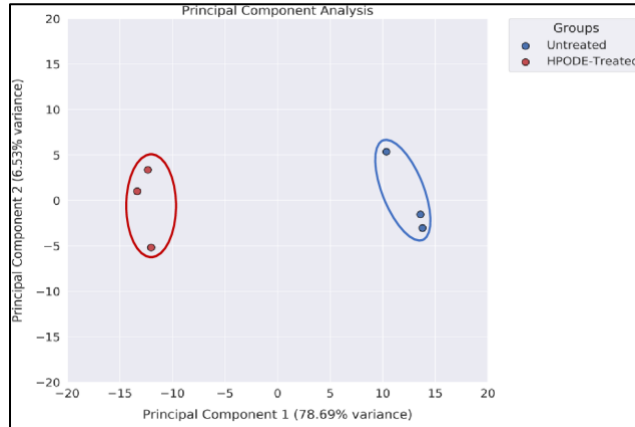
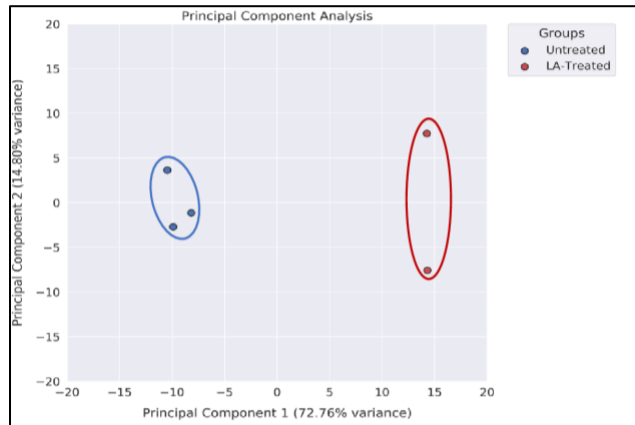


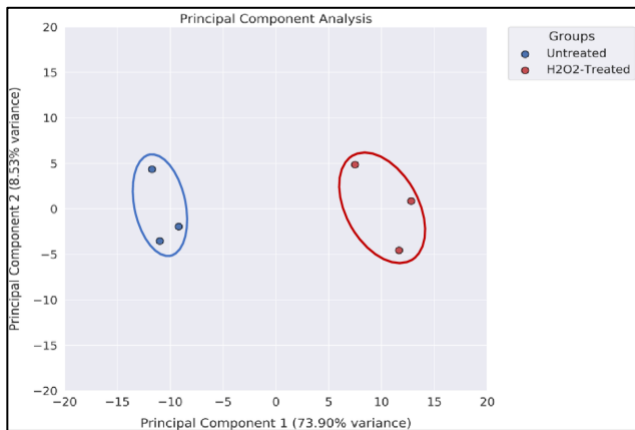
Figure S1. Leucomethylene blue (LMB) assay. LMB assay shows no significant difference (ns) in peroxide content before and after filter sterilization (FS) of 13-HPODE.



(a)



(b)



(c)

Figure S2. Principal component analysis (PCA). PCA shows distances between untreated and 13-HPODE-treated (a), LA-treated (b) or H₂O₂-treated (c) PDiff Caco-2 samples showing similarity based on treatment and good separation between untreated and treated groups.

