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Poster Abstract Form

A large molecular model of cancer harmonizes bioprinted PDAC co-cultures with patient biology

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Introduction

Durable benefit from emerging PDAC therapies depends on resolving the tumor-intrinsic and microenvironmental (TME) biology governing therapeutic vulnerability, combination rationale, and resistance. Co-culture models enable controlled study of this biology, while computational foundation models can extract interpretable biology linking these models back to patients. The Genialis Supermodel places PDAC co-culture models and patient tumors in a common biological space to nominate “biological twins” and clinically actionable subsets.

Methods

PDAC RNA-seq from the PanCAN SPARK Know Your Tumor (KYT) program, Inventia RASTRUM 3D-bioprinted PANC-1 and AsPC-1 monoculture or CAF co-culture models, and benchmarked patient-derived culture models were analyzed with the Genialis Supermodel. Each sample was decoded into biomodules quantifying tumor-intrinsic and microenvironmental programs. Model-to-patient concordance was quantified by biomodule correlation and embedding distance, unsupervised clustering defined biological classes, and classes were related to model drug responses.

Results

In the KYT cohort, biomodule scores span a broad range of stromal and immune-related activity defining the patient reference distribution. RASTRUM co-culture models reproduce canonical PDAC tumor-stroma biology relative to monoculture, with enrichment of TGF- β signaling, EMT, ECM remodeling, fibroblast activation, immune evasion, and hypoxia. CAF co-cultures shift toward the stroma-high region of patient space relative to monoculture, and resulting biological classes, defined by tumor-intrinsic (KRAS/MAPK) and microenvironmental (CAF, TGF- β) programs, map onto specific KYT patient subsets.

Conclusion

Embedding co-culture models and the KYT cohort in a shared biomodule space tests which models recapitulate patient biology and which subsets they represent, supporting an iterative model-to-patient strategy for prioritizing combination drug studies across therapeutic settings.