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3D Bioprinting the Tumor Microenvironment for Immunotherapy Development

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Abstract

The **tumor microenvironment (TME)** is a complex system that plays a crucial role in tumor progression, immune evasion and therapy resistance. Tumor associated macrophages (TAMs) are common in the TME where they play a strong anti-inflammatory role and promote tumor immune escape. Understanding the complex interactions within the TME is essential for developing effective anti-cancer immunotherapies.

3D bioprinting technology offers a novel approach for creating complex *in vitro* models of the TME, allowing for the rapid and cost-effective creation of tissue constructs that mimic the composition and spatial structure of native tissues. These models combine tumor cells, immune cells, and supportive cells to allow researchers to investigate the TME and screen the efficacy of novel drugs and anti-cancer immunotherapies.

Tumor Microenvironment

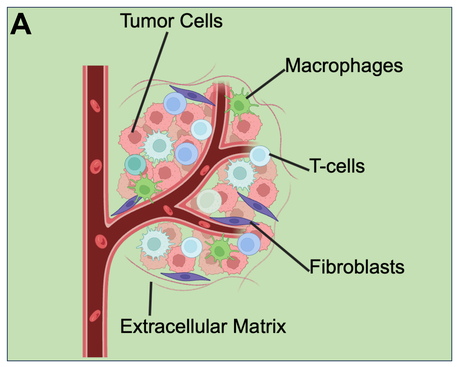
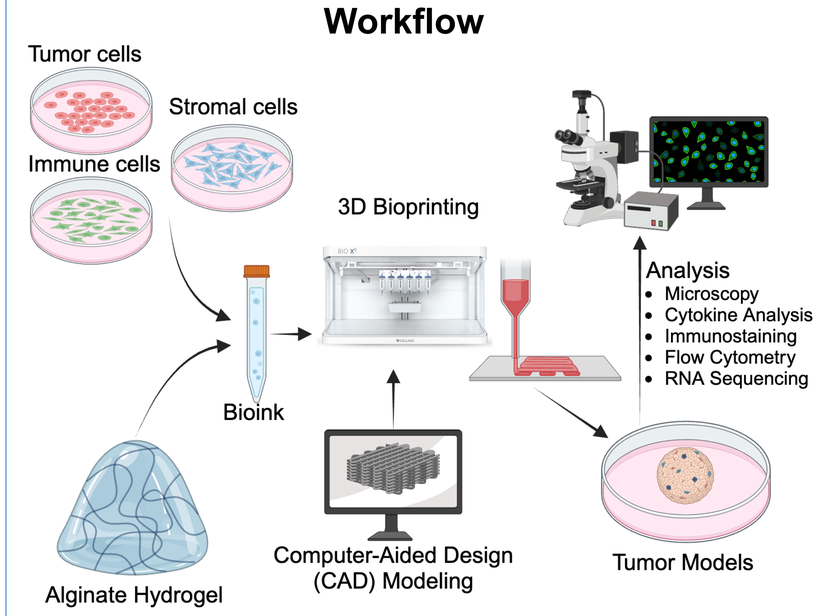


Figure 1.
A) The TME is composed of a variety of cell types which create an anti-inflammatory environment and prevent infiltration of cytotoxic immune cells.
B) Macrophages may exhibit pro-inflammatory or anti-inflammatory phenotypes. TAMs polarize toward an M2 state which contributes to the immunosuppressive TME.
C) M1 polarized macrophages gain MHCII expression by flow cytometry.
D) M2 polarized macrophages show increased CD206 expression by flow cytometry.
E) Macrophages can initiate an adaptive immune response via phagocytosis and antigen presentation.
F) Phagocytosis is measured with a fluorogenic probe to find that M1 macrophages engulf more cancer cells and thus are more immunogenic.