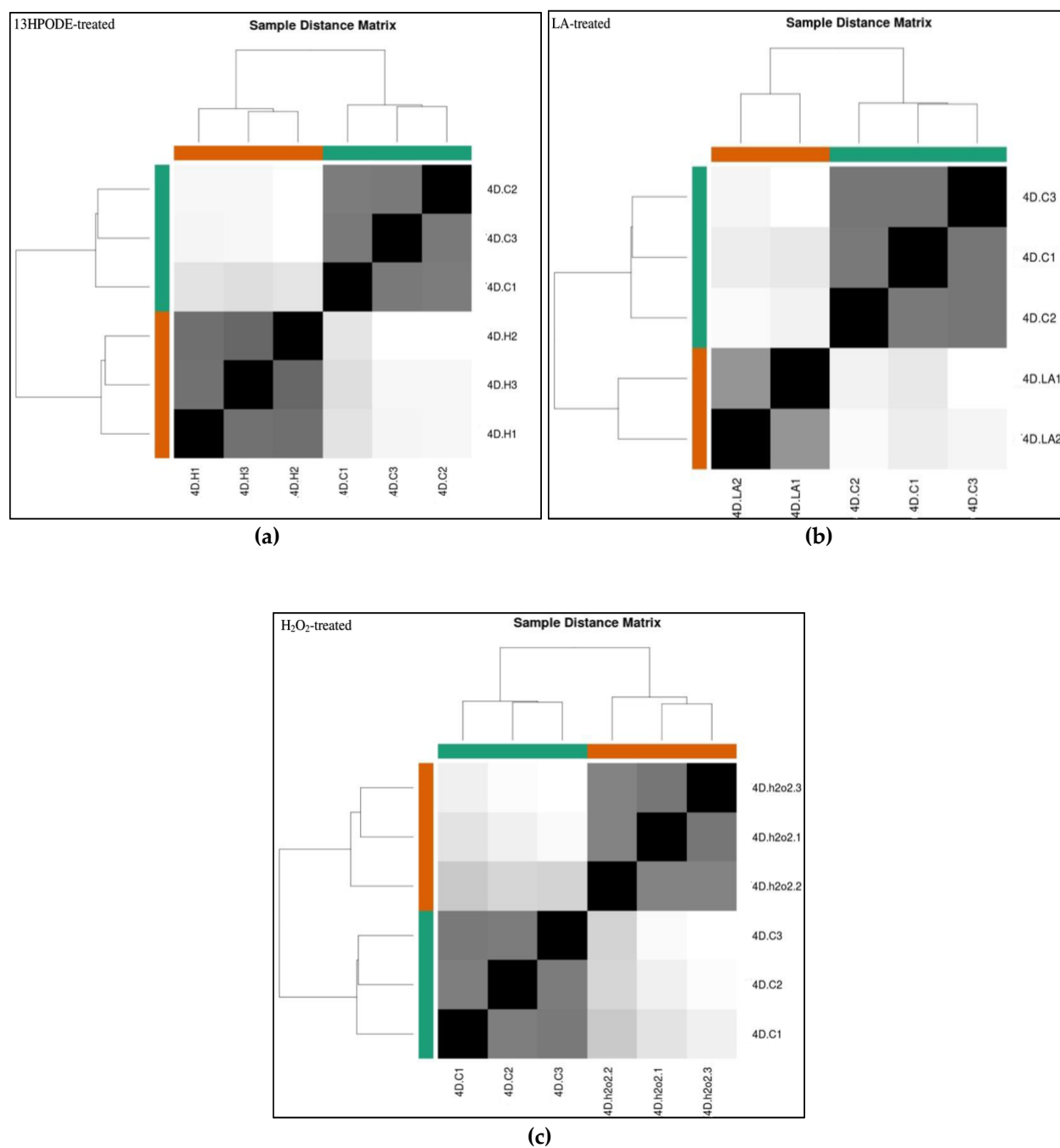
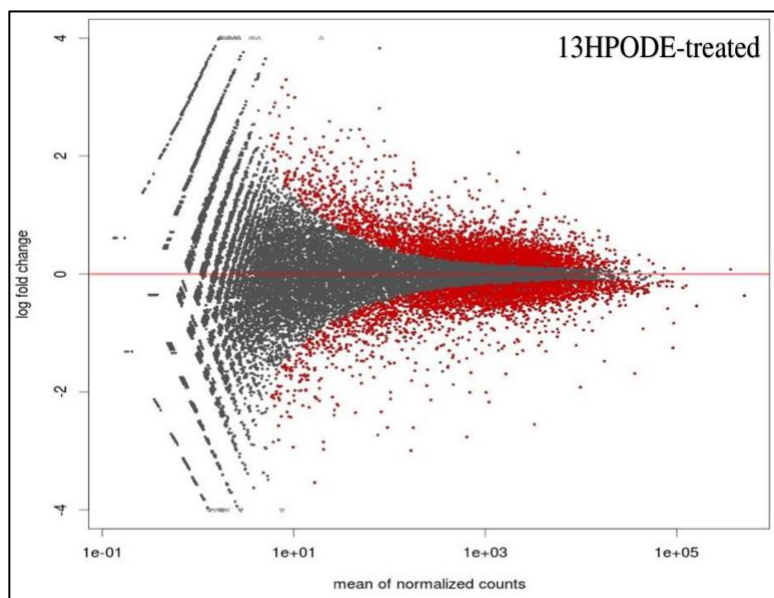
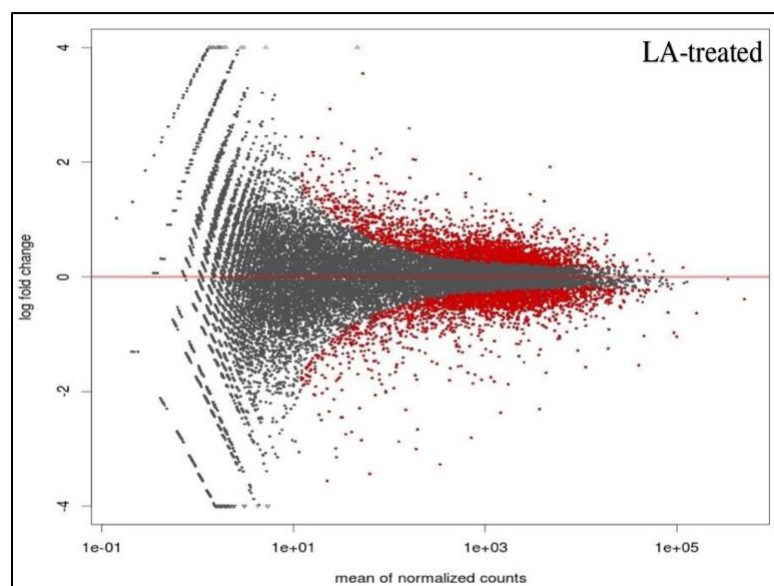


