Category :**Sepsis: basic mechanisms**

A213 - ***No interplay between gut microbiota composition and the lipopolysaccharide-induced innate immune response in humans in vivo***

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Introduction:

Animal studies have demonstrated the extensive interplay between the gut microbiota and immunity. Moreover, in critically ill patients, who almost invariably suffer from a pronounced immune response, a shift in gut microbiota composition is associated with infectious complications and mortality. We examined the relationship between interindividual differences in gut microbiota composition and variation in the *in vivo* cytokine response induced by bacterial lipopolysaccharide (LPS). Furthermore, we evaluated whether an LPS challenge alters the composition of the gut microbiota.

Methods:

Healthy male volunteers received an intravenous bolus of 2 ng kg^{-1} LPS (n = 70) or placebo (n = 8). Serial plasma concentrations of tumor necrosis factor-α, interleukin (IL)-6, IL-8 and IL-10 were measured, and subjects were divided into high and low cytokine responders. Gut microbiota composition was determined using 16s RNA gene sequencing of faecal samples obtained 1 day before (baseline) and 1 day and 7 days following the LPS challenge.

Results:

Baseline microbiota composition, analysed by principal coordinate analysis and random forest analysis, did not differ between high and low responders for any of the four measured cytokines. Furthermore, baseline microbiota diversity (Shannon and Chao indices) was similar in high and low responders. No changes in microbiota composition or diversity were observed at 1 and 7 days following the LPS challenge.

Conclusion:

Our results indicate that existing variation in gut microbiota composition does not explain the observed variability in the LPS-induced innate immune response. These findings strongly argue against the interplay between the gut microbiota composition and the innate immune response in humans.

Image :

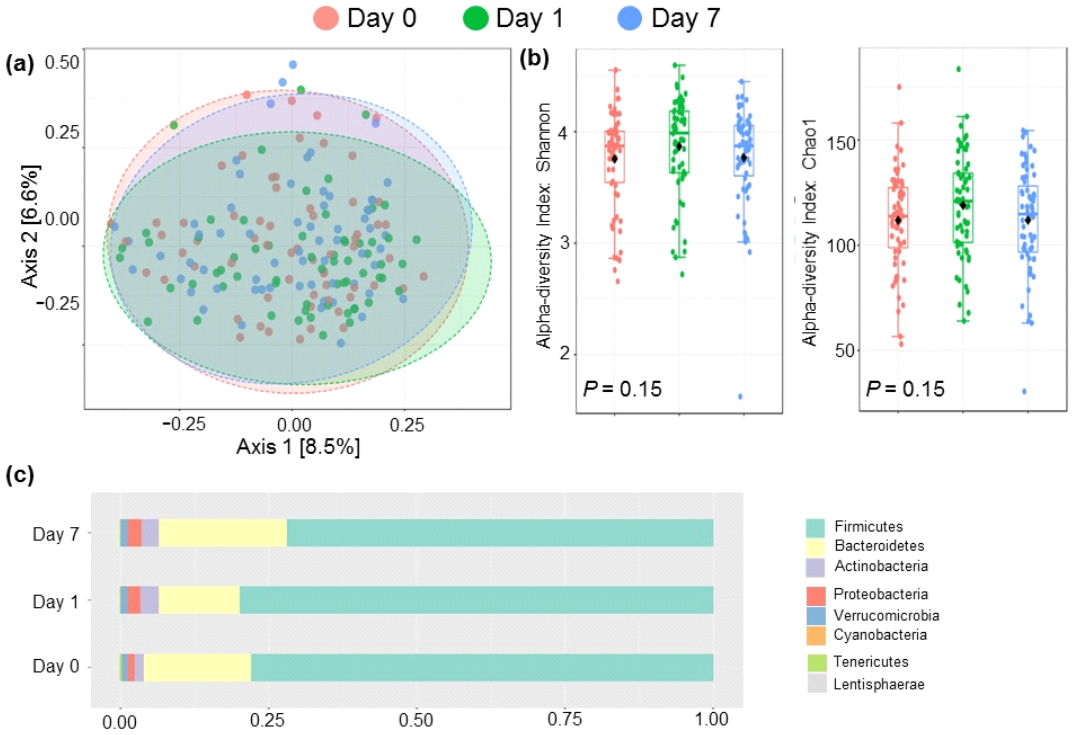

Figure 1. Effect of LPS challenge on gut microbiota composition. A) Principal coordinates analysis (PCoA) of microbiota composition over time following LPS challenge (n=63, paired samples across timepoints). PERMANOVA on the Bray–Curtis dissimilarity index: F-value: 0.44, R-squared=0.01, p=1.00 B) Gut microbiota diversity over time following LPS challenge (n=63, paired samples across timepoints), reflected by Shannon index and Chao1 index. p-values calculated by Friedman tests. C) Relative abundance of gut microbiota (phylum level) over time following LPS challenge (n=63, paired samples across timepoints).