Host–Microbiota Crosstalk in Ovarian Cancer

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Tumor-associated microbiota is increasingly recognized as an active component of the cancer microenvironment, yet its functional contribution to ovarian cancer progression and therapeutic response remains poorly defined. In this study, we experimentally investigated bidirectional host-microbe interactions in ovarian cancer and integrated whole-genome sequencing to identify the genetic basis underlying observed phenotypes. We isolated 45 bacterial strains from ovarian cancer and non-malignant ovarian tissues and performed extensive phenotypic characterization, including morphology, motility, biofilm formation, and antibiotic susceptibility testing. Chemotherapeutic drug-response assays showed that standard treatments (carboplatin, paclitaxel, and doxorubicin) reduced viability of ovarian cancer cell lines (SKOV3, OVCAR3, Kuramochi), the non-malignant fallopian tube epithelial model (FT190), and patient-derived ovarian organoids to ≤10–20%. In contrast, the majority of patient-derived bacterial isolates, including *Escherichia coli*, *Staphylococcus hominis, Streptococcus constellatus, Klebsiella michiganensis*, *Lactobacillus paracasei*, and *Lactobacillus zeae*, remained highly tolerant to these agents under both aerobic and anaerobic conditions. To directly assess functional host-microbe crosstalk, we performed soluble-factor interaction assays using bacterial and host-derived supernatants. Cell-free supernatants from all isolates (including tumor-associated, non-malignant tissue-derived, and reference strains) collected during logarithmic and stationary growth phases, induced divergent host responses ranging from approximately 70% growth inhibition to 45% proliferation enhancement, depending on bacterial species and growth state. Together, these findings demonstrate that tumor-associated bacteria engage in dynamic, context-dependent interactions with ovarian cancer cells through drug tolerance and soluble-factor–mediated effects, highlighting the importance of incorporating microbiological assays into ovarian cancer research and therapeutic evaluation.