Hypoxia-Inducing Cryogels (HICs) for Preclinical Anticancer Drug Screening

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Introduction

- Emulating the tumor microenvironment in-vitro is crucial to improving pre-clinical anti-cancer drug screening studies and drug development as a whole
- Two-dimensional (2D) models fail to recapitulate the complexity of the tumor microenvironment or induce a stable hypoxic oxygen gradient¹-²
- Three-dimensional (3D) Multicellular Tumor Spheroids (MCTS) models lack reproducibility³-⁴, a physiological environment⁵, and mechanical support⁶-⁷

To address these limitations, we developed an advanced 3D tumor model by combining:
- Biomimetic, macroporous, soft, cryogel-based scaffolds⁶ to facilitate cell seeding, proliferation, invasion, and extracellular matrix (ECM) formation
- A 3D, biomechanical support emulating tumor-associated hypoxia around tumor cells

We hypothesize that cryogel-based tumor models can be used as a platform for more reliable anti-cancer drug screening and can contribute to a better understanding of carcinogenesis.

Fabrication of Injectable Cryogels

Fabrication Process: Cryogelation

1. Cryogelation
2. Thawing
3. Injection

Cryogels vs Hydrogels: Macrostructure

- Cryogels possess highly interconnected macropores
- Cryogels are soft with shape memory properties

Cryogels vs Hydrogels: Physical Properties

- Cryogels are inter-connected & macroporous 3D scaffolds with highly tunable physio-chemical properties
- HICs induce cellular hypoxia all while retaining high cell viability.
- HICs induce phenotypic change of tumor cells, leading to therapeutic resistance against doxorubicin
- Evaluate the impact of HICs on tumor cells’ metabolic activity, and aggressiveness
- HIC-supported tumor models can potentially mimic human tumors more closely and be used as a platform for drug screening and predictive preclinical testing of emerging anti-cancer therapeutics

Conclusions & Future Directions

References