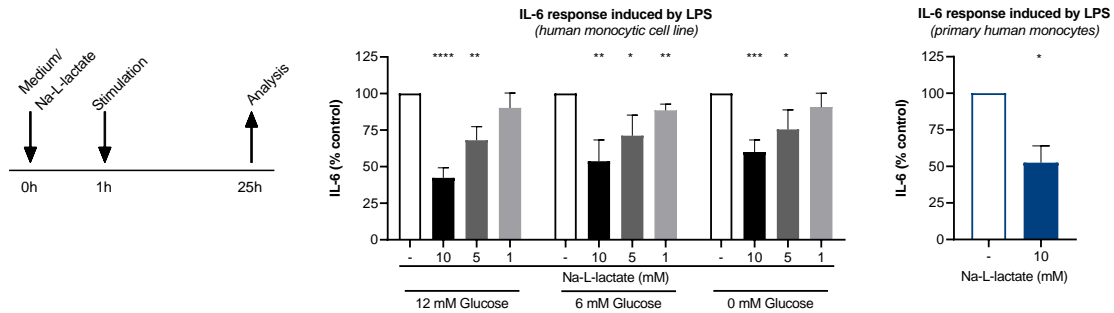
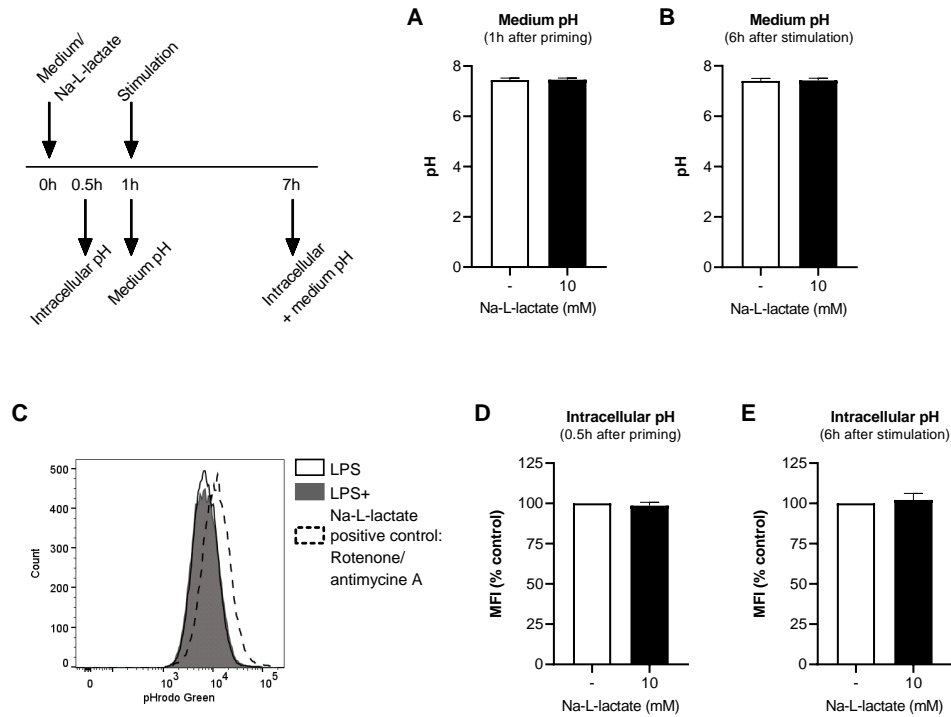


