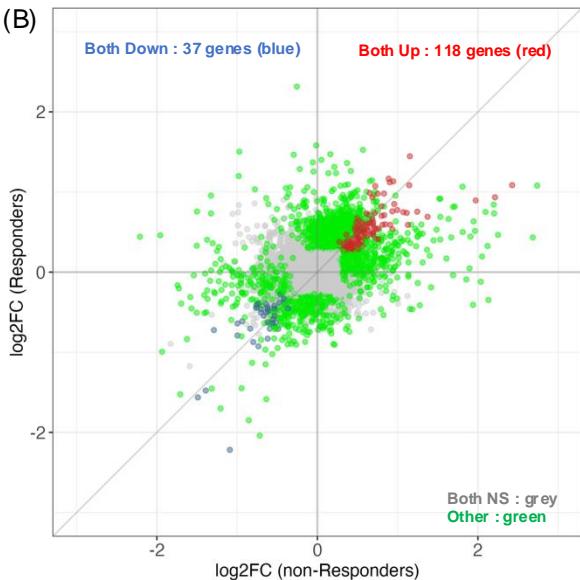
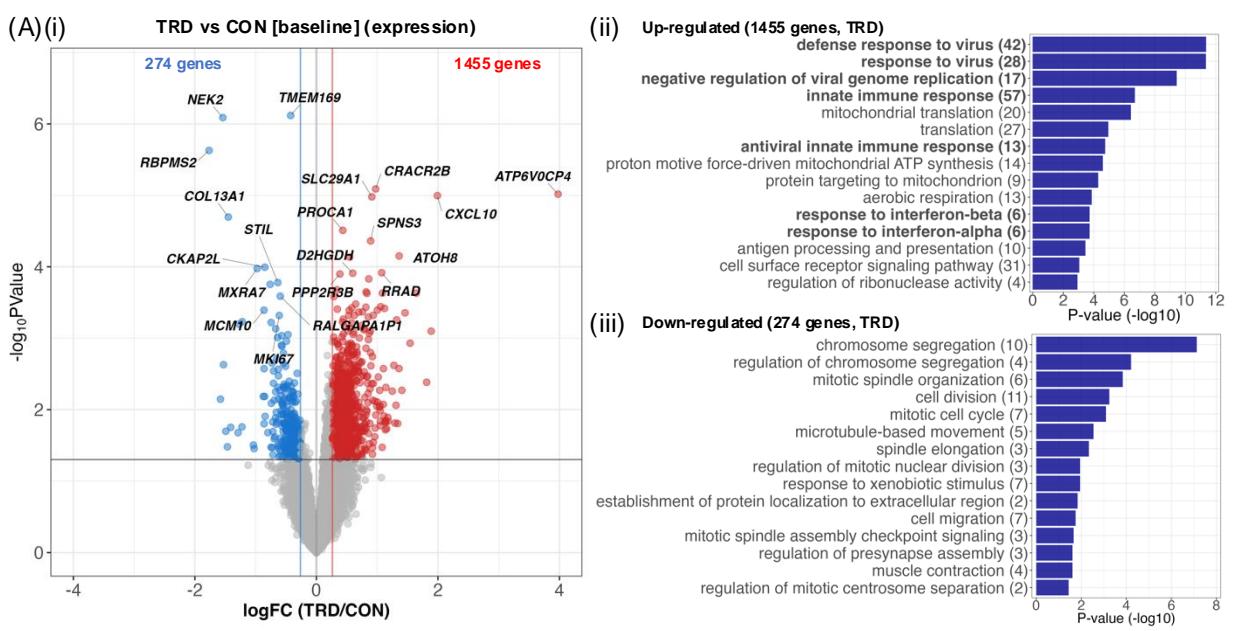
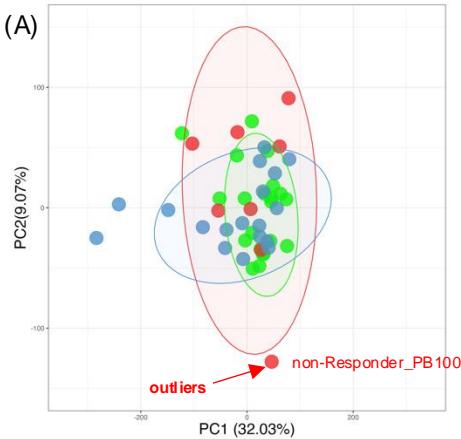


