World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:15, No:09, 2021

Construction of Ovarian Cancer-on-Chip Model by 3D Bioprinting and Microfluidic Techniques

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Abstract : Cancer is a major worldwide health problem that has caused around ten million deaths in 2020. In addition, efforts to develop new anti-cancer drugs still face a high failure rate. This is partly due to the lack of preclinical models that recapitulate in-vivo drug responses. Indeed conventional cell culture approach (known as 2D cell culture) is far from reproducing the complex, dynamic and three-dimensional environment of tumors. To set up more in-vivo-like cancer models, 3D bioprinting seems to be a promising technology due to its ability to achieve 3D scaffolds containing different cell types with controlled distribution and precise architecture. Moreover, the introduction of microfluidic technology makes it possible to simulate in-vivo dynamic conditions through the so-called “cancer-on-chip” platforms. Whereas several cancer types have been modeled through the cancer-on-chip approach, such as lung cancer and breast cancer, only a few works describing ovarian cancer models have been described. The aim of this work is to combine 3D bioprinting and microfluidic technics with setting up a 3D dynamic model of ovarian cancer. In the first phase, alginate-gelatin hydrogel containing SKOV3 cells was used to achieve tumor-like structures through an extrusion-based bioprinter. The desired form of the tumor-like mass was first designed on 3D CAD software. The hydrogel composition was then optimized for ensuring good and reproducible printability. Cell viability in the bioprinted structures was assessed using Live/Dead assay and WST1 assay. In the second phase, these bioprinted structures will be included in a microfluidic device that allows simultaneous testing of different drug concentrations. This microfluidic dispositive was first designed through computational fluid dynamics (CFD) simulations for fixing its precise dimensions. It was then be manufactured through a molding method based on a 3D printed template. To confirm the results of CFD simulations, doxorubicin (DOX) solutions were perfused through the dispositive and DOX concentration in each culture chamber was determined. Once completely characterized, this model will be used to assess the efficacy of anti-cancer nanoparticles developed in the Jean Lamour institute.

Keywords : 3D bioprinting, ovarian cancer, cancer-on-chip models, microfluidic techniques
Conference Title : ICB 2021 : International Conference on Bioprinting
Conference Location : Zurich, Switzerland
Conference Dates : September 16-17, 2021