Gut Microbiome as a Predictive Biomarker and Emerging Intervention Target in DLBCL

Woorim Kang
Department of Biological Science, Kangwon National University, Chuncheon, Korea

Diffuse large B-cell lymphoma (DLBCL) is accompanied by characteristic gut microbial dysbiosis, most notably expansion of Enterobacteriaceae. This dysbiotic shift correlates with disease burden and intensifies with advancing stage, suggesting cancer-driven remodeling of the gut microbiome. In treatment-naïve patients, elevated Enterobacteriaceae is associated with increased toxicity during R-CHOP immunochemotherapy and correlates with treatment response and progression-free survival, indicating that lymphoma-associated dysbiosis influences both treatment tolerance and efficacy. Patients undergoing CD19 CAR-T therapy for refractory/relapsed disease show similarly elevated Enterobacteriaceae compared to treatment-naïve patients, again correlating with treatment-related toxicities. In contrast, CAR-T response itself is associated with a distinct microbiome and metabolic signature characterized by enrichment of Bacteroides fragilis and inosine-related pathways, suggesting divergence between toxicity-linked dysbiosis and microbial features that support antitumor immunity. Longitudinal follow-up of patients achieving durable remission reveals gradual decline of Enterobacteriaceae over time, consistent with resolution of cancer-associated dysbiosis, although the rate and trajectory of this normalization vary markedly between individuals, potentially reflecting differences in baseline community structure and dietary patterns. Together, these findings support a model in which DLBCL induces stage-dependent dysbiosis that modulates treatment outcomes, while successful disease control permits microbiome recovery, providing rationale for microbiome-targeted interventions to improve therapeutic response and reduce adverse events in DLBCL.