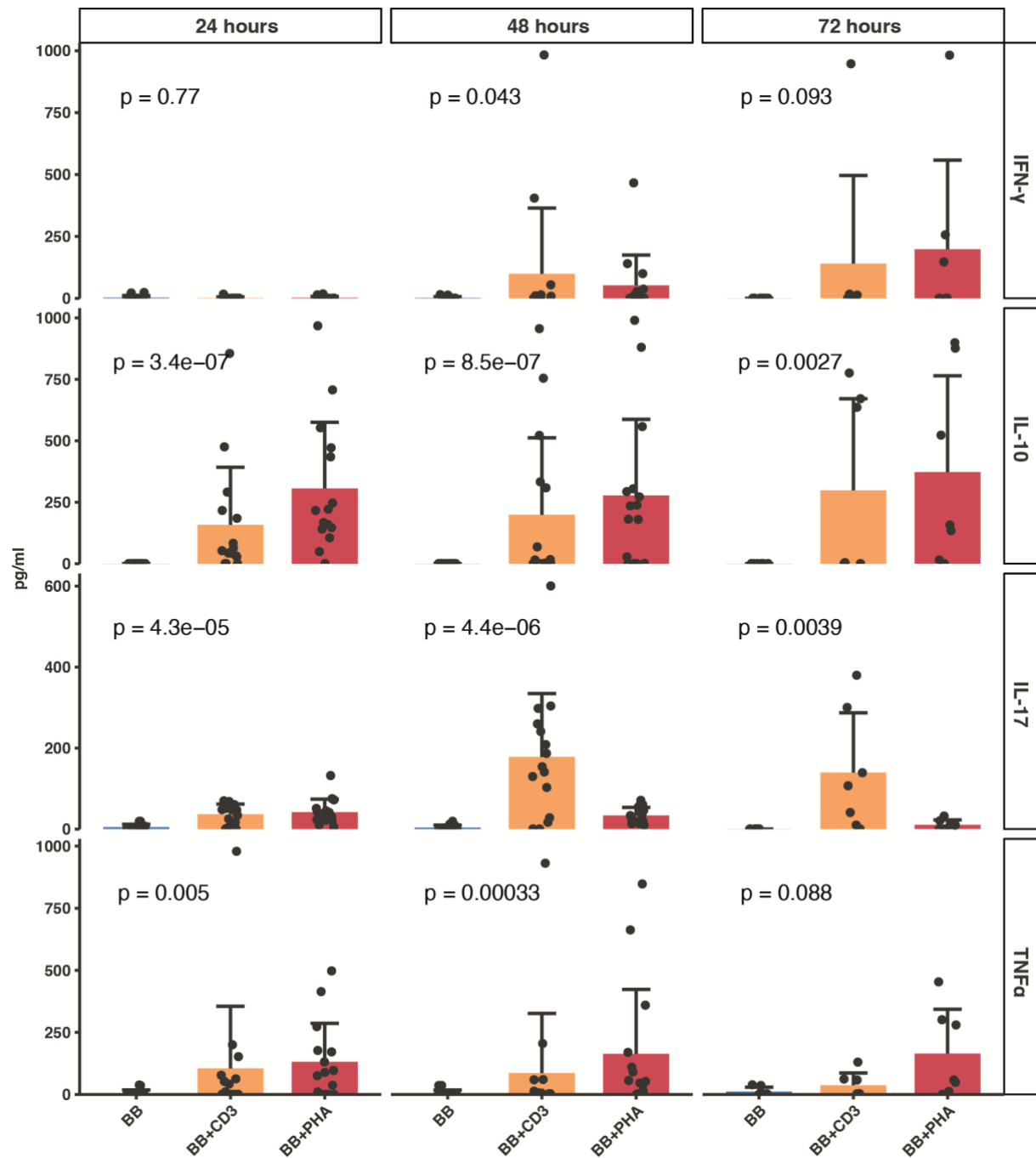
