An Organotypic Tumor Microenvironment (oTME) Model for High-throughput Discovery of Anti-cancer Therapeutics

Technology Summary

This technology provides a method to replicate the tumor microenvironment (TME) *ex vivo* for high-throughput discovery of anti-cancer therapeutics and therapeutic targets.

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Technology Overview

The development and growth of solid tumors relies on their surrounding tumor microenvironment (TME), which consists of several types of non-malignant cells. One of these cell types, named tumor-associated macrophages (TAMs), are of great interest to biomedical studies because they are critical to enhance proliferation, angiogenesis, and immune evasion of tumor cells. While the immunosuppressive TAMs are considered a highly promising therapeutic target for various solid tumors, researchers must rely on systems that are either non-scalable (e.g., mouse models) or incapable of accurately recapitulating the TME in patients (e.g., *in vitro* cell culture) when screening for drugs and drug targets. As such, there is a need for research tools that accurately model the TME to accelerate the discovery of therapeutics targeting the pro-tumorigenic functions of TAMs.

This technology provides an organotypic TME (oTME) model with remarkable scalability and a high resemblance to the TME in patients. The oTME is an *ex vivo* system derived from murine mammary tumors by integrating the tumor cells with the TME components (e.g., stromal cells, immune cells including T cells, NK cells and macrophages) from the same tumor, allowing for the maintenance of the intercellular interactions between tumor cells and other cells. Therefore, the oTME can recapitulate the human TME *in vivo* with high fidelity. Moreover, unlike conventional *in vitro* cell cultures, the oTME is exceptionally stable in culture (>2 month), scalable, self-sustained, with minimal requirement for the addition of growth factors or basement membrane proteins, which makes it suitable for high-throughput screening of TME immune-targeting therapeutics. In a proof-of-concept study, the inventors successfully identified novel anti-cancer drug targets and drug candidates that can revert TAMs to immuno-reactive state, block TAM proliferation and significantly inhibit tumor growth.

Potential Applications

- High-throughput anti-cancer drug target discovery
- High-throughput anti-cancer drug discovery
- Mechanistic research on tumorigenesis, metastasis, and immune evasion in TME

Advantages

- High resemblance to the human tumor microenvironment (TME)
- Scalability enables high-throughput screens
- Exceptional stability (>2 months) in culture
- Self-sustained (No requirement of growth factors or basement membrane proteins)