

# Bioengineering organotypic 3D microtumors for anti-cancer drug discovery

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Bioengineering human 3D tumor models that recapitulate major disease hallmarks has a unique potential to significantly accelerate anti-cancer therapeutics discovery and preclinical screening. The development of human tumor surrogates has however remained highly challenging owing to tumors' biological complexity and self-evolving features. Emulating living tumors' microenvironment in an *in vitro* setting requires the precise inclusion of distinct cell populations that dynamically interact and interface with the tumor extracellular matrix (ECM). The tumor-ECM is recognized to support cancer and stromal cell proliferation and differentiation. In the context of tumor progression, ECM alterations also play a critical role in resistance to therapeutics and metastatic processes.

Envisioning to recapitulate the major components of human breast cancer microenvironment, this research employed breast tissue-derived decellularized extracellular matrix (dECM) for *in vitro* fabrication of organotypic 3D tumor models envisioning to augment biomimicry. The bottom-up fabrication strategy

involved dECM-microfibrillar fragments combined with major human cell components, enabling to analyze leading chemotherapeutics for breast cancer therapy. This methodology facilitated the preservation of microarchitectural features of native ECM, therefore providing an alternative route for facile dECM components inclusion without requiring extensive processing. Foreseeably, such closer-to-human avatars are envisioned to be used for large scale screening of next-generation precision therapeutics that may provide more tractable advances in the management of breast cancer, as well as other solid human neoplasias.

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**FIGURE 1**  
3D Breast cancer microtumor models bioengineered with native tumor microenvironment components. Microtumors' cellular invasion into surrounding artificial tissues modelled in a preclinical setting.

