

Gut Microbiota Predicts Chemo-Immunotherapy Response in Small Cell Lung Cancer

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Introduction

Small cell lung cancer (SCLC) is a highly malignant neuroendocrine tumor with poor prognosis. Chemotherapy combined with immune checkpoint inhibitors (ICIs) has become the standard first-line treatment for extensive-stage SCLC. However, treatment response varies considerably among patients, and reliable predictive biomarkers remain scarce. The gut microbiota regulates systemic immunity and anti-tumor therapeutic responses via the gut-lung axis, but its association with progression-free survival (PFS) in SCLC patients treated with chemo-immunotherapy has not been fully elucidated.

Methods & Results

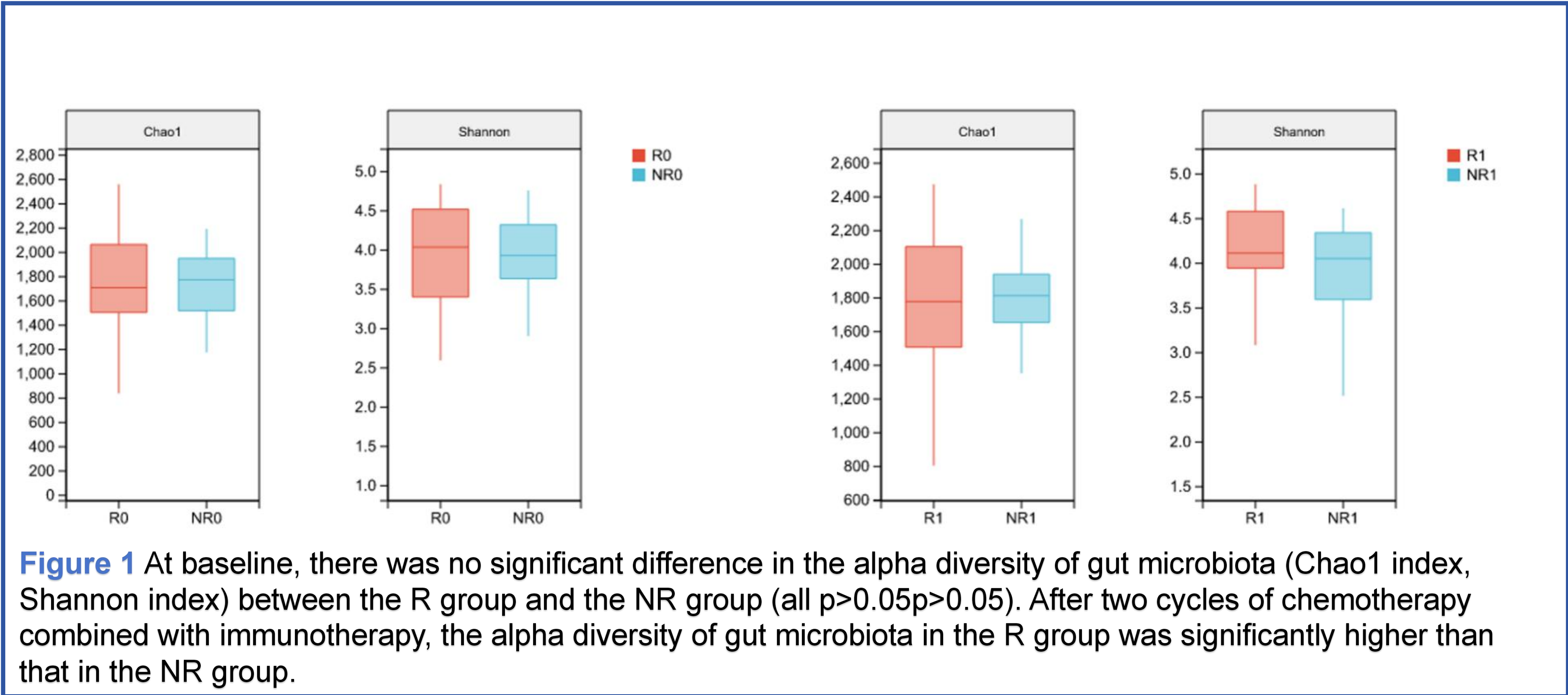


Figure 1 At baseline, there was no significant difference in the alpha diversity of gut microbiota (Chao1 index, Shannon index) between the R group and the NR group (all $p > 0.05$). After two cycles of chemotherapy combined with immunotherapy, the alpha diversity of gut microbiota in the R group was significantly higher than that in the NR group.

