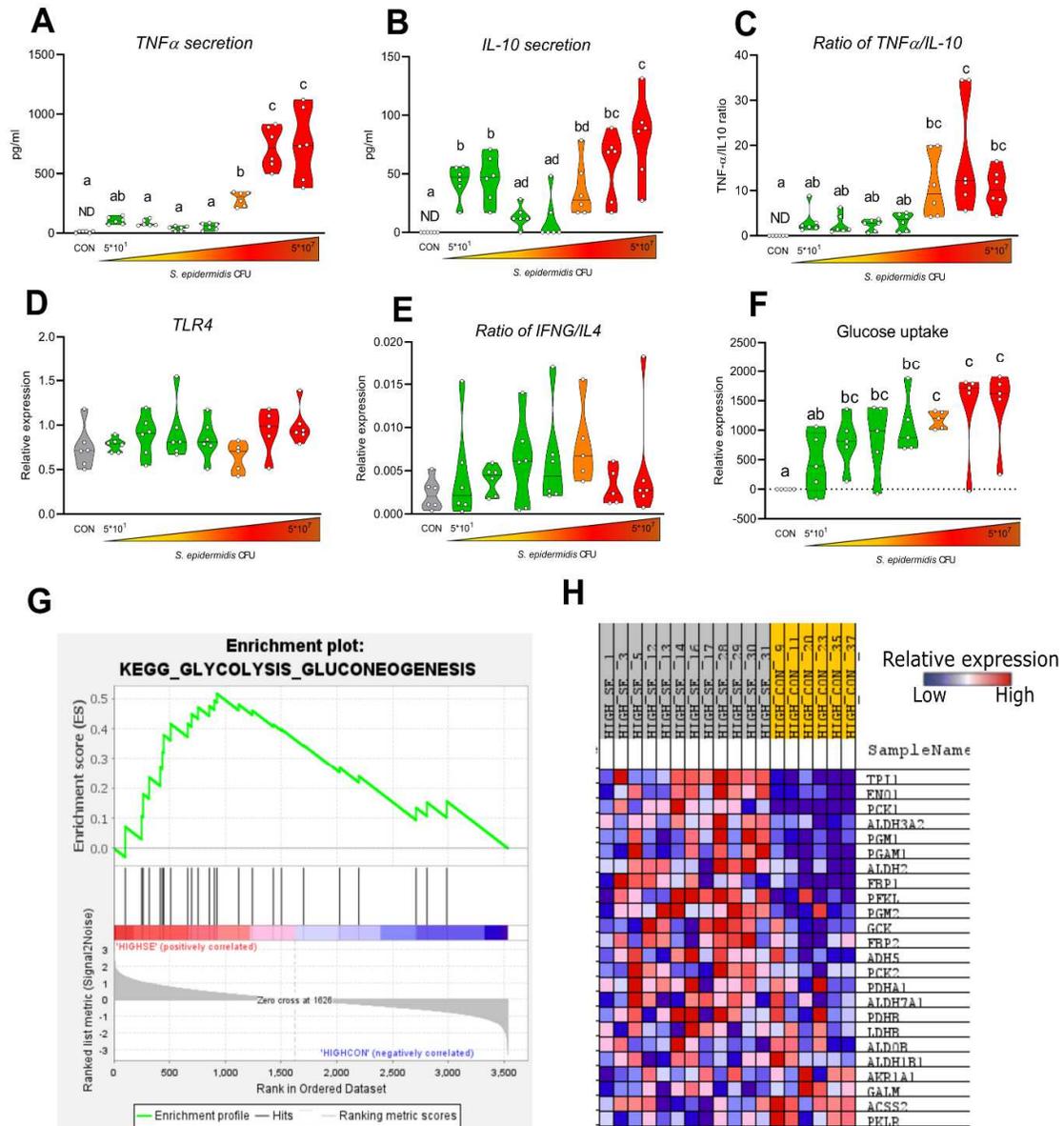
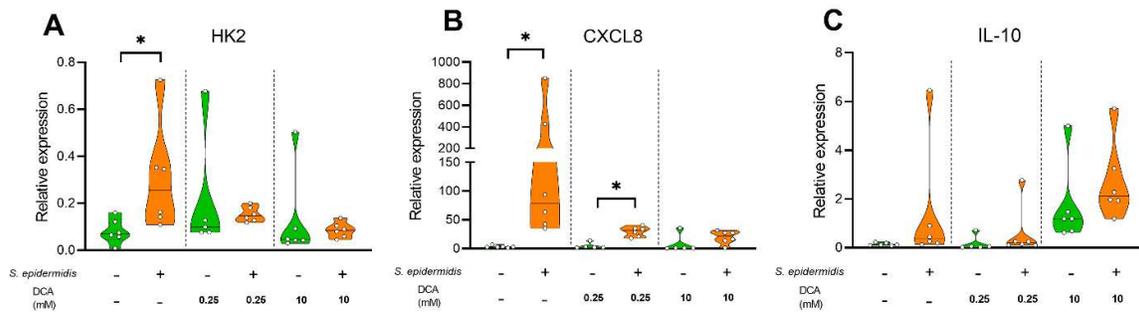


