

Supplement 1

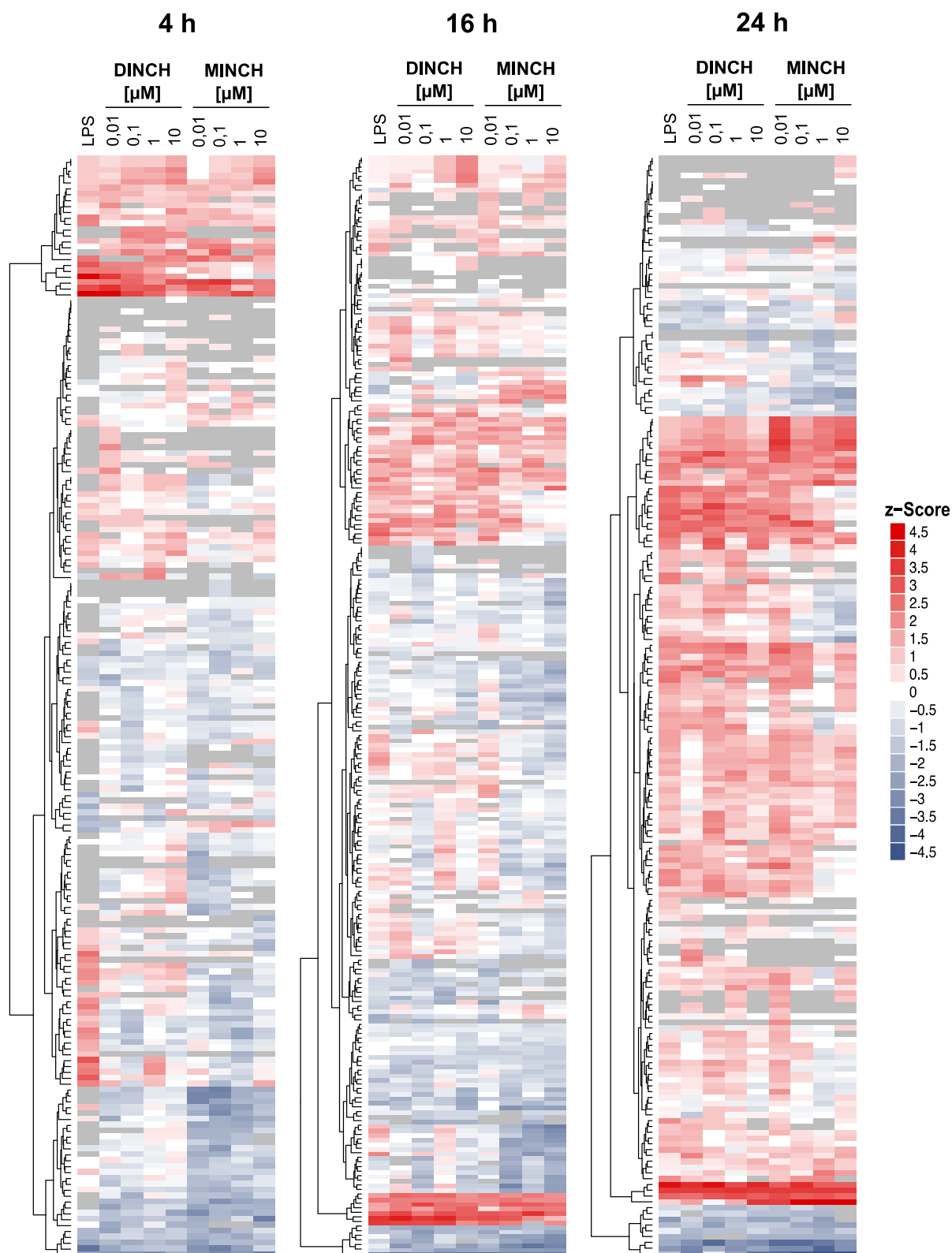


Figure S1: All enriched pathways obtained by Ingenuity Pathway Analysis (IPA) for the exposure of THP-1 macrophages to DINCH and MINCH. THP-1 macrophages were exposed to 10 nM – 10 μM of compound for 4 h, 16 h, and 24 h. Fold changes were calculated relative to the unstimulated control containing equivalent amounts of solvent (0.01% MeOH). Significant changes are labeled with asterisks (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, $n=4$).