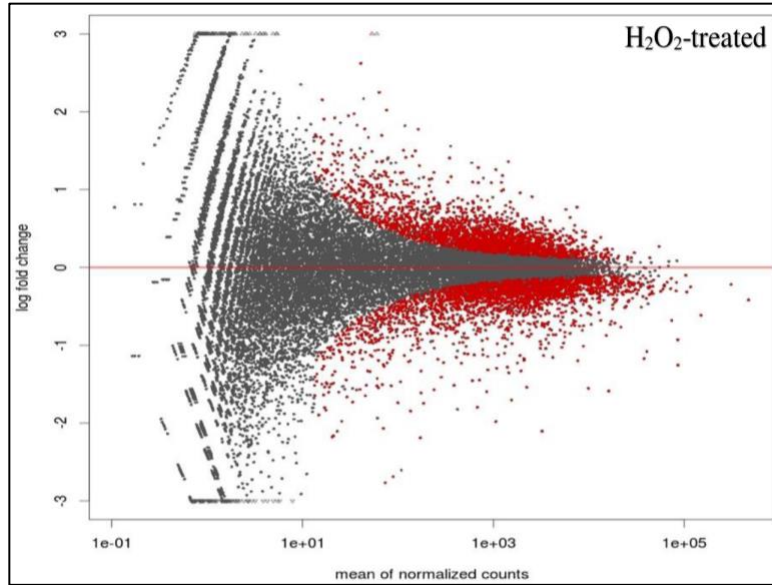
Figure S3. Sample-to-sample distance heatmaps generated by DESeq2. The heatmaps show similarity between Caco-2 samples of each group based on normalized gene expression. Samples are clustered by replicate. **(a)** 13-HPODE-treated (4D.H1, 4D.H2, 4D.H3); **(b)** LA-treated (4D.LA1, 4D.LA2); **(c)** H₂O₂-treated (4D.h2o2.1, 4D.h2o2.2, 4D.h2o2.3); Untreated controls (4D.C1, 4D.C2, 4D.C3).



