3D tumor spheroids

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Abstract

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Introduction

PDAC belongs to the top five of cancer-related deaths in the world and the poor prognosis is primarily due to its advanced stage at diagnosis , the progress in its treatment remains too slow as a consequence of the complex physiopathology of this tumor characterized by a heterogeneous cellular composition and the accumulation of a very dense fibrotic tissue [**???**]: Due to that pancreatic cancer is a heterogeneous disease, is often modelled using established cell lines in the laboratory.

In recent years, three-dimensional (3D) culture systems have gained increasing recognition as an effective tool for biological research. One widely used 3D culturing technique is the application of multicellular spheroids (MCS).Cells cultured in 3D more closely mimic the physiological environment compared to conventional monolayer culture systems. Spheroids are three-dimensional spherical cellular aggregates with high cell-density, that more closely simulate conditions existing in solid tumors where hypoxia and alterations related to intracellular metabolism occur due to poor availability of nutrients from blood vessels.@doi:10.1371/journal.pone.0177737

Pancreatic tumor microenvironment

In Pancreatic ductal adenocarcinoma (PDAC), the major components of the tumor microenvironment are a complex population of fibroblasts forming the bulk of the stroma, vasculature, inflammatory and immune cells [2]. PDAC is associated with evolving alterations in the tumor microenvironment, including increasing fibrosis and extracellular matrix deposition (desmoplasia). Increasing desmoplasia accompanies progressive disease and creates intratumoral pressure that compresses the vasculature, resulting in limited blood flow to the tumor and consequent hypoxia and low nutrient delivery [3].

2D and 3D cell cultures

Cell culture is a widely used *in vitro* tool to improve the understanding of cell biology, cellular mechanisms, tissue morphology, drug action, protein production and the development of tissue engineering [4].

The structure of multicellular spheroids.

Methods for the generation of MCS

MCS and PDA

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