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Creating a Mammary Duct Model to Study the Effects of Cancer Heterogeneity on Tumor Metastasis

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ABSTRACT

During tumor progression, the process of clonal evolution gives rise to a variety of cell subpopulations that cause differential sensitivity to drugs and give rise to cell populations with the ability to metastasize, there are many mouse models available that can be used to study tumor progression and metastasis. However, there is a lack of models to study the effect of tumor heterogeneity using human cancers. Xenograft based systems require the use of immunodeficient mice, which limits the use of the model to evaluate microenvironmental factors involved in metastatic dissemination. Humanized mouse models with established human immune systems have been developed. However the high cost, and deficiencies in the immune system limit their clinical utility. One way to combat these issues is through tissue-engineered models. A mammary duct model was created to study the effects of breast cancer cell heterogeneity on metastasis. A 3D printed mold was fabricated to create a lumen, representative of the hollow mammary duct using type I collagen. After lining the interior of the lumen with Matrigel to mimic the basement membrane, normal human epithelial cells (HMLEs) were seeded into the lumen. Future studies will use this physiologically relevant tissue model to systematically evaluate microenvironmental factors that drive human breast tumor initiation, progression, and metastasis. This model can further be used to study the effect of cancerous oncogenes that are activated by the presence of a common cancer drug, such as doxycycline, as well as systematically investigate the role of the tumor microenvironment on tumor progression.

KEYWORDS

Mammary duct model, metastasis, collagen lumen