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Three-Dimensional Tumor Cell Cultures and the Role of Tissue Biorepositories in Personalized Medicine

Klara Valyi-Nagy

Research Assistant Professor, Department of Pathology, University of Illinois at Chicago, USA

***Corresponding author:** Department of Pathology, University of Illinois at Chicago, 840 South Wood Street, Room 130 CSN, M/C 847, Chicago, IL 60612, USA, Tel: 312-996-0029; E-mail: klaravn@uic.edu

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Tissue biorepositories have long been critically important for medical research by providing human tissues for scholarly investigations. In addition to this traditional research role, tissue banks are rapidly assuming new roles in the clinical side of medicine. In the modern era of personalized medicine, tissue biorepositories are increasingly expected to establish close collaborations with clinical and laboratory units and provide banked tissues for a variety of tests that in turn will guide clinical decision making tailored to the patient [1-4]. This new role of biorepositories requires the development of novel complex standard operating procedures (SOPs) for tissue collection, processing and storage that can provide tissues ideal for a variety of novel molecular and other tests [1,3,4].

The introduction of three-dimensional (3D) tumor cultures has revolutionized anticancer drug research as these cultures allow for the study of drug resistance mechanisms that cannot be explored in traditional two dimensional (2D) monolayer cultures. The behavior of cells in vivo is controlled by their interactions with neighboring cells and with the extracellular matrix (ECM) [5-7]. Cancer cells grown in 3D cultures in a polymeric ECM closely mimic the biology of tumor development in vivo and numerous studies indicate that 3D cultures are superior to traditional 2D monolayer cultures for studies of key cellular behaviors like differentiation, proliferation, invasion and apoptosis [8,9]. Cancer cells grown in 3D culture are more resistant to chemotherapeutic agents, radiation and oncolytic virotherapy than cells in 2D culture and 3D tumor cell cultures are useful for preclinical evaluation of the cytotoxic effect of anticancer agents [6,8,10-14].

Analysis of clinical tumor specimens by molecular and other tests that can guide individualized therapy is a cornerstone of personalized medicine [2]. Short-term primary cultures of tumor cells derived from pieces of solid tumors have been used for predicting anticancer drug responses [2,15].There are several lines of observations suggesting a significantly increased use of 3D tumor cultures in personalized medicine in the near future. The concept of personalized therapy of tumors based on tumor stem cells is based on the notion of targeting slowly-dividing and inherently therapy-resistant tumor stem cell populations. Tumor stem cells isolated and amplified from individual clinical tumor specimens could be tested for sensitivity to antineoplastic treatment modalities and molecular markers for improved personalized tumor therapy [2]. 3D culturing of tumor cells provides a niche for enrichment in tumor stem cells [7,16-19]. Importantly, 3D cultures also have been reported to augment isolation and characterization of circulating cancer cells, a development potentially highly relevant to personalized tumor therapy [20].

As 3D tumor cultures are emerging as excellent in vitro experimental platforms for studies of tumor resistance against a variety of antineoplastic modalities, it is likely that there will be an increasing demand on tissue biorepositories to be able to prepare and perhaps even process tumor tissues for 3D tumor cell cultures. This will require the adjustment of SOPs, consent procedures and institutional review board (IRB) protocols to include routine isolation of cell lines at the time of tumor tissue collection or viable cryobanking that will process and store tumor tissues in a way that will allow for the establishment of tumor cell lines at a later time [21].

In summary, processing of tumor tissues in ways that allow for the establishment of 3D tumor cell cultures is likely to become a regular activity of modern tissue repositories as they expand from their traditional research role to active participation in personalized medicine. Pathologist and other personnel involved in tissue banking will need to adapt to the new expanded roles of modern biorepositories that will likely include routine isolation of cell lines at the time of tumor tissue collection or viable cryobanking that will allow for the establishment of tumor cell lines at a later time.

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