## Supplementary Figures



**Figure S1: *In vitro* and *in vivo* immunometabolic response of preterm pig cord blood to increasing doses of *S. epidermidis*.** (A-C) Plasma cytokine levels of TNFA, IL10, and TNFA/IL10 ratio in response to increasing bacterial dose (5×10<sup>1</sup>-5×10<sup>7</sup> CFU/mL, stimulated for 2 h at 37°C and 5%CO<sub>2</sub>, n = 6). (D-E) mRNA levels of *TLR4*, and *TNGF/IL4* ratio from the same blood samples (n

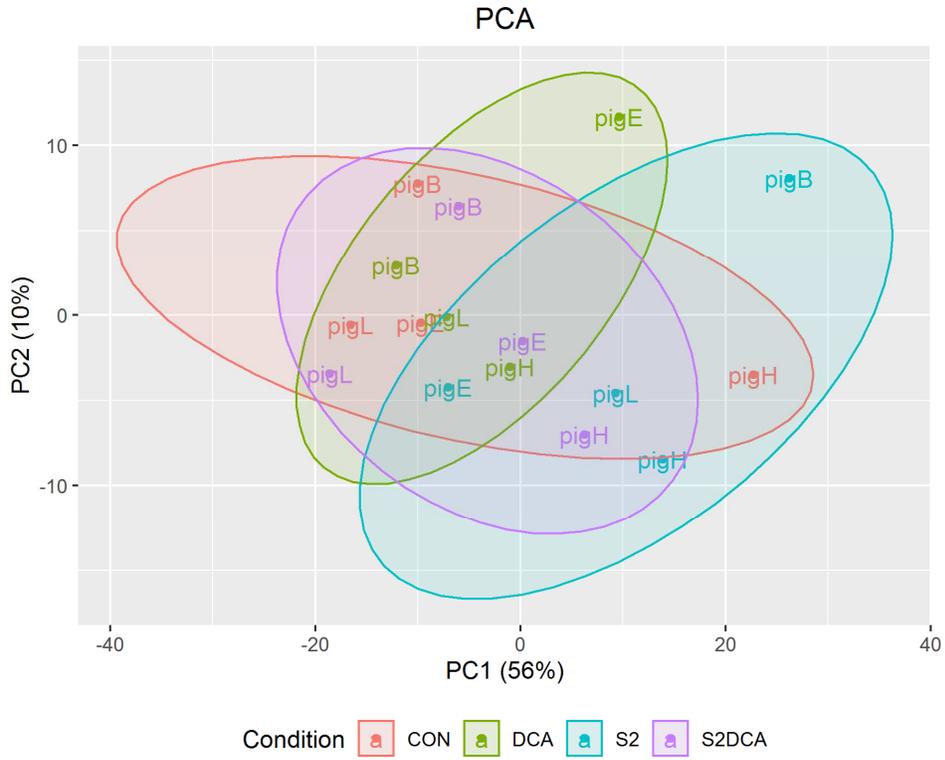
= 5-6). **(F)** Cellular glucose uptake measured by the differences in supernatant glucose levels of stimulated and unstimulated samples (n = 5). **(G-H)** Liver transcriptomics of control (n = 6, HIGH\_CON group) and infected animals (n = 12,  $10^9$  CFU/ml *S. epidermidis*, 12h, HIGH\_SE group) with gene set enrichment analysis (GSEA) showing enrichment plot (G) and heatmap (H) with representative DEGs involved in glycolysis/gluconeogenesis pathway. Data in (A-F) are presented as violin dot plots with median (solid line) and interquartile range (dotted lines) and were analyzed using linear mixed-effect model followed by Tukey Post-hoc comparisons. Values not sharing the same letters are significantly different ( $P < 0.05$ ). GSEA were performed using GSEA 4.2.2 (UC San Diego and Broad Institute). Pathways with adjusted P-value  $< 0.05$  was considered statistically significant.



