Generation of a Perfusable 3D Lung Cancer Model by Digital Light Processing

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INTRODUCTION

Lung cancer still has one of the highest morbidity and mortality rates among all types of cancer. Its incidence continues to increase, especially in developing countries [1, 2]. Although the medical field has witnessed the development of targeted therapies, new treatment options need to be developed urgently [3, 4]. For the discovery of new drugs, physiologically relevant human cancer models are required to study drug efficiency.. In this respect, 3D printed organs have proven to be a promising tool in the field of cancer biology in recent years [5].

MATERIALS AND METHODS

We designed a perfusion model using Rhino 6 (McNeel) software, and then printed it utilizing a Lumen X Digital Light Processing bioprinter (Cellink) using GelMa PhotoInk (Cellink). Afterwards, the viability/cytotoxicity kit, XTT assays, and EdU (5-ethynyl-2'-deoxyuridine) Cell Proliferation Imaging Kit were used to detect the cell viability and cell proliferation in the model.Four days post perfusion with gemcitabine, cryosections of the model were immunofluorescently labelled to analyze the effects of drug-mediated apoptosis. ,

RESULTS AND DISCUSSION

In our study we used non-small cell lung cancer cells and a clinically used cytostatic drug. We connected the vascularized lung cancer model to a perfusion system and demonstrated the advantages of dynamic cultivation over conditions. Furthermore, the gemcitabine was applied via the perfusion system simulating intravenous injection in a human patient. Finally, we investigated the mode of action of the drug and demonstrated its ability to induce apoptosis in the cancerous cells. Compared to the high efficacy of gemcitabine found in 2D culture, the diminished cytostatic effect observed in 3D culture more closely resembles the biology of human patients; compared to static cultivation of 3D models. Further details can be found in our publish [International journal of molecular sciences vol. 24,7 6071. 23 Mar. 2023, doi:10.3390/ijms24076071]

CONCLUSIONS

This is the first published study on the use of Lumen X digital light processing bioprinting technology to generate a perfusable lung cancer model. We have shown that H358 cell survives the printing process, and this model can be used to study the toxicity of cytostatic substances. In addition, channels included in the model allow connection to perfusion systems that that rudimentarily reflects some properties of the vasculature of living organisms. Perfusion of the model resulted in higher cell viability compared to static conditions. In proof-of-concept studies, we use this setup to study the activity of the approved cancer drug gemcitabine and investigate its mechanisms of action. Therefore, we consider this model suitable for testing new substances with potential antitumor activity. In order to increase the physiological relevance of the model, it is planned to make it more complex in terms of its cellular composition, such as endothelial lining.

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