(a)

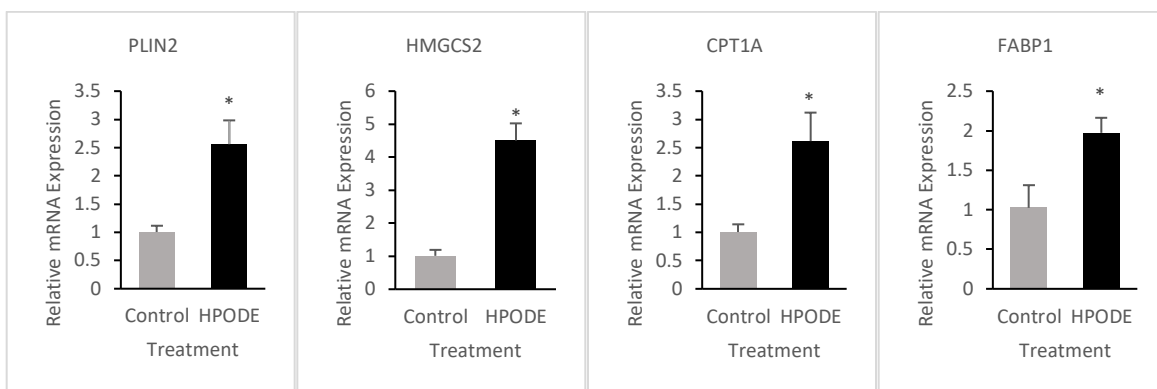


(b)



(c)

Figure S4. Log ratio vs. mean average (MA) plots of differentially expressed genes (DEGs) between untreated and treated PDiff Caco-2 cells. MA plots show DEGs (red dots; adjusted p-value < 0.05) between untreated PDiff Caco-2 cells and 13-HPODE-treated (a), LA-treated (b), or H₂O₂-treated (c) PDiff Caco-2 cells. x-axis represents the mean expression across untreated and treated cell groups, y-axis represents the log₂ fold change between untreated and treated groups.

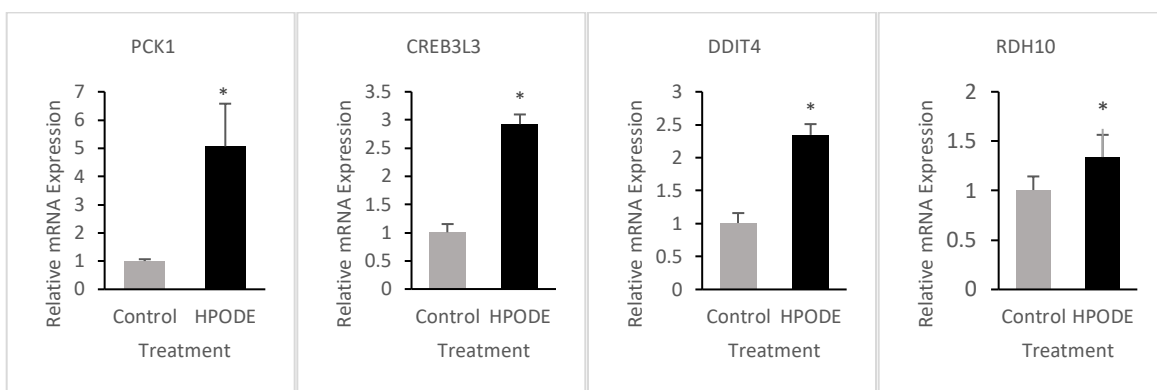


(a)

(b)

(c)

(d)

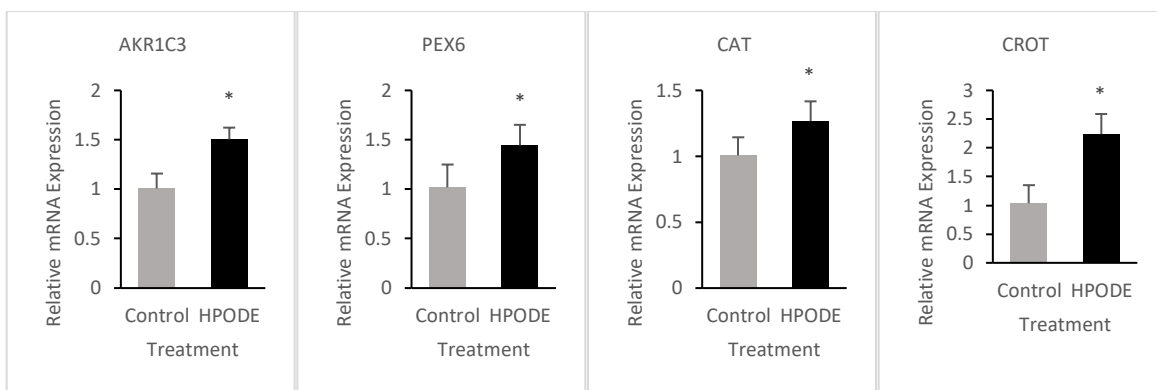


(e)