3D Bioprinting the TME



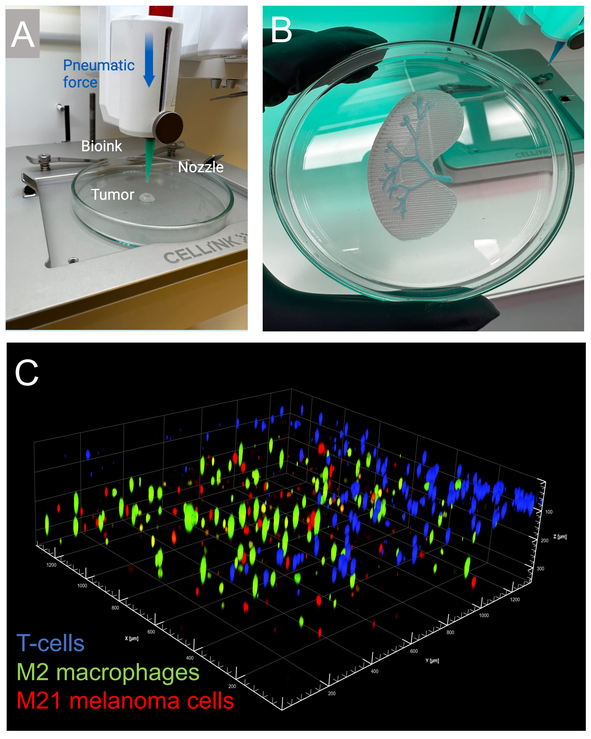
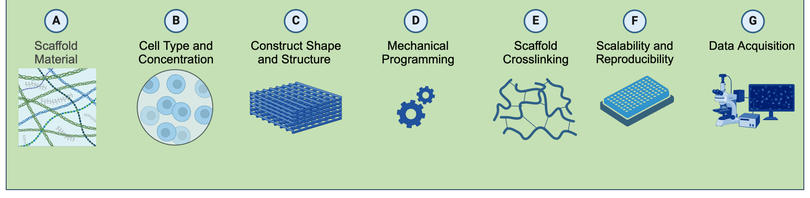
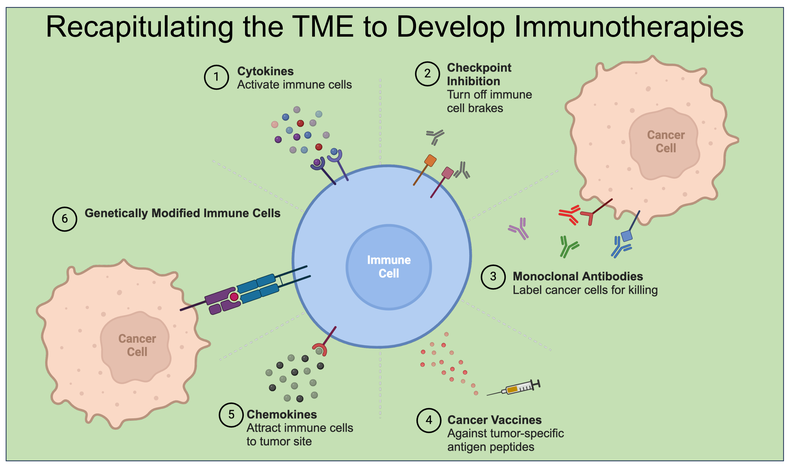


Figure 2.
A) CELLINK extrusion-based BioX6 printer with an intelligent printhead.
B) Bioprinted kidney model demonstrates the versatile capabilities of utilizing six intelligent printheads.
C) 3D rendered confocal microscopy image of bioprinted tumor model allows visualization and spatial analysis of T-cell infiltration.

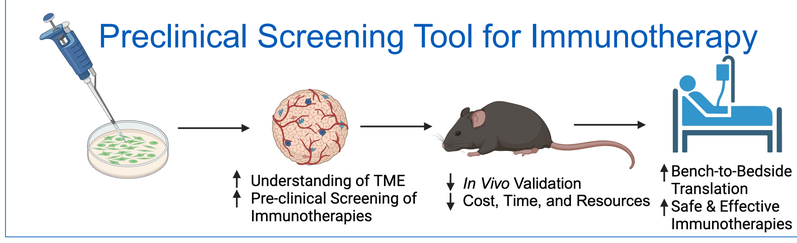
3D Bioprinting Optimization



Future Directions



- Utilize bioprinted tumor models to more efficiently develop novel cancer immunotherapies.
- Enhance tumor model complexity by introducing cancer-associated fibroblasts, myeloid-derived suppressor cells, and regulatory t-cells.
- Utilize tumor models to evaluate efficacy of iPSC-derived immune cells and novel immunotherapeutic CAR-T cell and CAR-Macrophage treatments.
- 3D bioprint patient-derived tumors for use in preclinical drug discovery and personal diagnostics.



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