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DEFENSE OF THE DOCTORAL

DISSERTATION

"DEVELOPMENT OF BONE MARROW-MIMETIC HYDROGEL FOR 3D BIOPRINTING OF IN VITRO BONE MARROW MODELS"

by

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10:00 A.M.
WebEx TBD

ABSTRACT

Biomedical research and translational medicine thrive by bringing data from bench to bedside and then back to the bench. This iterative cycle is critical for our understanding of the human body in health and disease as well as for the development of therapeutic approaches. Three-dimensional (3D) in vitro models are an important bridge between conventional two-dimensional (2D) cell culture systems and preclinical in vivo models, such as mice and rats. 3D culture systems provide a more physiologically relevant environment for cells in vitro, eliciting phenotypes which more closely represent that of cells in vivo and subsequently increasing translational efficiency of generated data.

Bone marrow (BM) is a historically difficult organ to model in vitro for a variety of reasons, including its weak mechanical properties, complex niche arrangement, and heterogeneous cellular composition. BM biopsies and aspirates and traditional 2D co-cultures do not adequately represent the BM microenvironment in an in vitro setting. State-of-the-art 3D models more closely mimic microenvironment of BM but often lack proper physical imitation of endogenous BM tissue. Additionally, these 3D models are limited by difficulties in implementation, model customization, and scalability. 3D bioprinting technology can be leveraged to address these challenges through the fabrication of tunable, high-throughput in vitro BM models by using a BM-mimetic hydrogel, or ‘bioink’.

Through a comprehensive evaluation and characterization process, we have developed a novel methylcellulose (MC)-alginate based hydrogel bioink that is amenable to bioprinting, mimetic of mechanical and architectural aspects of native BM, and supports primary human BM cells. Furthermore, this bioink facilitates customizability and scalability of in vitro models with which to investigate BM-focused research questions.

Models created using this MC-alginate hydrogel have the potential to provide critical insights into the role of the BM microenvironment in a variety of physiological states. For instance, we have demonstrated that scaffolds created using the BM-mimetic bioink support viability and cellular dormancy of BM-metastatic triple negative breast cancer cells (BCCs). Dormant BCCs in BM are known to be a major source of cancer resurgence and to pose a continual challenge for current and prospective oncology treatments. Future studies using this model can uncover new non-toxic therapeutic targets and strategies to eradicate dormant BCCs and improve patient outcomes.