Biomimetic tumor engineering to enhance drug discovery - BioengineeredTumor

Bojana Obradović[1,*], Jasmina Stojkovska[1], Jovana Zvicer[1], Milena Milivojević[2], Radmila Janković[3], Miodrag Dragoj[4] and Ivan Jančić[5]

[1]*University of Belgrade, Faculty of Technology and Metallurgy, Belgrade, Serbia*
[2]*University of Belgrade, Institute of Molecular Genetics and Genetic Engineering, Belgrade, Serbia*
[3]*University of Belgrade, Faculty of Medicine, Belgrade, Serbia*
[4]*University of Belgrade, Institute for Biological Research "Siniša Stanković" - National Institute of the Republic of Serbia, Belgrade, Serbia*
[5]*University of Belgrade, Faculty of Pharmacy, Belgrade, Serbia*

Keywords: 3D cell culture; cancer; perfusion bioreactor; carcinoma; osteosarcoma

Hem. Ind. **78(1S)** 22 (2024)

Available on-line at the Journal web address: http://www.ache.org.rs/HI/

Development of novel, effective, and safe anti-tumor drugs is still a slow and cumbersome process, which is often attributed to weaknesses of current preclinical assays and low correlation of the preclinical *in vitro* and *in vivo* data with the results obtained in clinical trials. Consequently, there is a clear need for development of more reliable *in vitro* three dimensional (3D) tumor models, which will capture key features of the *in vivo* tumor cell microenvironment and provide drug testing results relevant for human patients. The aim of the project "Biomimetic tumor engineering to enhance drug discovery – BioengineeredTumor" funded by the Science Fund of the Republic of Serbia is to develop 2 novel, simple and robust 3D models for cultures of carcinoma and osteosarcoma cells by applying systematic and integrated methodology to comprehensively define the key model components. In specific, the aim is to use different human and animal cancer cell lines in conjunction with alginate-based biomaterials as artificial extracellular matrices imitating tumor environments and to cultivate the obtained constructs in perfusion bioreactors providing enhanced transport of nutrients, gases and biochemical signals to the cells as well as adequate levels of hydrodynamic shear stresses. Thus, the strategic goal is to establish an adaptable platform suited to the use by scientists without technical expertise for long-term *in vitro* studies of cancer cells for applications in anti-cancer drug discovery and validation, development of personalized medical treatments, and cancer research.

The project is structured based on 3 concept points: (*i*) development of a longer-term *in vitro* 3D tumor model relies on the use of biomimetic scaffolds and bioreactors providing adequate biochemical and physical signals, (*ii*) bottom-up approach starting form single well-defined components can yield controlled, reproducible and physiologically relevant 3D tumor models, and (*iii*) simple *in vitro* 3D tumor models capturing some of the key features of the tumor environment *in vivo* can present a useful and expandable platform for reliable anti-cancer drug testing and cancer research. The planned methodology is designed accordingly so that the project will comprise 3 phases: I) development of 3D tumor models, II) validation of the models, and III) utilization of the optimized 3D tumor models in short-term (up to 7 days) and longer-term (up to 28 days) studies of the effects of standard anti-cancer drugs (*e.g*. cisplatin, doxorubicin, 5-fluorouracil, or paclitaxel) on the cultured cells. In addition, the second phase of the project will include development or adaptation of analytical methods for comprehensive characterization of the cells in 3D cultures as well as mathematical modelling in order to assess the effects of culture conditions on cell viability, morphology, apoptosis and cytokine profiles. Such a systematic experimental and analytical approach will provide significant insights in cancer cell biology regarding 3D environment and guidelines for further optimization of 3D tumor models in general.

Overall, the project BioengineeredTumor is addressing an urgent clinical problem, aiming to provide important fundamental insights in cancer cell biology as well as usable products and methods for advancements in pharmaceutical and healthcare sectors.

Acknowledgements: This project is supported by the Science Fund of the Republic of Serbia grant no.7503, Biomimetic tumor engineering to enhance drug discovery – BioengineeredTumor

*Corresponding author E-mail: bojana@tmf.bg.ac.rs