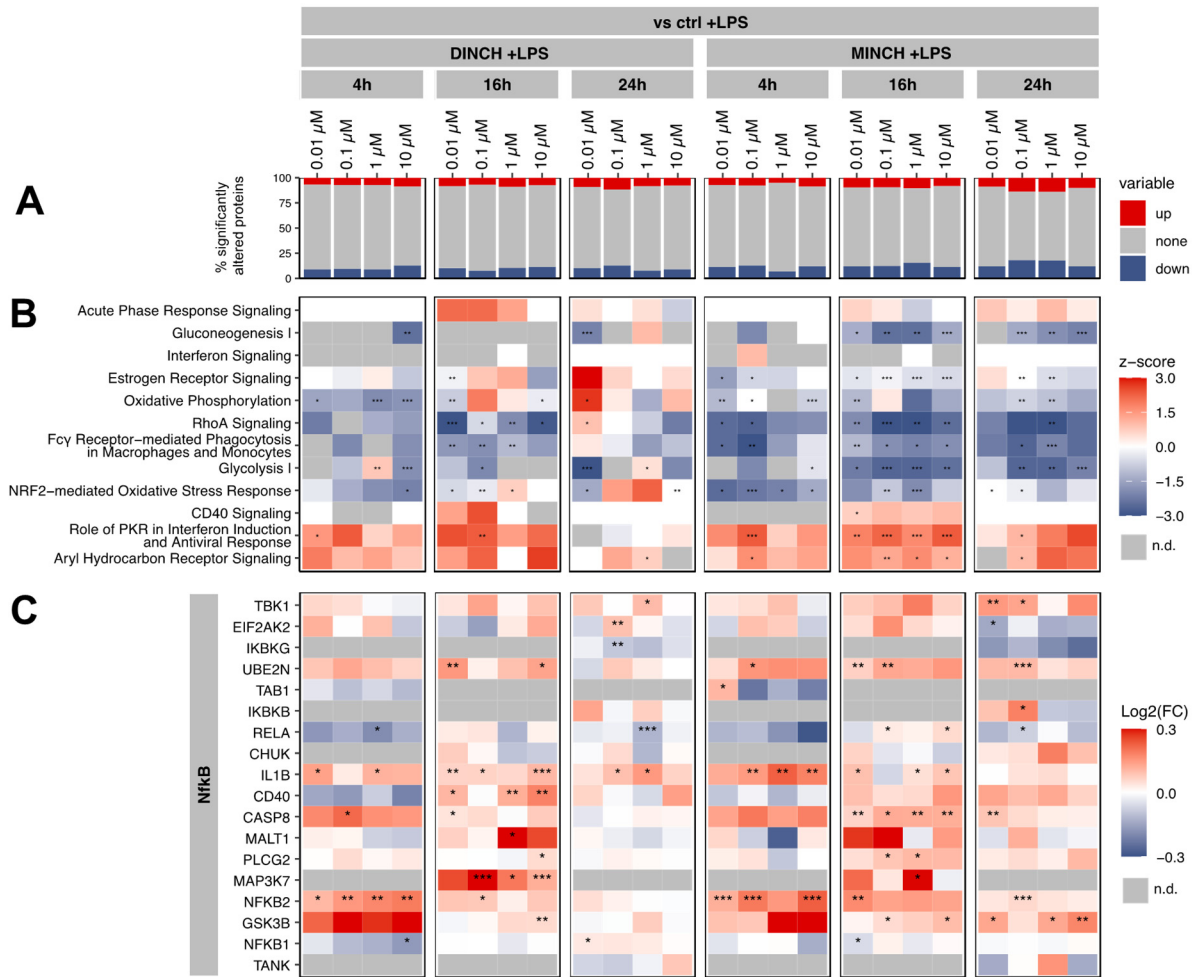


Figure S2: Proteomics analysis of DINCH and MINCH in THP-1 macrophages using Log₂(FCs) of treatment vs LPS-stimulated control. Differentiated THP-1 cells were treated with increasing concentrations of DINCH and MINCH for 4, 16, and 24 h. Fold changes (FCs) of the treatments to the LPS-stimulated control containing an equivalent amount of MeOH were calculated. (A) Percentage of significantly ($p \leq 0.05$, $n=4$) altered proteins after exposure of THP-1 cells which were subjected to Ingenuity Pathway Analysis (IPA). (B) Heatmap of selected significantly (adjusted $p \leq 0.05$) enriched pathways in treated THP-1 cells. The heatmap is colored based on z-scores calculated by IPA, indicating the direction of pathway regulation (z-score > 0 pathway is up-regulated, z-score < 0 pathway is down-regulated, not detected is marked in grey). Significant changes are labeled with asterisks (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, $n=4$). (C) NF- κ B associated proteins for the exposure of THP-1 macrophages to DINCH and MINCH. Significant changes are labeled with asterisks (* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, $n=4$).