# **Supplementary figures**

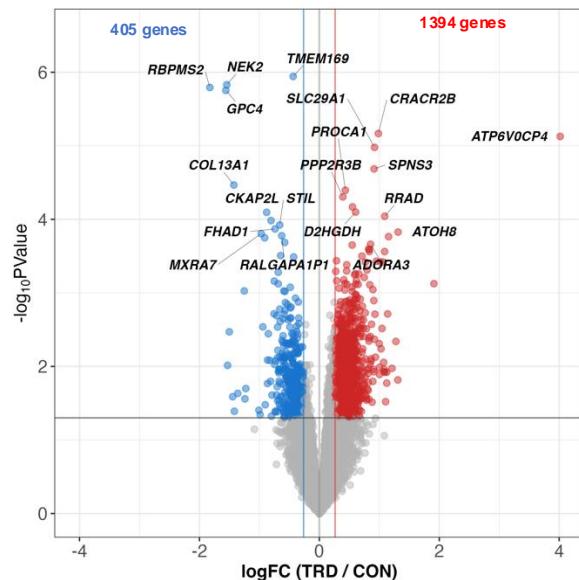


**Fig. S1. RNA expression comparison and GO enrichment analysis**

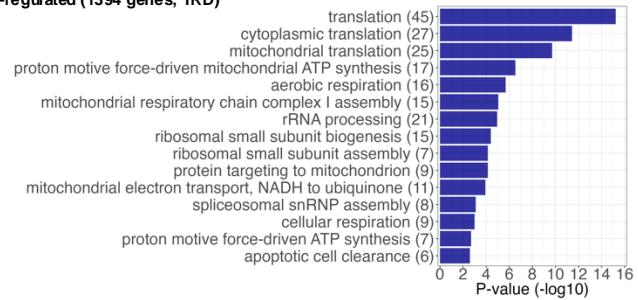
(A) DEGs analysis between TRD and CON (baseline). (i) Volcano plots of RNA expression comparisons are shown. The vertical axis shows  $-\log_{10} P$ -values and the horizontal axis shows  $\log_2$  fold-change. Genes showing significant changes are shown in red (up-regulation) and blue (down-regulation) (threshold:  $P < 0.05$  and fold-change  $> 1.2$ ). Symbols for the top 10 genes with the lowest  $P$ -values among the respective genes that were up- and down-regulated are shown. (ii, iii) GO enrichment analysis using up-regulated (ii) and down-regulated (iii) genes in TRD. Horizontal axis indicates  $-\log_{10} P$ -values. Vertical axis indicates the enriched GO term and the number of genes corresponding to that term in parentheses. Bold indicate GO terms related to innate immunity. (B) Scatterplot of fold-change in expression between non-responders and responders. The vertical axis shows  $-\log_2 FC$  of non-responders and the horizontal axis shows  $\log_2 FC$  of responders group. Red is both significantly up-regulated; Blue is both significantly down-regulated; Gray is both not significantly changed; Green either showed significant change.



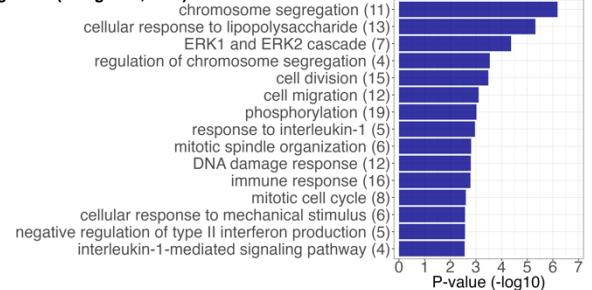
(B) (i) TRD vs CON [baseline] (expression)



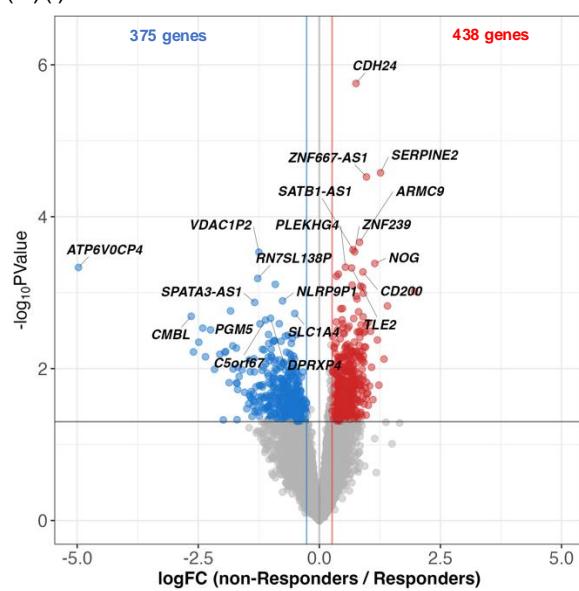
(ii) Up-regulated (1394 genes, TRD)



