The role of human microbiota in breast cancer pathogenesis and treatment

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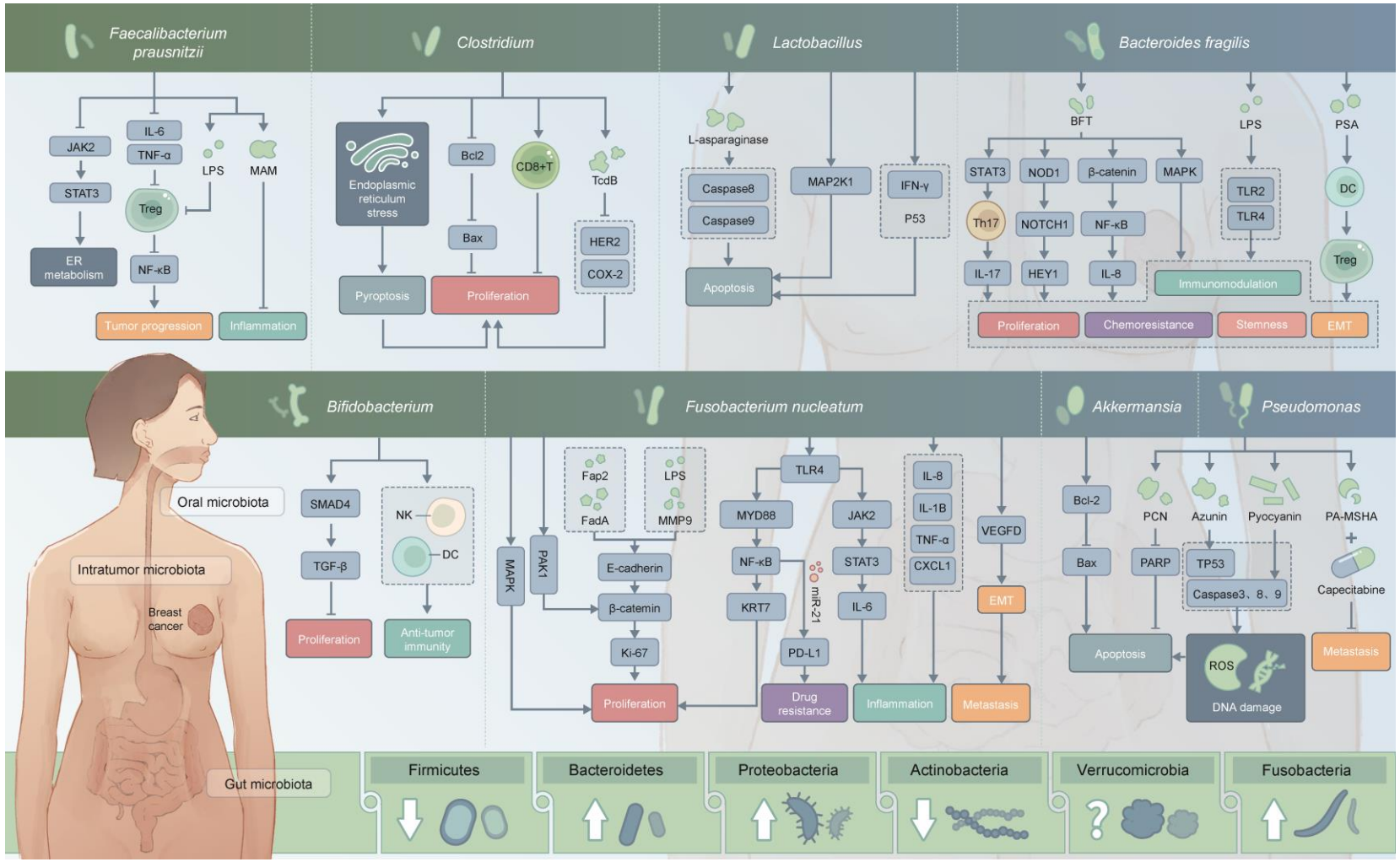
Research Background