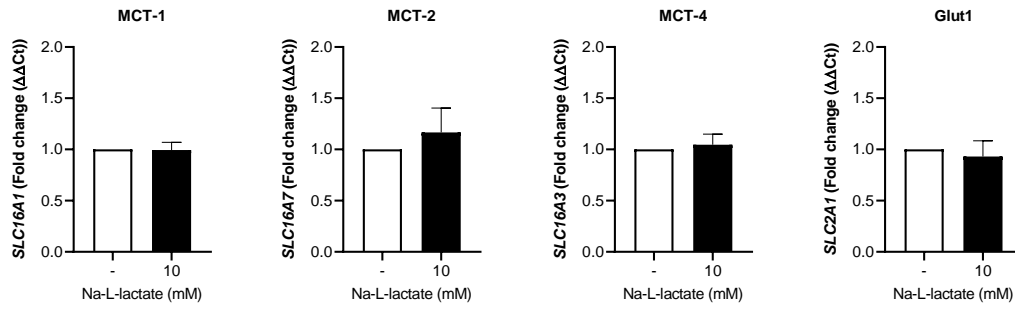
Supplementary Material



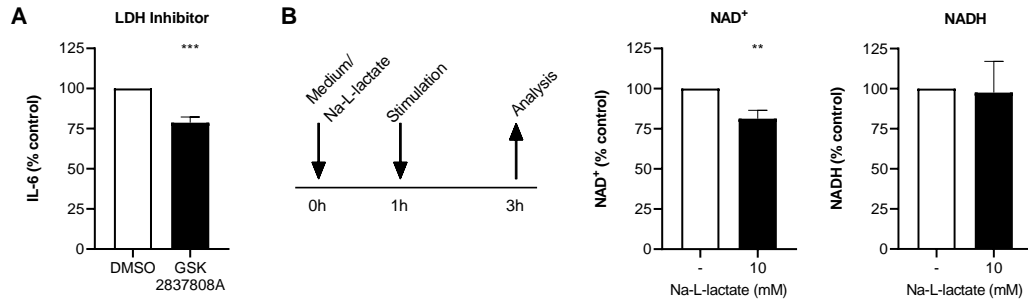
Supplementary Figure 1. **Extracellular lactate reduces cytokine response upon stimulation.** IL-6 secretion from MM6 primed with Na-L-lactate at the indicated concentrations for one hour and stimulated with LPS for 24 hours in medium with 12mM, 6mM, or without glucose (n=5) and from primary human monocytes primed with Na-L-lactate for one hour and stimulated with LPS for 24 hours in medium with 12mM glucose (n=3). Data are shown as mean + SD. One sample t test was performed against the theoretical value 100 (**** $P < 0.0001$, *** $P \leq 0.001$, ** $P \leq 0.01$, * $P \leq 0.05$).



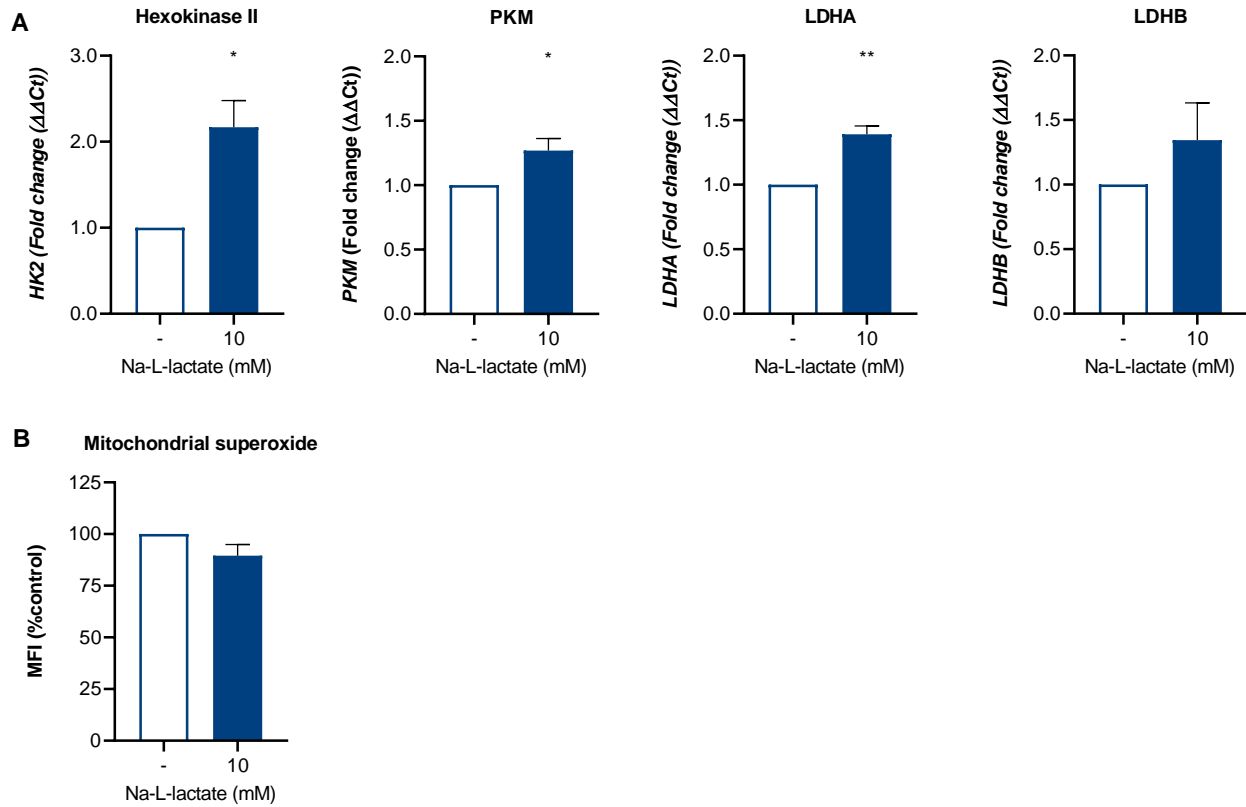
Supplementary Figure 2. **Physiological pH is maintained despite lactate priming.** Medium pH after (A) one-hour priming with Na-L-lactate and (B) additional six hours stimulation with LPS. (C) Intracellular pH after (D) 30min priming with Na-L-lactate or (E) one-hour priming with Na-L-lactate and six hours stimulation with LPS. Data are shown as (A, B) mean + SEM or (D, E) mean + SD (n=3).