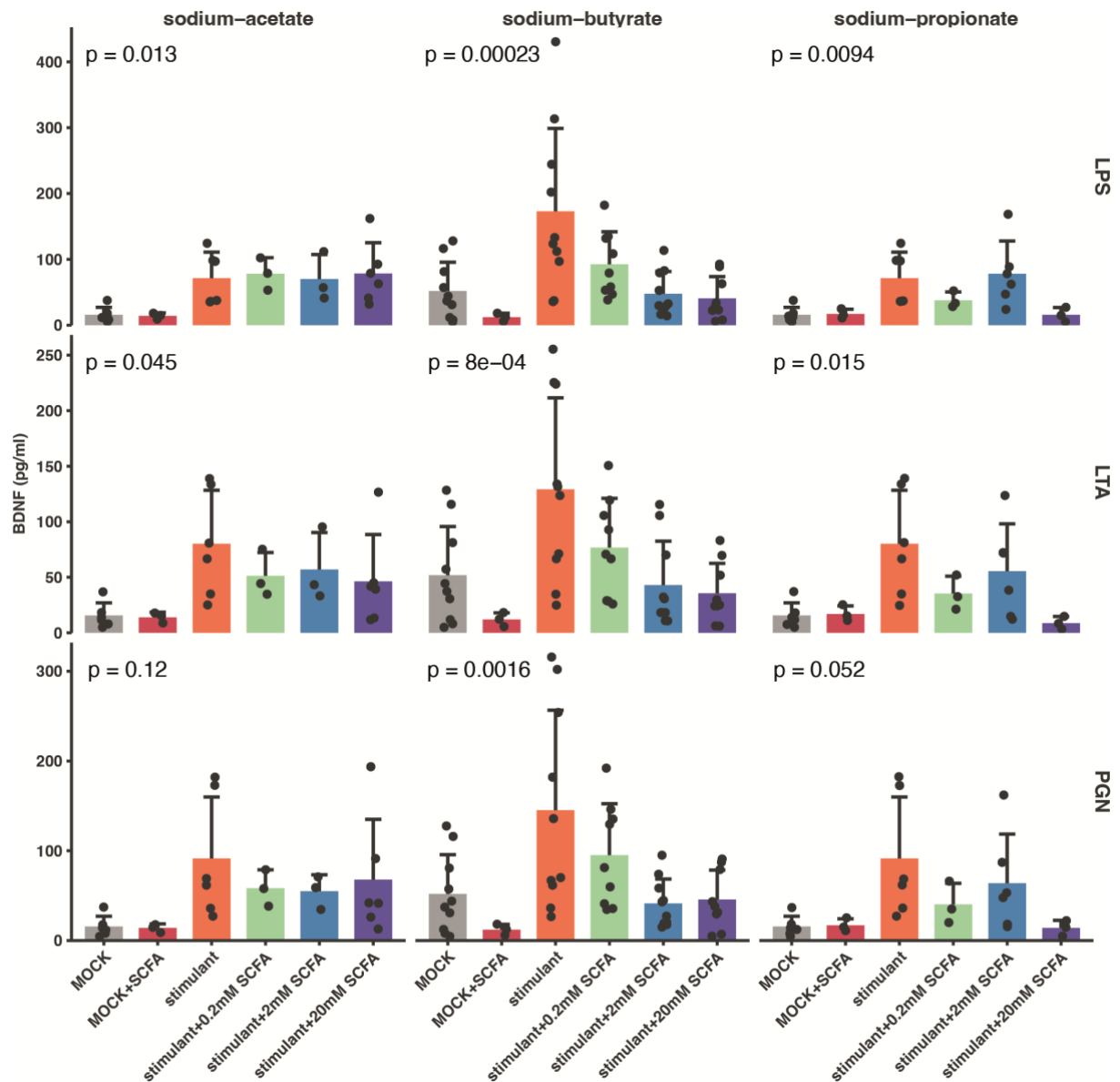