(f)

(g)

(h)



(i)

(j)

(k)

(l)

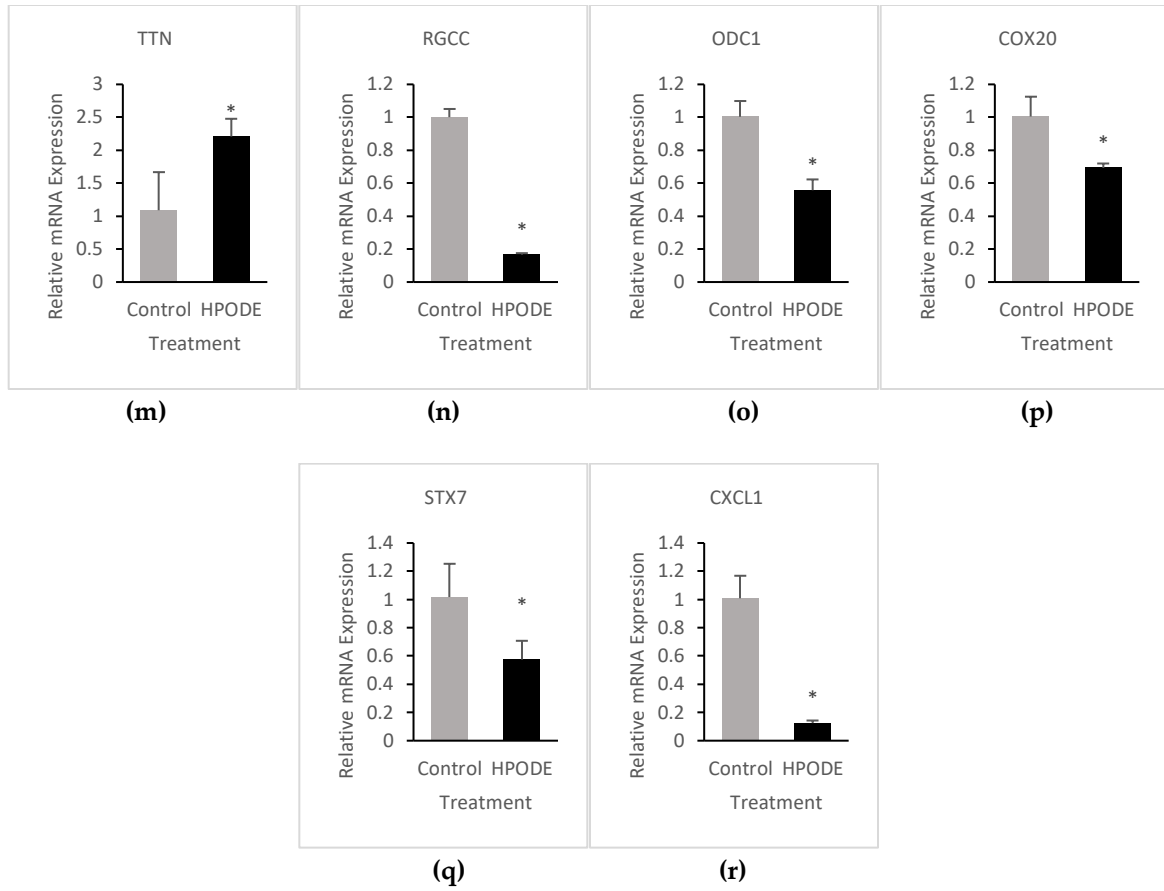


Figure S5. Quantitative RT-PCR validation of RNA-seq data in 13-HPODE-treated PDiff Caco-2 cells. qRT-PCR of DEGs from RNA-seq data. Relative mRNA expression levels in 13-HPODE-treated (HPODE) cells are presented with statistical significance of $*p < 0.05$ relative to untreated (control) cells. Results were normalized to *GAPDH*.