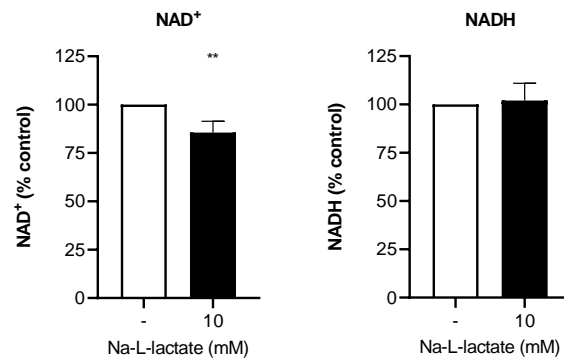
Supplementary Figure 3. **Expression levels of lactate and glucose transporter are maintained.** Gene expression of *SLC16A1*, *SLC16A7*, *SLC16A3*, and *SLC2A1* after one-hour priming with 10mM Na-L-lactate and six hours stimulation with LPS. Data are shown as mean + SD (n=5).



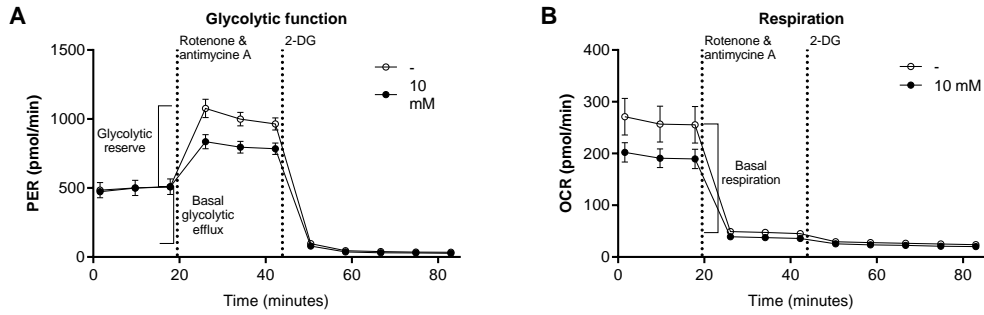
Supplementary Figure 4. **Role of LDH.** (A) IL-6 secretion after inhibition of LDH starting one hour prior to a six-hour stimulation with LPS. (B) Intracellular NAD⁺ and NADH levels after one-hour priming with 10 mM Na-L-lactate and two hours stimulation with LPS. Data are shown as mean + SD (n=5). One sample t test was performed against the theoretical value 100 (***) $P \leq 0.001$.



Supplementary Figure 5. **Glycolytic enzyme gene expression and mitochondrial superoxide production in primary monocytes.** (A) Gene expression of *HK2*, *PKM*, *LDHA*, and *LDHB* in primary human monocytes after one-hour priming with 10mM Na-L-lactate and six hours stimulation with LPS. (B) Production of mitochondrial superoxide in primary human monocytes after one-hour priming with 10mM Na-L-lactate and three hours stimulation with LPS. Data are shown as mean + SD (n=3). One sample t tests were performed against the theoretical values 100 or 1 respectively (** $P \leq 0.01$, * $P \leq 0.05$).



Supplementary Figure 6. **Extracellular lactate alone is sufficient to reduce NAD⁺ level.** Intracellular NAD⁺ and NADH level safter six hours priming with 10mM Na-L-lactate. Data are shown as mean + SD (n=5). One sample t test was performed against the theoretical value 100 (** $P \leq 0.01$).



Supplementary Figure 7. **Calculation of glycolytic and respiratory indices.** (A) Calculation of the glycolytic indices basal glycolytic efflux and glycolytic reserve and (B) calculation of basal respiration after a 24-hour priming with 10mM Na-L-lactate. Data are shown as mean \pm SEM (n=5).