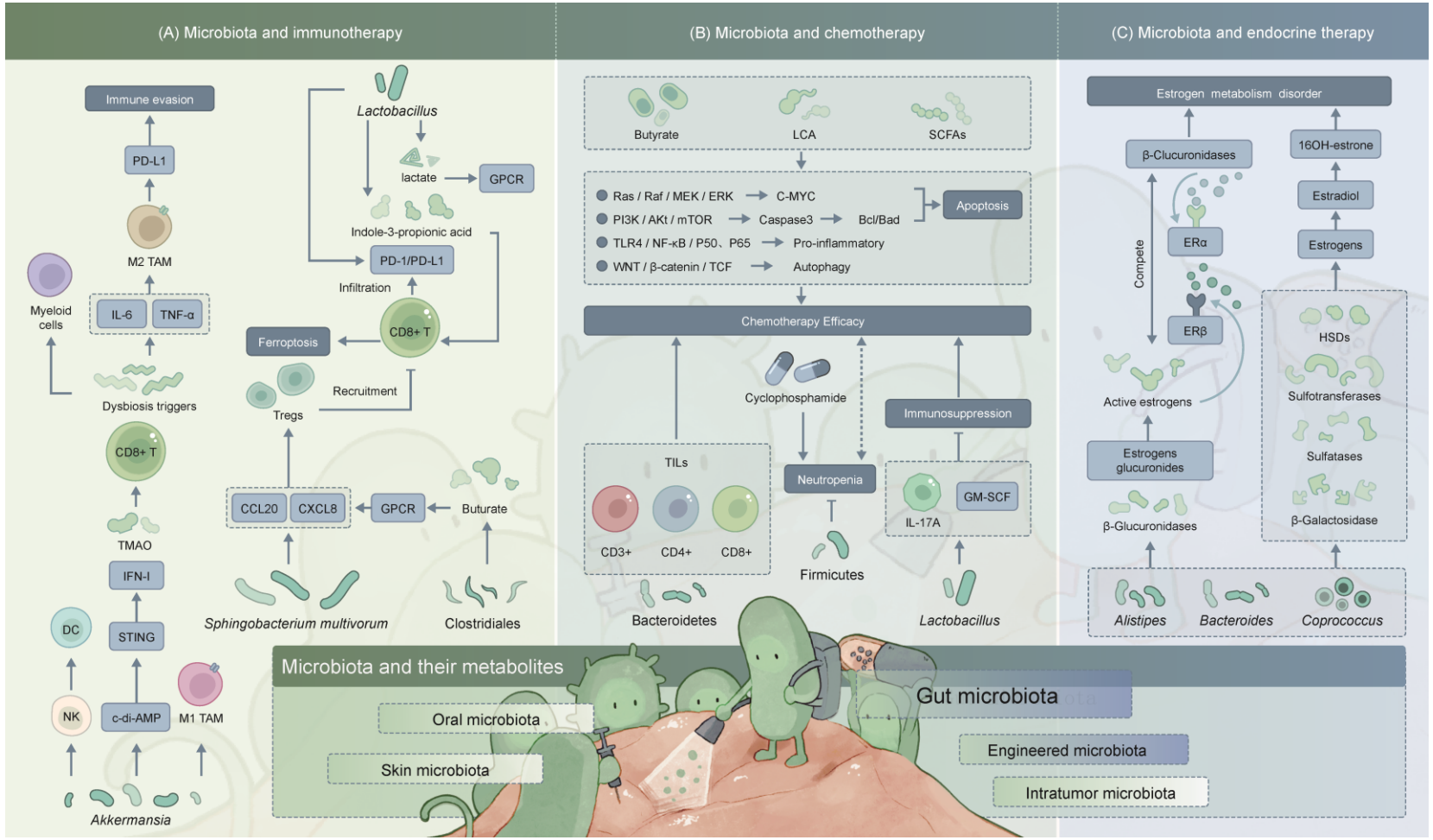
- Breast cancer remains the most common malignancy among women worldwide, with treatment resistance and interindividual variability in therapeutic response representing major clinical challenges.
- For a long time, the breast was considered a sterile organ. However, recent studies have revealed that breast tissue actually harbors a low-biomass microbiota, with significant compositional differences between healthy and malignant tissues, suggesting that local microorganisms may participate in tumor initiation and progression.
- Further research has demonstrated that, in addition to the local breast microbiota, the gut and oral microbiota also influence breast cancer biological behavior through local and systemic crosstalk, and may modulate treatment responses.
- Of particular note, accumulating evidence indicates that core breast cancer treatment modalities—including immunotherapy, chemotherapy, endocrine therapy, and HER2-targeted therapy—may all be regulated by the microbiota.
- A deeper understanding of these complex interactions holds promise for the discovery of novel biomarkers, optimization of therapeutic strategies, and development of microbiota-targeted interventions in breast cancer, ultimately improving the level of diagnosis, prognosis assessment, and precision medicine for this disease.

Crosstalk between the microbiota and the malignant progression of breast cancer.



- Microbiota from the breast, gut, and oral cavity participate in breast cancer development through local and systemic crosstalk.
- Tumor and normal breast tissues differ in microbiota composition (e.g., Firmicutes, Bacteroidetes), though study results vary.
- Specific bacteria, including *Fusobacterium nucleatum* and *Bacteroides fragilis*, are linked to tumor initiation, proliferation, metastasis, and drug resistance.
- These microbes regulate T cell infiltration, inflammation, and estrogen metabolism, thereby shaping the tumor microenvironment and breast cancer progression.

Microbiota and their metabolites in breast cancer therapy



- Gut/intratumoral microbes modulate immune infiltration and cytokines to affect immunotherapy response.
- Microbiota and metabolites regulate drug metabolism and apoptosis; composition changes correlate with chemotoxicity.
- Microbiota mediate estrogen enterohepatic circulation and local reactivation, influencing endocrine therapy response.
- Microbiota-targeted interventions (e.g., probiotics, FMT, engineered microbes) show promise but remain early-stage clinically.

Summary

- The human microbiota is closely associated with breast cancer biology, involving multiple ecological niches including the breast, gut, and oral cavity;
- Microbiota and their metabolites influence the tumor microenvironment and breast cancer development through diverse pathways, such as immune, metabolic, and inflammatory;
- Microbiota and their metabolites may correlate with responses to systemic therapies, including immunotherapy, HER2-targeted therapy, chemotherapy, and endocrine therapy;
- Microbiota-targeted interventions (e.g., probiotics, fecal microbiota transplantation, and engineered microbes) hold promise for improving the efficacy of various breast cancer treatments; however, clinical translation remains at an early stage, and future efforts should strengthen mechanistic and translational research.

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