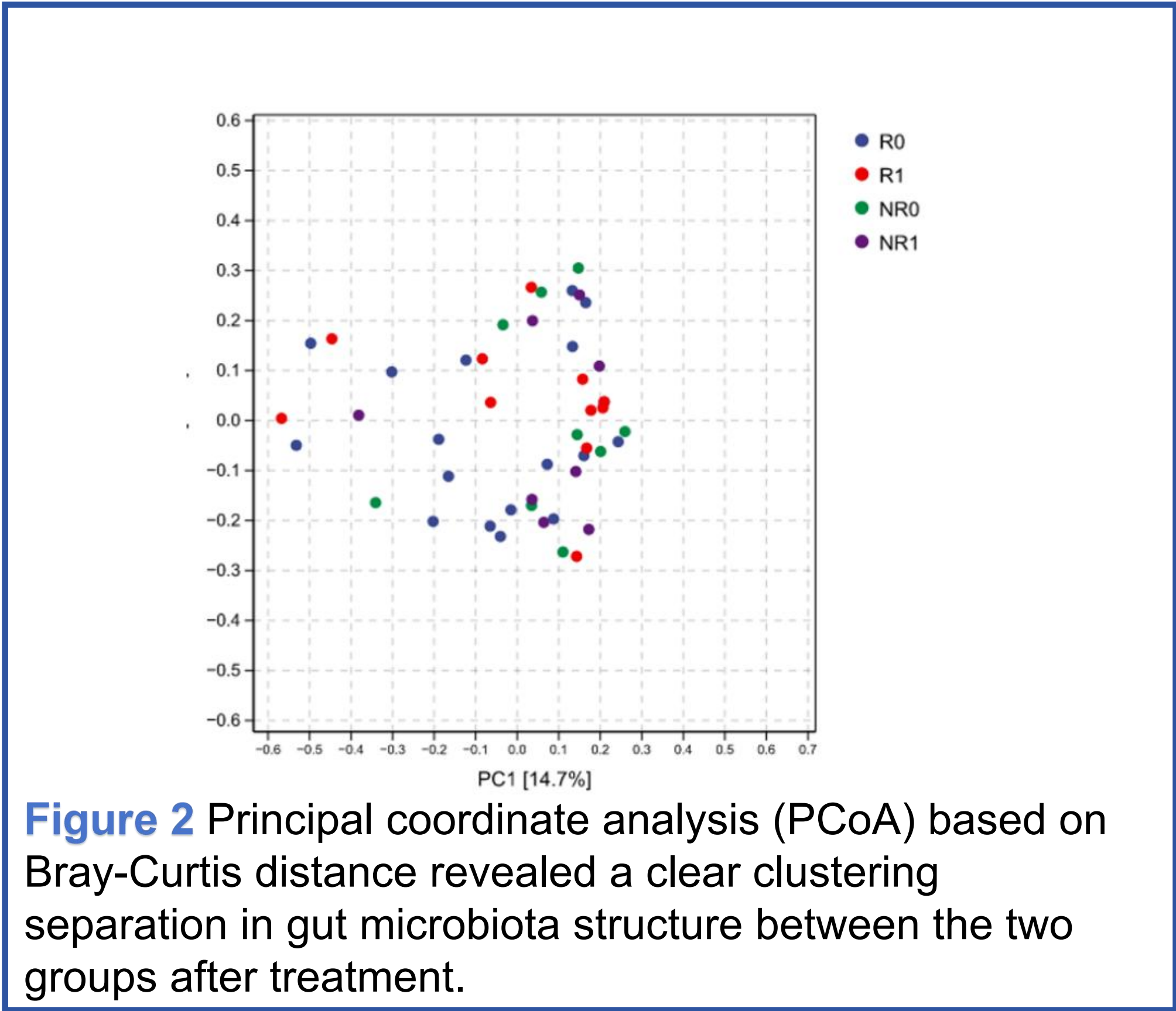


Figure 2 Principal coordinate analysis (PCoA) based on Bray-Curtis distance revealed a clear clustering separation in gut microbiota structure between the two groups after treatment.



Figure 3 At the species level, at baseline, the R0 group was significantly enriched with short-chain fatty acid (SCFA)-producing bacteria, including *Ruthenibacterium* and *Anaerostipes*, among others. In contrast, the NR0 group was enriched with genera such as *Clostridium* and *Lachnospira*. After two cycles of treatment, the R1 group was significantly enriched with *Ruminococcus_B* and *Anaerostipes*, while the NR1 group was significantly enriched with *Bifidobacterium*, among others. Notably, there were substantial differences in the composition of the intestinal microbiota between the R group and the NR group at both baseline and after two cycles of treatment.

Conclusions

Dynamic changes in the gut microbiota are closely associated with PFS in SCLC patients receiving chemo-immunotherapy. Enrichment of SCFA-producing bacteria (*Ruthenibacterium*, *Anaerostipes*, *Clostridium*, *Lachnospira*) and elevated post-treatment microbiota diversity may correlate with longer PFS. These gut microbiota signatures could serve as potential predictive biomarkers for the efficacy of chemo-immunotherapy in SCLC and provide novel targets for microbiota modulation to improve patient outcomes.

Key words

SCLC, Chemo-immunotherapy, Gut microbiota, Metagenomics, Biomarker