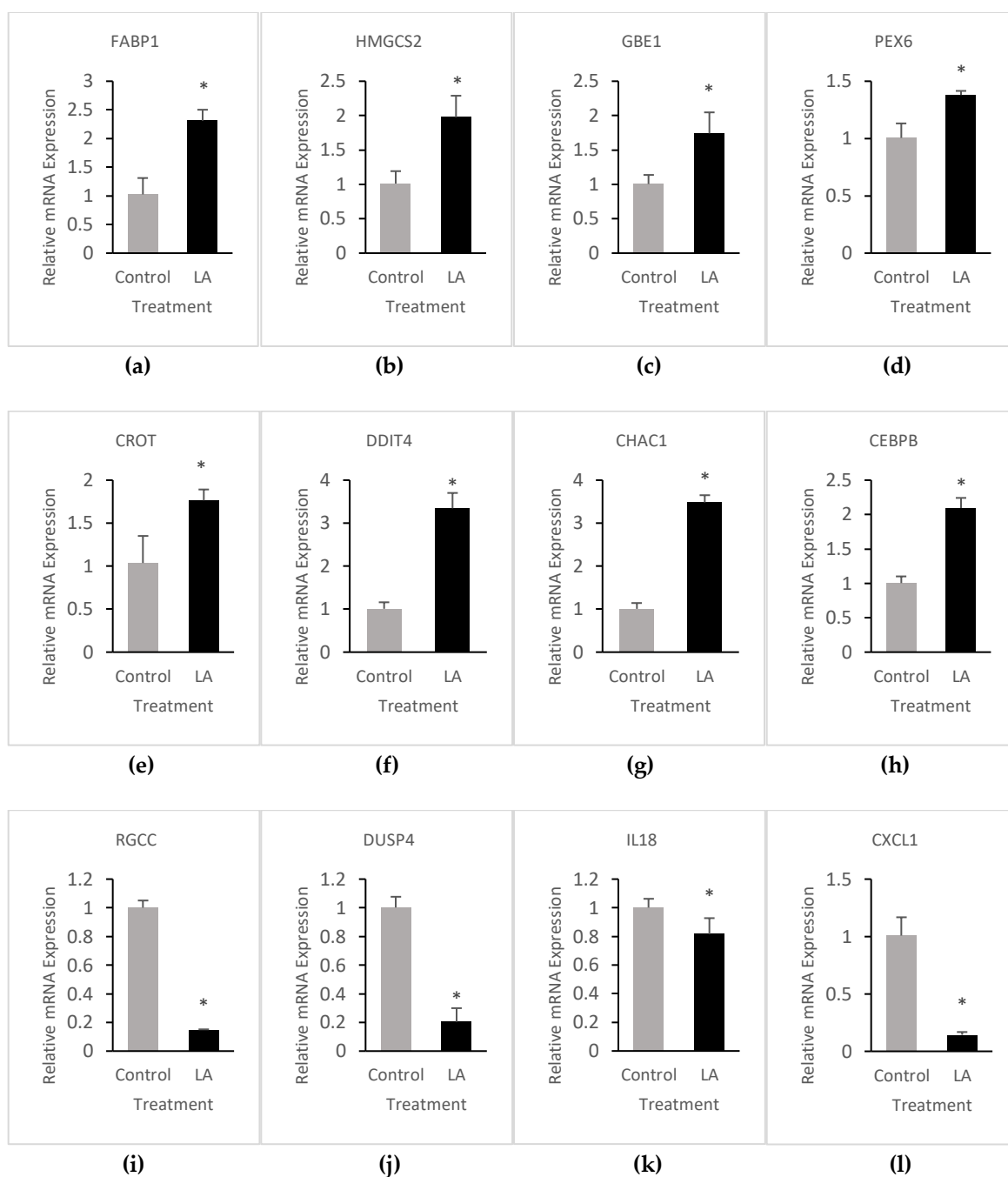


Figure S6. Quantitative RT-PCR validation of RNA-seq data in LA-treated PDiff Caco-2 cells. qRT-PCR of DEGs from RNA-seq data. Relative mRNA expression levels in LA-treated (LA) cells are presented with statistical significance of $*p < 0.05$ relative to untreated (control) cells. Results were normalized to *GAPDH*.