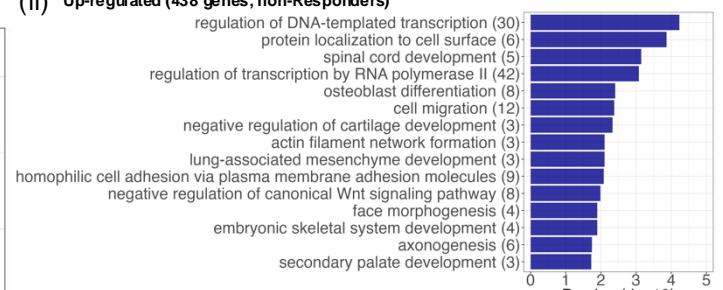
(iii) Down-regulated (405 genes, TRD)



(C) (i) non-Responders vs Responders [baseline] (expression)



(ii) Up-regulated (438 genes, non-Responders)



(iii) Down-regulated (375 genes, non-Responders)

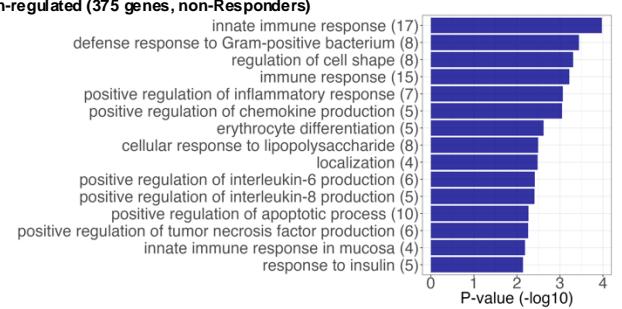
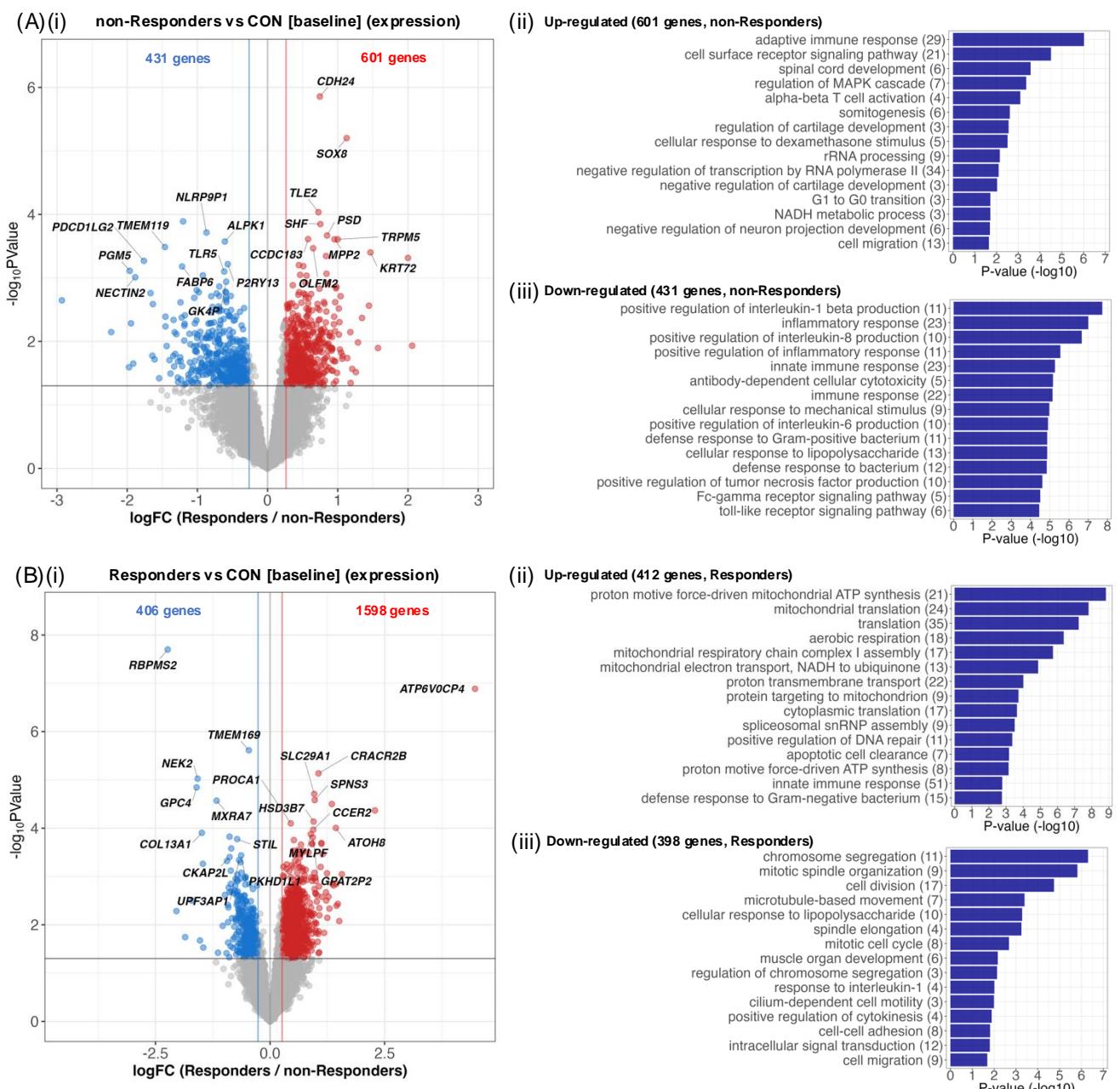


