



Short Article

Stem Cell 2018:Development and application of bioengineered artificial tumor tissues to effectively model breast cancer generation, progression and metastasis - Timothy Lyden - University of Wisconsin, USA

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Abstract

Tissue engineering and regenerative medicine have developed in various different directions while collectively growing into the burgeoning new fields that we see today. One area of interest to our laboratory seeks to apply engineered or artificial tissues as alternatives to cell cultures and live animals in modeling cancer. Our laboratory at the TCIC has been applying engineered tissue approaches over the past 14 years to explore the use of these technology solutions to study normal and cancerous tissues. From initialization/colonization to long-term progression, metastasis and target attachment/invasion we are exploring artificial tumor tissues using a variety of different natural and synthetic substrates as well as several different culture conditions. Here work focused on two specific types of tumors which will be presented, melanoma and breast cancer. In each of these cases, we have successfully developed in vitro tumor models which present with many features observed in patient samples while providing a platform to directly study cellular and tissue interactions and mechanisms involved at various stages of these diseases. In the case of melanoma, models of tumor generation and progression using a hydrogel-based matrix combined with B16F1 and B16F10 mouse melanoma cell-lines will be the focus. These studies demonstrate the capacity of in vitro 3D models to very closely replicate clinical observations of cutaneous melanoma. In addition, since these in vitro models are maintained intact for extended growth periods, out to 6 months in these studies, the resultant artificial tumors effectively demonstrate the process of tumor progression as well.

A hallmark of this progression is the generation of two-three cellular populations that display clearly distinct morphological and behavioral characteristics. In the second case, human breast adenocarcinoma cell line MCF-7 was employed with several different natural matrix materials in addition to our standard hydrogels, to generate a library of studies with artificial tumors tissues extending over very long-term culture periods, up to 4 years in some cases. Results from several types of scaffold and their implications as evidence of the value of this modeling system will be presented. In these studies collectively, tumor progression leads to the staged development of single cell release followed by cancer cell cluster release and definitive spheroid formation followed by distant colonization of the culture wells. Our working hypothesis is that these stages and the released products, particularly the clusters/spheroids, represent a direct correlate to clinical metastasis. We are also studying the nature and behaviors of these released cells under various conditions and using a variety of methods include immunolabeling, flow cytometry, and western blotting. Taken together, these presented studies demonstrate the power and efficacy of in vitro 3D artificial tissues as models of clinical disease in cancer and support our assertion that these essentially represent designer Lab-Animals-in-a-Dish.