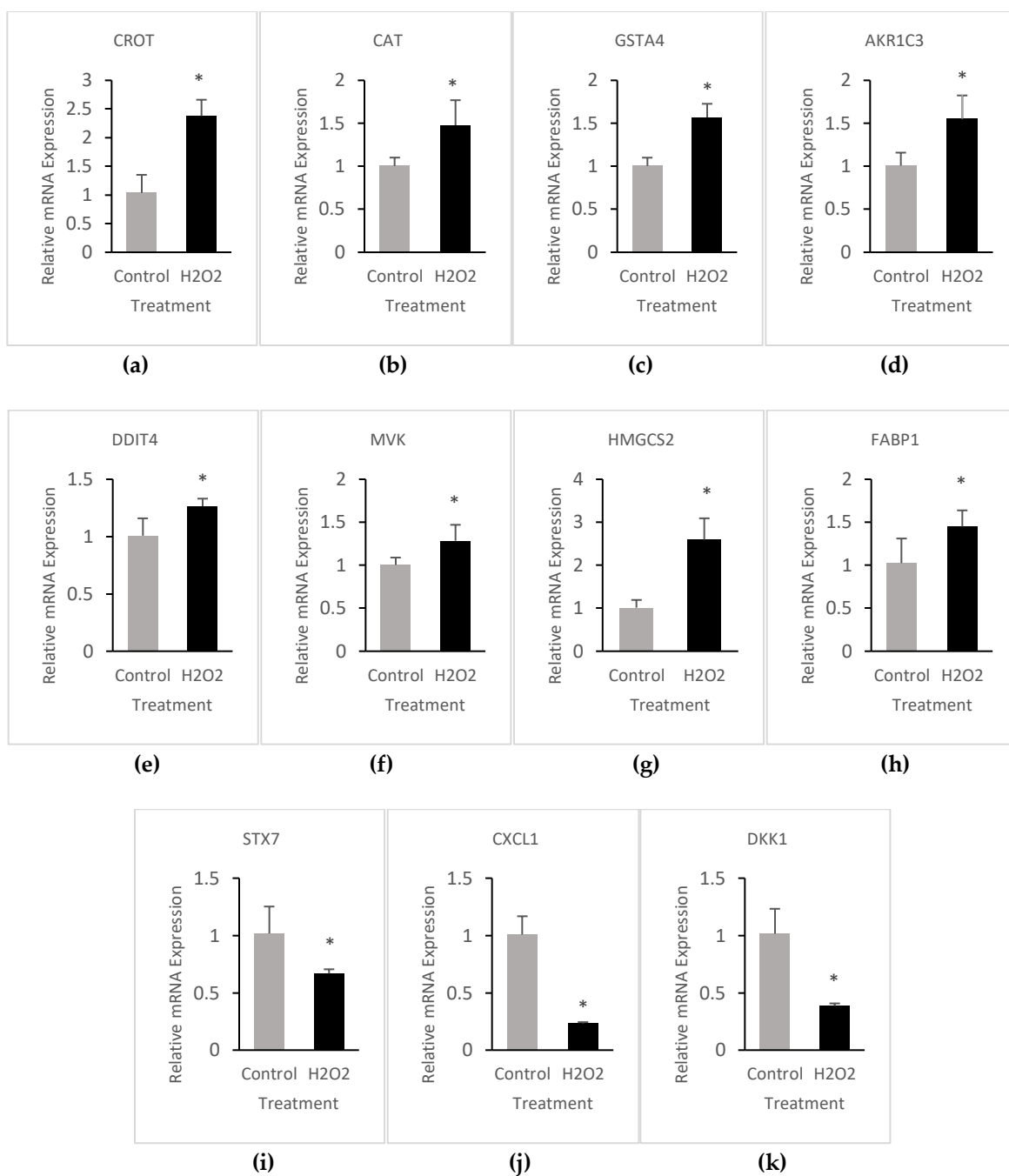


Figure S7. Quantitative RT-PCR validation of RNA-seq data in H₂O₂-treated PDiff Caco-2 cells. qRT-PCR of DEGs from RNA-seq data. Relative mRNA expression levels in H₂O₂-treated (H₂O₂) cells are presented with statistical significance of $*p < 0.05$ relative to untreated (control) cells. Results were normalized to *GAPDH*.