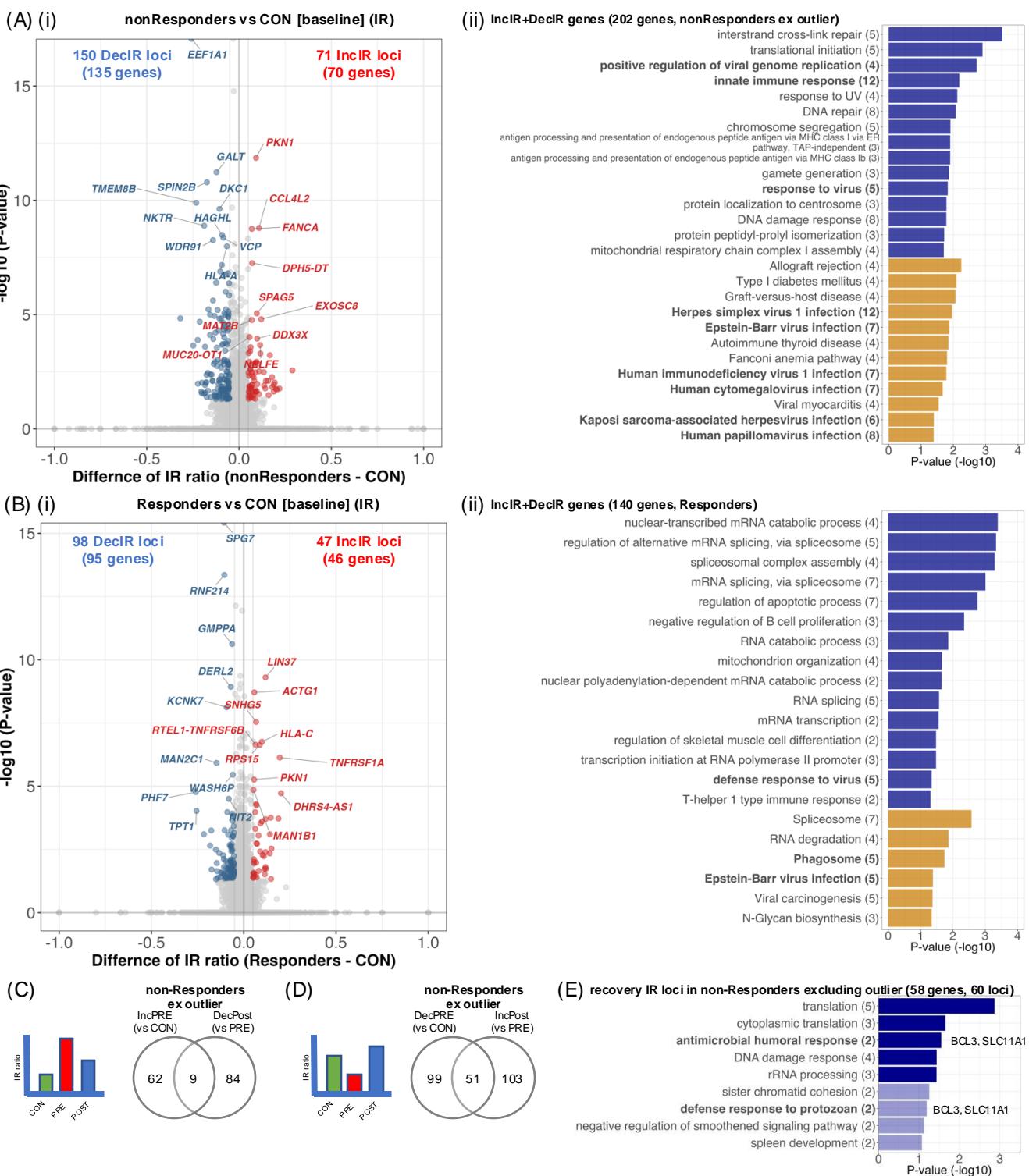
Fig. S2. RNA expression comparison and GO enrichment analysis excluding outliers (1)

