Patient-derived mini-colons enable long- term modeling of tumor–microenvironment complexity

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Date/Time: 2024/12/12, 15:10 -16:00
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Background:

Traditional organoid models are limited in fully replicating the complexity of cancer, particularly in terms of multicellular diversity, tissue organization and biological durability. These limitations hinder the study of multifactorial cancer processes, especially those involving the tumor microenvironment (TME). Existing colorectal cancer (CRC) models often fail to accurately mimic the interactions between cancer cells and their native TME, which includes stromal components, immune cells, and vascular elements.

Objective:

To validate a patient-specific mini-colon model that replicates colorectal cancer (CRC) tumor dynamics, serves as a drug testing platform, and enables the study of tumor microenvironment (TME) interactions, including mechanisms of invasion, immune evasion, and immunotherapy.

Results:

The mini-colon model successfully mimics patient-specific CRC tumor formation, progression, and invasion, with long-term culture capability. It accurately evaluates drug efficacy and toxicity, distinguishing between effective and ineffective therapies while enabling real-time observations of tumor cell dynamics. The model reveals that cancer-associated fibroblasts (CAFs) drive CRC invasion EMT and upregulation of MMP7. Additionally, tumor-infiltrating lymphocytes (TILs) showed cytotoxic potential and promote immune evasion by inducing PD-L1 expression in cancer cells. Furthermore, PD-L1 blockade restores TIL-mediated tumor killing, demonstrating the model's utility in studying immunotherapy strategies.

Conclusion:

The mini-colon model represents a significant advancement over traditional organoids by integrating patient-specific cancer cells with their native TME in a stable, long-term culture system. It provides a versatile platform for studying tumor dynamics, testing anticancer drugs, and exploring mechanisms of tumor invasion and immune evasion. By enabling high-resolution analysis of TME interactions, the mini-colon offers new opportunities for personalized medicine, immunotherapy optimization, and identifying novel therapeutic targets for CRC.