ACTA SCIENTIFIC CANCER BIOLOGY

Volume 2 Issue 8 October 2018

Editorial

Investigating Metastatic Cancer: Pre-Clinical Models

Enza Lonardo*

Researcher, Gastrointestinal Cancer Laboratory, Molecular Oncology Department, Institute of Genetics and Biophysics, Naples, Italy

***Corresponding Author:** Enza Lonardo, Researcher, Gastrointestinal Cancer Laboratory, Molecular Oncology Department, Institute of Genetics and Biophysics, Naples, Italy.

Received: July 19, 2018; **Published:** September 01, 2018

Xenotransplantation of human cancer cells or fresh tumour tissue into immunodeficient mice has been used for several years as a main tool to study cancer biology and for preclinical screening to develop novel cancer therapeutics. Whereas subcutaneous inoculation is most commonly used and represents a valuable tool for tumour biology studies and drug screenings, thanks to its low cost and simplicity, it fails to recapitulate the microenvironmental complexity and metastatic profile of human tumours. The organ-specific orthotopic implantation (e.g. the caecum or the pancreata), while more challenging to generate, offers a more realistic model to study the biology of metastasis. Remarkably, both types of xenografts generated from integral tumour pieces recapitulate the histological features including stroma and preserve genetic heterogeneity of the original tumour better than cell lines. However, both models lack a fully intact TME (tumor microenvironment), both due to mismatch between some murine and human signalling molecules and because of the absent or abrogated immune system required for xenotransplantation. To address these problems, mouse models are being generated that correct known signalling deficits as well as feature humanized immune components, potentially leading to patient-specific immune environments. These future advances promise to clearly enhance these already potent tools for cancer biology and preclinical oncology.

Three-dimensionally cultured tumour organoids are increasingly exploited as an alternative to xenotransplantation and have already made a strong impact on cancer biology as they retain much of the genetic heterogeneity of the original tumour and can be easily manipulated for high-throughput screening. When injected, especially in orthotopic implantation, tumour organoids can give rise to histologically complex tumours that closely relate to the original cancer. Remarkably, taking advantage of the CRISPR/CAS9 technology, studies have modelled the tumour progression from "adenoma to carcinoma" through the introduction of sequential mutations in human different types of cancer. These advances will considerably speed up the modelling of combinations of mutations (or their reversion) on large solid tumour panels to study the adenoma-carcinoma sequence. Taken together, most recent data emphasize the importance of tumour heterogeneity as a mixture of malignant and non-malignant cells modulating cancer progression and chemoresistance. The evaluation of stromal cells as putative biomarkers and therapeutic targets has opened a range of original possibilities to ameliorate the outcome of patient with cancer. However, the complex network of cell sub-populations forming the TME will need to be further investigated in order to improve actual therapies.

Volume 2 Issue 8 October 2018