Application of Cell-Mate,... 3D matrix to modeling artificial breast cancer and “normal” ductal tissues.

Timothea Lyden Ph.D, Brun Stilpen Justen, Ronald Louiere, Tissue Innovation Center, Biology Imaging Center, University of Wisconsin-River Falls, River Falls, WI

Abstract

In collaboration with BRTI Lifesciences, LLC., the UWRF TCIC has been engaged in testing and evaluating a new synthetic, 3D tissue engineering matrix material called Cell-Mate. This new material is based on a combination of bioactive hydrogels that can be used to generate artificial tissues. In the series of studies, breast ductal adenocarcinoma cells (MCF7) and ‘normal’ breast ductal cells (MCF10A) were grown in Cell-Mate ATTs and these studies were used to evaluate the behavior of these cells. MCF-7 ATTs were generated from 40, 20 and 10 million cells respectively and ATs from MCF10A were generated from 20 and 10 million cells. In all cases, successful ATTs resulted in significant areas of tissue or tumor formation. The architecture and distinct evidence of cellular differentiation as well as tumor cell progression. MCF-7 ATTs generated evidence of tumor progression and eventual metastasis-related spherical, clump and single cell release. In the case of 40 million cell loading, spheroid production occurred first within the week of culture while at 20 and 10 million cell load, the timing of spheroid generation/release was significantly longer, at 2-3 weeks. Also, in the case of 40 million cell load, 20 and 10 million cell load showed different results on the surfaces of the developing ATs. Interestingly, one single cluster generation was seen in the “normal” MCF10A cell ATTs, while a multitude of these were present. Also in the case of MCF10A ATTs, single clusters formed in the bottom of the wall which did not differentiate cell associated atoms and clusters after 2-3 weeks of ATT development. These results contrasted dramatically from those seen in the original culture monolayers which strongly supports the interpretation that the ATs microenvironment induce further changes in cell behavior. Continuing studies are evaluating the impact of Cell-Mate ATTs on the progression patterns of breast cancer cell lines.

In collaboration with BRTI Lifesciences, LLC., the UWRF TCIC has been engaged in testing and evaluating a new mass of tumor tissue (figure 4, below). In our initial studies, many of these features contain materials which appear to be in the process of being secreted as a flaccid material. Ongoing and future studies will examine and further define/characterize each of these observed features as well as seek to understand the in-vitro developmental pathways involved. The architecture of life.

Summary and Future Directions.

In this pilot study, we have demonstrated that the utilization of 3D Matrix media and does work as a viable approach for the growth of ductal adenocarcinoma cells as well as “normal” breast ductal epithelial tissues. In both cases, the resultant structures contained a high cell density with the various nucleated sinks of the original cells. In the case of MCF-7 adenocarcinoma cells, we observed the generation of large clusters of tumor tissue and the development of numerous attachment points in figure 4A and B. In the case of MCF10A “normal” ductal cells, we saw the generation of excellent tubular ducts with evidence of secretion from these features, potentially including the generation of milk fats. Ongoing and future studies will examine and further define/characterize each of these observed features as well as seek to understand the in-vitro developmental pathways involved.