Unravelling the tumor-stroma interaction in biomaterials-based 3D cancer models

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Cancer associated fibroblasts, cancer cells, endothelial and immune system cells are the main players in the tumor progression. The non-reductionist view of tumor microenvironment makes aware researchers and oncologists that flat two-dimensional cell cultures are not the best standard to investigate cancer, since they do not recapitulate the complex interaction between the tumor cells and the surrounding microenvironment. Moreover, animal models face ethical challenges and do not mimic the human cancer microenvironment. Drug development is a high-costly process and may last 7-10 years with no guarantees for the final drug approval and efficacy. There is an urgent need to develop new tools able to copycat the tumor microenvironment and allow more realistic drug screening able to efficiently predict the drug efficacy and toxicity. Biomaterials support the grow of cancer cells together with the other cellular and acellular players, offering different options to recapitulate the tumor microenvironment.[1,2] Here, we presented a 3D cancer model based on the co-culture of fibroblast and pancreatic cancer cells seeded on gelatin porous microcarriers. The pancreatic adenocarcinoma (PDAC) *in vitro* model is able to recapitulate the main features of the tumor in vivo as shown by gene array analysis and histological staining. Moreover, in the dynamic system the cells are able to synthesize and remodelling their own extracellular matrix [3]. Based on the same dynamic system, breast cancer model is also developed and used as screening platform for conventional drugs and nanoparticles [4,5]. In the second part, we present some attempts to develop 3D *in vitro* cancer models based on naturally-derived biomaterials as silk fibroin, gelatin and gellun gum. These materials show good biocompatibility, suitable mechanical properties, tunable biodegradability. Both hydrogels and freeze-dried scaffold from the different materials have been produced in order to evaluate the best approach to faithfully recapitulate the tumor microenvironment. Firstly, breast cancer cells and normal mammary fibroblast are seeded or embedded in the scaffold/hydrogels [5]. The platforms may represents promising models for understanding the crosstalk between cancer cells, fibroblasts and extracellular matrix. Moreover, the developed 3D *in vitro* cancer models are also useful as drug screening platform.

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BioSketch

Virginia Brancato, PhD, got her Ph.D. in Enviromental Microbiology and cutaneous ecosystem from the “Luigi Vanvitelli” University of Naples, Italy, in 2010. In 2011, she joined the Virology Division of National Institute of Medical Research (London, UK) under the supervision of Alan Hay, world leader in virology. In 2012, she got a fellowship as postdoctoral researcher at the University of Naples, under the scope of the project entitled: NEWTON Advanced nano system for a new molecular oncology. Here, she developed heterotypic 3D tumor models (breast and pancreas) that can be exploited as drug screening platform. In 2017, Virginia Brancato joined 3Bs research group at the University of Minho, Portugal, as Assistant Researcher, supported by the H2020 ERA-Chair project FoReCaST. Her research activity is focused on development of *in vitro* 3D tumor model for drug testing. During her scientific career, she also supervised PhD candidates and masters students. Recently, she got FCT grant as principal investigator to study the interaction among macrophages and tumor microenvironment. She is member of the Tissue Engineering & Regenerative Medicine International Society (TERMIS), European Association for Cancer Research (EACR), and Association of Italian researcher Abroad (AIRIcerca).