Project title: Utlizing organoids to investigate organotropism of breast cancer metastasis

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Aim of the Project

This project aims to develop advanced 3D organoid models, or "oncomaterials," that mimic the breast cancer metastatic niche to improve understanding and therapeutic targeting of metastasis. By generating organoids from primary, metastatic and normal tissue sites for subsequent co-cultures and integrating these models with 3D microfluidic organ-on-chip systems that emulates in vivo tissue structures and the tumor microenvironment (TME), we aim to enhance understanding of intravasation, an early step in metastasis. This model seeks to reveal mechanisms of tumor cell attraction, colonization, and growth within specific organs, focusing on the metastatic niches commonly affected by breast cancer.

Project Description

Breast cancer (BC) is the second most common cancer worldwide, with metastasis accounting for over 90% of BC-related deaths. Metastasis is now understood to be a non-random process and dependent on intricate tumor-stroma interactions at the target organ. The most common sites of BC metastasis include the lung, liver, bone and brain, with the microenvironment at each site playing a critical role in facilitating metastasis. For instance, HER2-positive BC patients experience a higher incidence of brain metastasis compared to those with HER2-negative or hormone receptor-positive BC, highlighting how both tumor cell properties and host organ factors contribute to metastatic efficiency.

Characterizing metastatic progression is challenging, especially with current tumor models. While animal models provide valuable complexity, they do not fully mimic human physiology and rarely develop clinically relevant metastases, limiting their translational relevance. Furthermore, few models capture the essential roles of immune and stromal cells, as well as soluble factors, in orchestrating metastasis—an important gap that this project aims to address. Recently, 3D organoid technology has gained traction in cancer research. Organoids are three-dimensional cultures that mimic organ-specific cell organization, self-organizing from stem cells or progenitor cells in a way that closely resembles in vivo conditions. As “biological twins” of the patient’s own tissue, organoids are a promising platform for drug testing, biomarker discovery, and guiding personalized treatments in clinical practice.

This project aims to develop a metastatic organoid model system that advances the understanding and therapeutic targeting of the pre-metastatic niche. The approach will focus on two primary goals: First, generating organoids from paired primary and metastatic tumors to reveal potential mechanisms by comparing these two organoid types. While this approach provides valuable insight, it does not capture interactions between tumor cells and the native microenvironment. Therefore, the project’s second goal

will involve creating organoids from normal tissue, then co-culturing these with tumor-derived cells or organoids to better mimic the metastatic niche. These experiments will be further enhanced by integrating 3D microfluidic organ-on-chip systems. These chips will simulate in vivo-like conditions, incorporating multiple cell types and physical forces to study organ-specific tumor microenvironment cues and their role in primary BC spread.

By elucidating the interactions between immune cells, soluble factors, extracellular matrix proteins, and stromal cells, this research will deepen insights into tumor cell attraction, colonization, and proliferation within the metastatic niche. The ultimate objective is to leverage these "oncomaterials" for early detection of metastatic events, prevention of niche formation, and inhibition of metastatic progression. Through this work, the project aims to open new avenues for therapeutic intervention and provide foundational models for translational research in BC metastasis.

Requirements:

Familiarity with cell culture techniques, as well as knowledge of tumor microenvironment interactions, immunology, or metastasis mechanisms will be advantageous. Candidates with experience in molecular biology and cell biology are encouraged to apply.