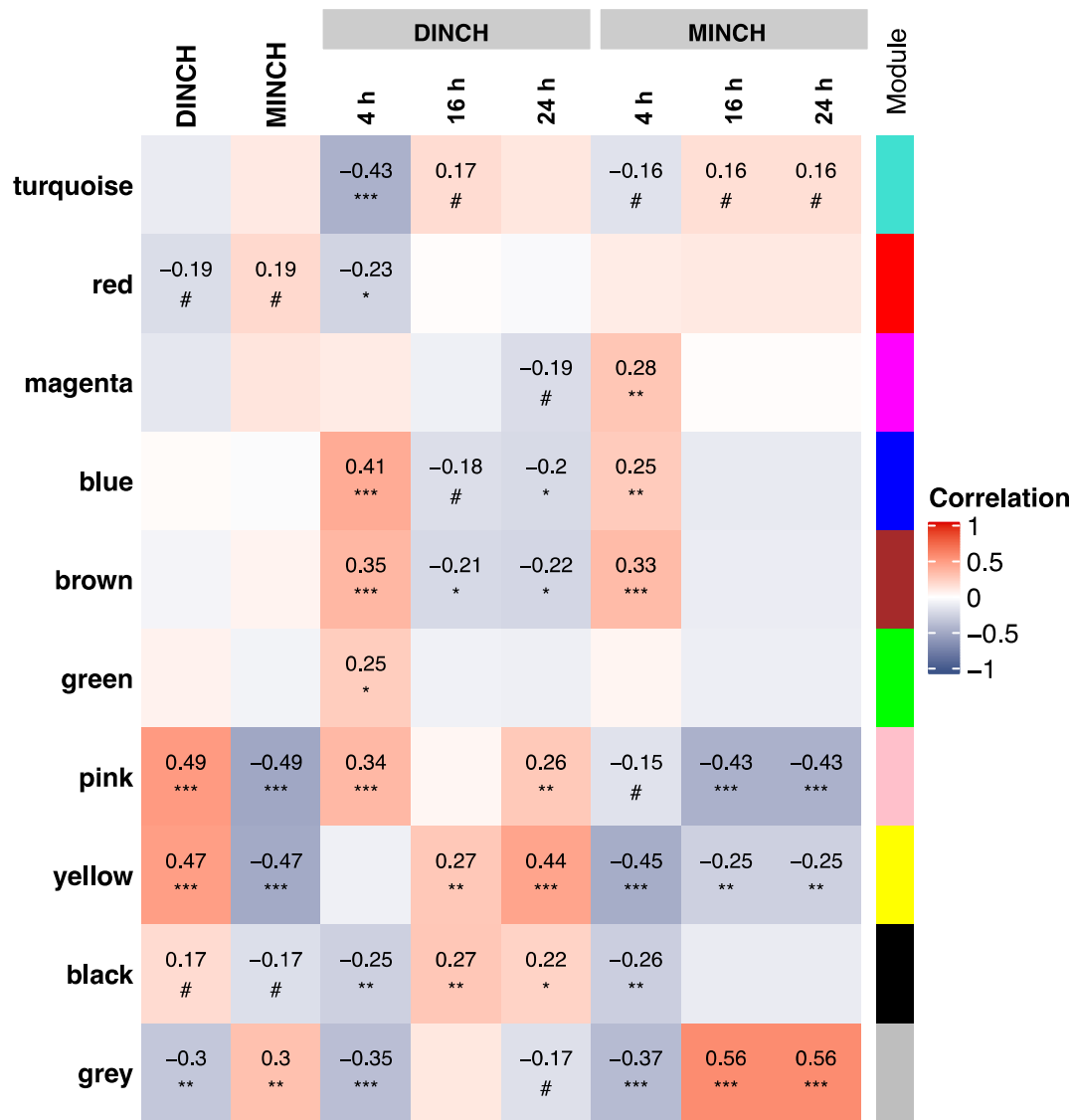


Figure S3: Full module-trait correlation obtained by WGCNA of treatment vs LPS-stimulated control. Displayed are all ten obtained modules of co-expressed proteins correlated with compound treatment (DINCH/MINCH) and time point (4 h, 16 h, 24 h). The heatmap is colored according to the correlation and significance of correlation is indicated (# $p \leq 0.01$, * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$).

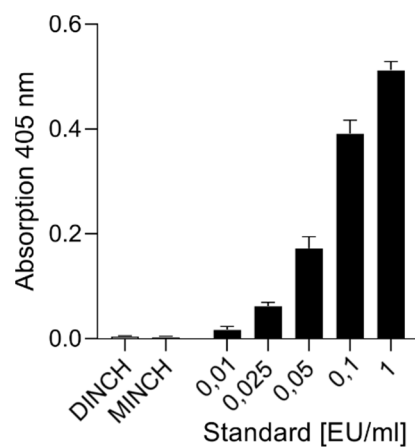


Figure S4: Endotoxin-Assay of 10 μ M DINCH und MINCH. Displayed are the absorbances of the highest tested concentration (10 μ M) of DINCH and MINCH and endotoxin standard dilutions. Data are depicted as mean \pm SD, $n=3$.