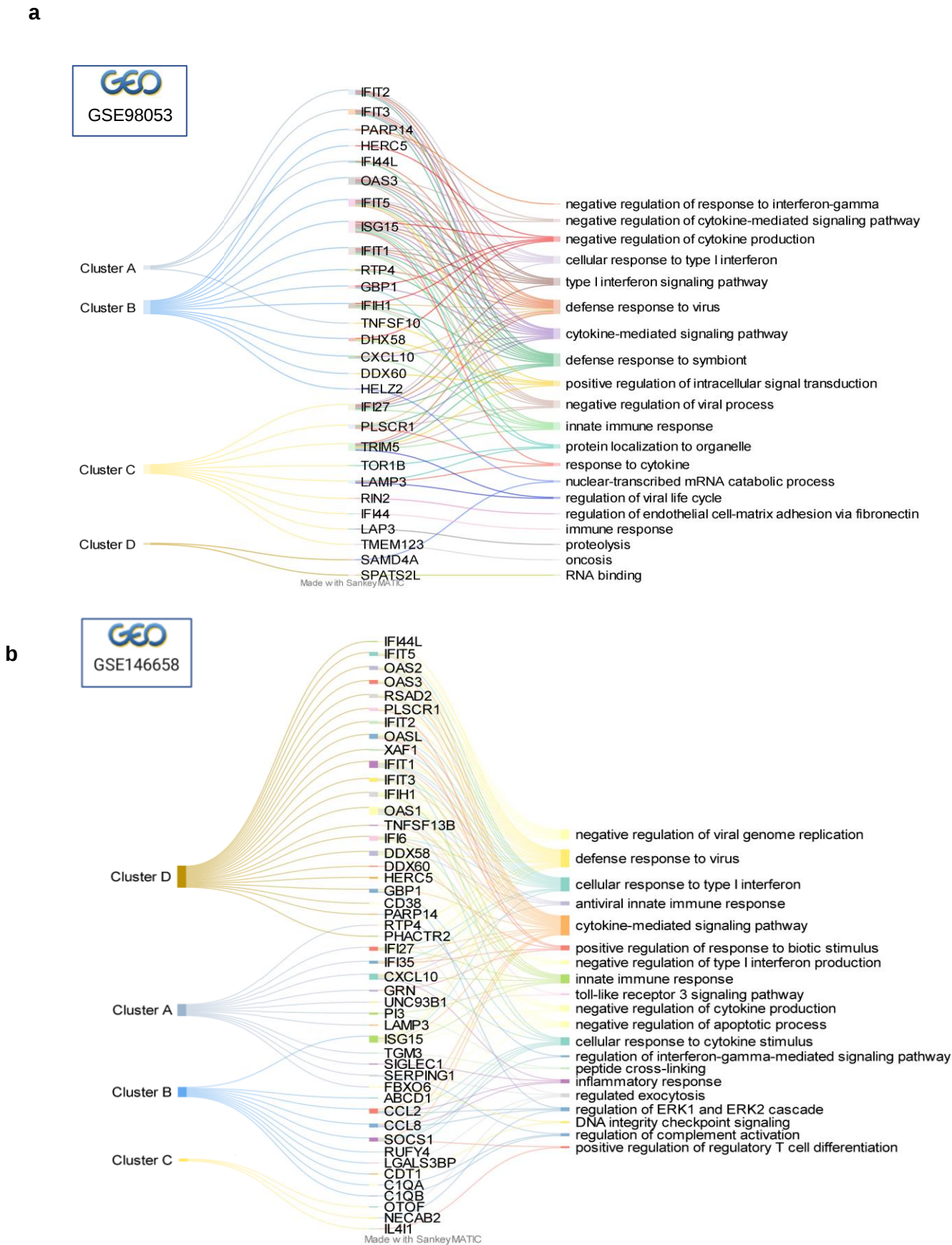


Supplementary Figure 1. Biological processes enriched by the common differentially expressed genes between the dengue acute phase in natural infection. Barplot of biological processes (BPs) enriched by the (a) 164 common up-regulated and (b) 48 common down-regulated DEGs during the acute phase (Suppl.Tables S7-8). The bar color denotes the adjusted p-value of enriched pathways. Graphs were created using the Cluster Profiler R package.