**Supplemental Figure 1. Cytokine secretion after bacterial stimulation of human PBMCs.**

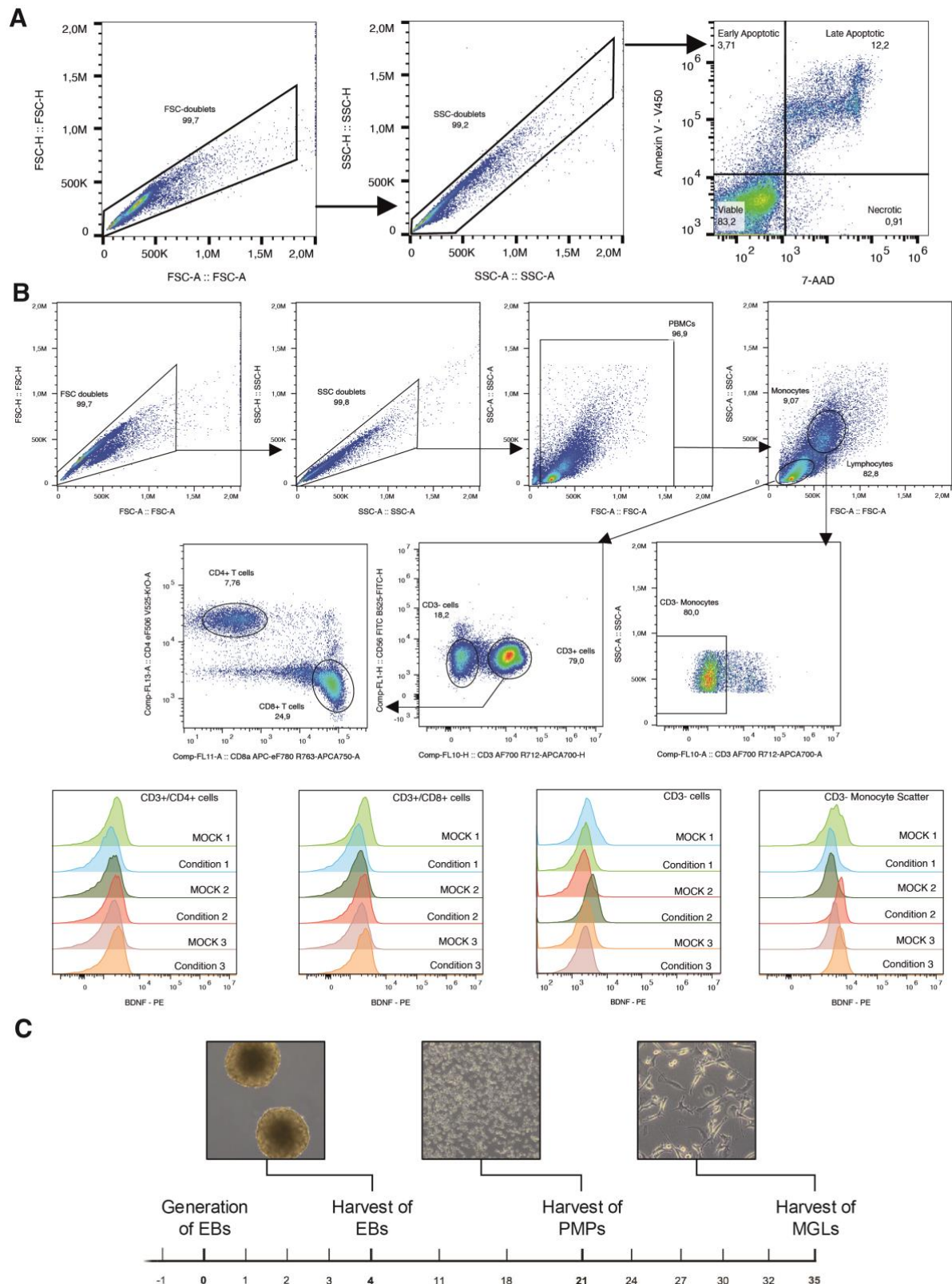
The secretion of TNF $\alpha$ , IFN- $\gamma$ , IL-17, IL-10, and BDNF after concomitant stimulation of PBMCs ( $1 \times 10^6$  cells,  $n=10$  per stimulation, 10 independent experiment) with phytohemagglutinin (PHA; 5  $\mu\text{g/ml}$ ) and heat-killed *S. epidermidis* (SE), *E. faecalis* (EF), *E. coli* (EC), and *K. pneumoniae* (KP, each  $1 \times 10^6$ ) grown under aerobic (A) and anaerobic (B) conditions. Cells were stimulated for 24 hours and cytokine secretion measured via ELISA. Bar graphs represent the mean concentration with SD (pg/ml). The Kruskal-Wallis-Test was used for statistical analysis.



**Supplemental Figure 2. Cytokine secretion after bacterial stimulation with *Bifidobacterium breve* (BB) of human PBMCs.** PBMCs (n=6-15, 8 independent experiments) were stimulated with *B. breve* (BB;  $1 \times 10^6$ ) as well as PHA (5  $\mu\text{g/ml}$ ) or CD3/CD28 (CD3; 10  $\mu\text{g/ml}$ ) and cytokine as well as BDNF secretion was analyzed after 24, 48, and 72 hours via ELISA. Bar graphs represent the mean concentration with SD (pg/ml). The Kruskal-Wallis-Test was used for statistical analysis.



**Supplemental Figure 3. Cytokine secretion after bacterial antigen stimulation with short chain fatty acids of human PBMCs.** BDNF concentration after co-stimulation of PBMCs (n=3-10, 4 independent experiments) with increasing doses of sodium-acetate (left panel), sodium-butyrate (middle panel), and sodium-propionate (right panel), as well as LPS (1 $\mu$ g/mL; upper panel), LTA (1 $\mu$ g/mL, middle panel), or PGN (10 $\mu$ g/mL, lower panel). Cells were stimulated for 72 hours and BDNF was measured via ELISA. Bar graphs represent the mean concentration with SD (pg/ml). ANOVA was used for statistical analysis.



**Supplemental Figure 4. Gating strategy and microglia generation overview.** Used gating strategy for the apoptosis assay (A) as well as the intracellular BDNF staining panel 1 (B). Figure were generated using FlowJo. (C) Human microglia were generated *in vitro* from the human embryonic stem cell line WA09. The differentiation process

involved sequential stages, including embryoid body (EB) formation, primitive macrophage progenitor (PMP) development, and maturation into microglia-like cells (MGLs) over 35 days.