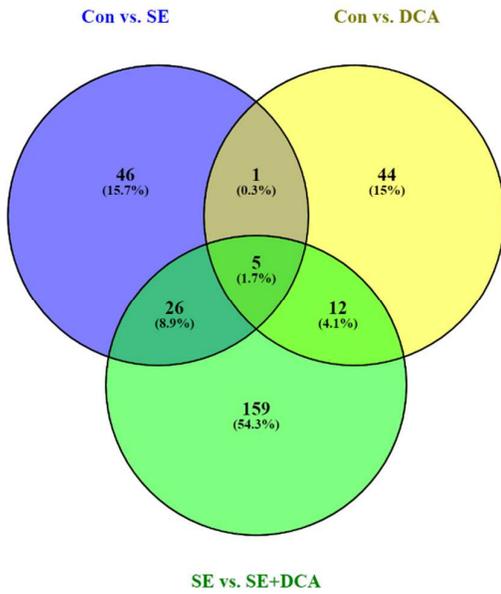
**Figure S2: *In vitro* immunometabolic response of preterm pig cord blood to *S.epidermidis* and dichloroacetate (DCA) supplementation. (A-C) mRNA levels of *HK2*, *CXCL8*, *IL10* of cord blood from preterm piglets stimulated with and without *S. epidermidis* ( $5 \times 10^5$  CFU/ml), with and without presence of glycolysis inhibitor DCA (0.25mM or 10mM DCA), for 2 hours at 37°C and 5% CO<sub>2</sub> (n = 5-6). Data are presented as violin dot plots with median (solid line) and interquartile range (dotted lines) and were analyzed using linear mixed-effect model followed by Tukey Post-hoc comparisons.**

\* , P < 0.05.

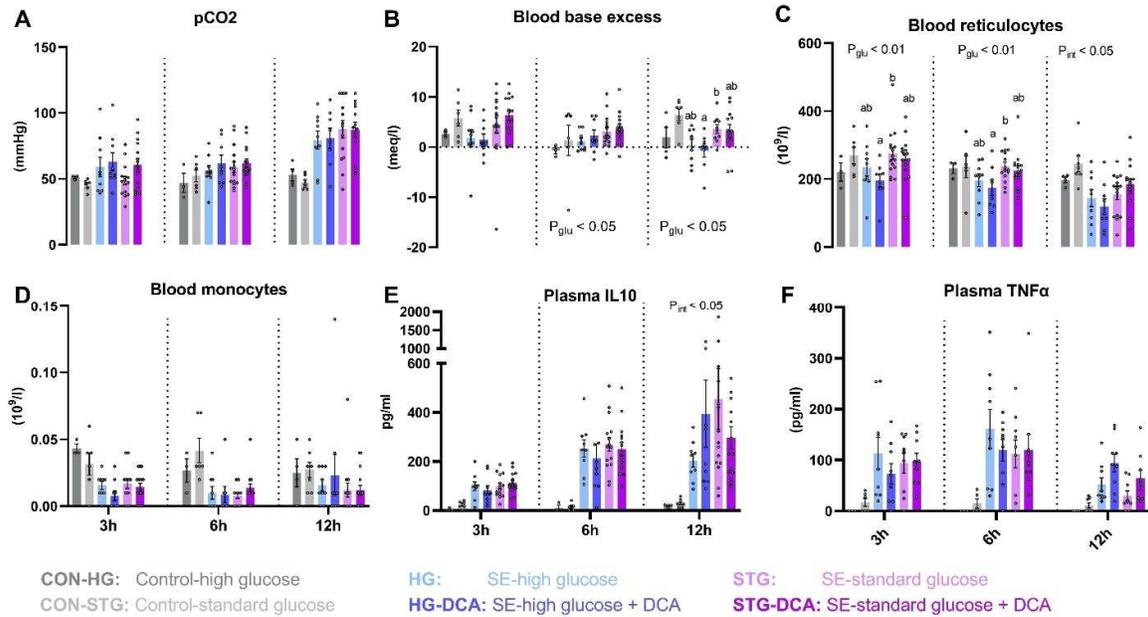
**A**



**B**



**Figure S3: Transcriptomic analysis of preterm pig cord blood following *S.epidermidis* stimulation and/or DCA supplementation.** (A) Principle component analysis plot based on gene expression profiles in treatment groups (n = 4/group). (B) Venn diagram demonstrating numbers of differentially expressed genes (DEGs) across group comparisons. Venn diagram was generated by venny 2.1 (<https://bioinfogp.cnb.csic.es/tools/venny/index.html>).



**Figure S4. The impact of parenteral glucose levels and glycolysis inhibition by DCA on clinical response to *S. epidermidis* infection.** (A-B) Arterial blood gas parameters, (C-D) Numbers of blood reticulocytes and monocytes, and (E-F) Plasma IL10 and TNF $\alpha$  levels 3, 6, and 12 h after *S. epidermidis* infusion. Data are presented as bar graphs including mean and standard error with individual dots and are analyzed separately for each time point using a linear mixed-effect model including glucose and DCA interaction. All analyzed data represents three independent experiments using separate litters. Among infected groups,  $P_{DCA}$ ,  $P_{glu}$  and  $P_{int}$  at each time point denote probability values for overall effects of DCA, glucose and their interaction, respectively, among the four infected groups in the linear mixed-effect model. Values at each time point not sharing the same letters are significantly different ( $P < 0.05$ ).

**Supplementary Tables:** uploaded separately due to the nature of big datasets