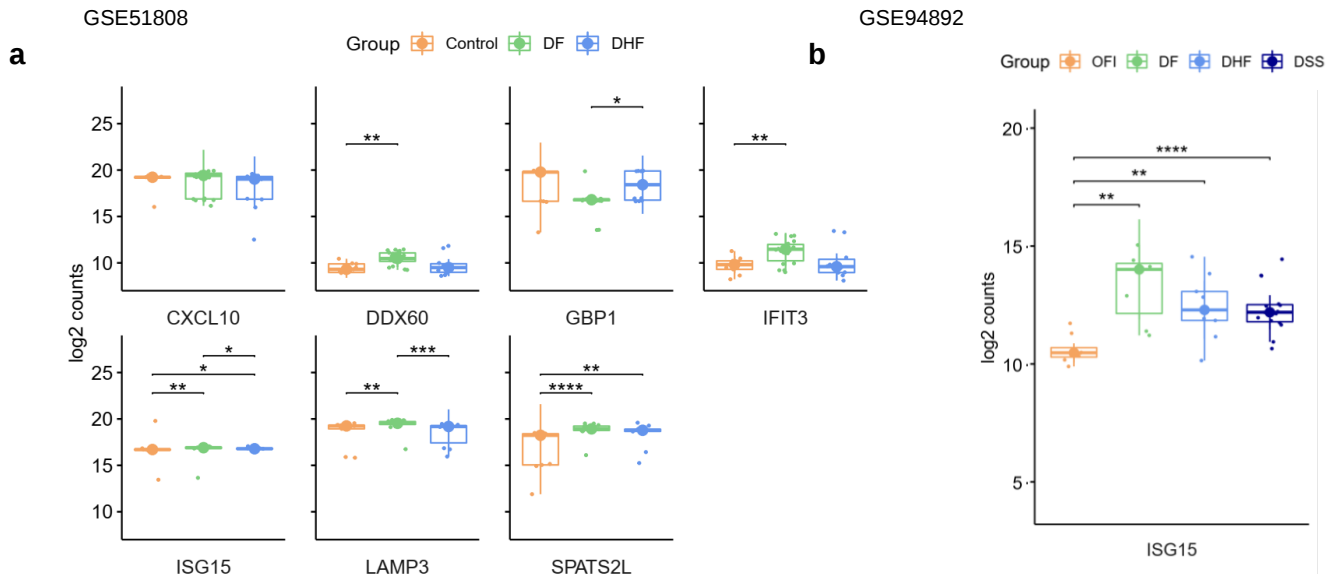


Supplementary Figure 2. Common enriched biological processes between NDI and DVT1 during acute and convalescent phases. (a-b) Bubble heatmaps with hierarchical clusters by Euclidian distance of common biological processes (BP) in at least two data sets across NDI (GSE28405, GSE28988, GSE28991) and DVT1 (GSE152255) data sets during (a) acute (days 4-8 versus day 0-3) and (b) convalescent (days 15-28 versus days 0-3) phases after infections. Bubble sizes are proportional to the -log10 adjusted p-value and colors according to the number of DEGs by BP term across the data sets. The complete lists of significant enriched BPs are provided in **Suppl. Tables S14 and S15**.





Supplementary Figure 4. Enrichment of genes overlapping in NDI/DVT1 and additional vaccine trials DVT2 and DVT3. (a-b) Alluvial diagrams of 28 common genes from NDI/DVT1-DVT2 (a) and 60 genes from NDI/DVT2-DVT3 (b) separated by clusters, showing their functional enrichment. BPs were obtained using the enrichR⁴ web tool. Complete enrichment tables are available in **Suppl. Tables S17 and S19**.



Supplementary Figure 5. Expression pattern of genes classified as most predictors of dengue severity across disease severity groups from other data sets. (a-b) Boxplots showing log₂ counts of variables classified as predictors for disease severity in the random forest model from groups of the natural dengue infections (NDI) data set **(a)** GSE51808 (Control, DF, and DHF, n=9, n=18, and n=10, respectively) and **(b)** GSE94892 (OFI, DF, DHF, and DSS, n=8, n=7, n=9, and n=15, respectively). All statistics were obtained by wilcoxon.test: * p value < 0.05; ** p value < 0.01; *** p value < 0.001; **** p value < 0.0001. DF: Dengue Fever; DHF: Dengue Hemorrhagic Fever; DSS: Dengue Shock Syndrome; OFI: Other Febrile Illness; Control: healthy controls