(A) Principal component analysis (PCA) plots based on gene expression of CON, non-responders and responders group in baseline. Green: CON group, Red: non-responders group, Blue: responders group. Circles were drawn by calculating probability ellipse on R. (B) DEGs analysis between TRD group excluding outliers and CON. (i) Volcano plots of RNA expression comparisons are shown. (ii, iii) GO enrichment analysis using up-regulated (ii) and down-regulated (iii) genes in TRD excluding outliers. (C) DEGs analysis between non-responders group excluding outliers and responders. (i) Volcano plots of RNA expression comparisons are shown. (ii, iii) GO enrichment analysis using up-regulated (ii) and down-regulated (iii) genes in responders excluding outliers.



**Fig. S3. RNA expression comparison and GO enrichment analysis excluding outlier (2)**

(A) DEGs analysis between non-responders excluding outlier and CON (baseline). (i) Volcano plots of RNA expression comparisons are shown. The vertical axis shows  $-\log_{10} P$ -values and the horizontal axis shows  $\log_2$  fold-change. Genes showing significant changes are shown in red (up-regulation) and blue (down-regulation) (threshold:  $P < 0.05$  and fold-change  $> 1.2$ ). Symbols for the top 10 genes with the lowest  $P$ -values among the respective genes that were up- and down-regulated are shown. (ii, iii) GO enrichment analysis using up-regulated (ii) and down-regulated (iii) genes in POST. Horizontal axis indicates  $-\log_{10} P$ -values. Vertical axis indicates the enriched GO term and the number of genes corresponding to that term in parentheses. (B)(i, ii, iii) DEGs analysis between responders and CON (baseline).



**Fig. S4. IR comparison and GO enrichment analysis excluding outlier**

(A) Intron retention analysis between non-responders excluding outlier and CON (baseline). (i) Scatter plots of IR ratios comparisons are shown. The vertical axis shows  $-\log_{10} P$ -values and the horizontal axis shows difference of IR ratio ( $\Delta IR$ ). Genes showing significant changes are shown in red (InclR genes) and blue (DeclR genes) (threshold:  $P < 0.05$  and absolute  $\Delta IR > 0.05$ ). Symbols for the top 10 genes with the lowest  $P$ -values among the respective genes that were InclR and DeclR genes are shown. (ii) GO and KEGG enrichment analysis performed by merging InclR and DeclR genes. Horizontal axis indicates  $-\log_{10} P$ -values. Deep blue bars indicate GO terms and orange bars indicates KEGG pathway name. Vertical axis indicates the enriched GO/KEGG term and the number of genes corresponding to that term in parentheses. Bold indicate GO terms related to innate immunity. (B)(i, ii) Intron retention analysis between responders excluding outlier and CON (baseline). (C) Venn diagram comparing genes whose IR ratio is InclR loci in non-responders and DeclR loci by ketamine treatment (reverse V-shape). (D) Venn diagram comparing genes whose IR ratio is DeclR loci in non-responders and InclR loci by ketamine treatment (V-shape). (E) GO enrichment analysis performed by recovery IR genes. Horizontal axis indicates  $-\log_{10} P$ -values. Dark blue bars are GO terms with  $P$ -values  $< 0.05$ , light blue bars are those with no significant difference. Gene symbols indicate innate immunity related genes. Using 58 genes, including the recovered 60 IR loci in non-responders excluding outlier.