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Placenta-on-a-chip model for assessing the transport and toxicity of xenobiotics *in vitro*

Evgeny Knyazev[1,2], Sergey Nikulin[1,3], Anna Khristichenko[1,4], Tatyana Gerasimenko[1], Olga Kindeeva[1,3], Vladimir Petrov[1,5] and Dmitry Sakharov[1,6]

[1]Scientific Research Centre Bioclinicum, Moscow, Russian Federation; [2]Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russian Federation; [3]Far Eastern Federal University, Vladivostok, Russian Federation; [4]Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation; [5]Institute of Nanotechnologies of Microelectronics of the Russian Academy of Sciences, Moscow, Russian Federation; [6]D. Mendeleev University of Chemical Technology of Russia, Moscow, Russian Federation

Objectives

The study of the transport and toxicity of xenobiotics in women is limited for ethical reasons. *Ex vivo* placenta models have high variability and low success rates. Animal models *in vivo* differ from a human in anatomy, genotype, and proteome. The placenta-on-a-chip model is a compromise. The cells BeWo b30 in combination with endothelial cells are often used as models of the placenta *in vitro* [1-4]. Cultivation of cells with the circulation of the medium allows the microenvironment to be brought closer to the real organism [5]. We studied the transport of the components of the FAC chemotherapy regimen for breast cancer in this model.

Methods

BeWo b30 cell line was grown in the DMEM with L-glutamine, 4.5 g glucose/l and Earle's salts containing 10% FBS, 1x MEM NEAA, 100 U/ml penicillin and 100 µg/ml streptomycin in inserts cut from 96-well Transwell plate and placed in a microfluidic chip. Cells were seeded with a density of 10,000 cells per insert. After 7 days, 5-fluorouracil (25 µg/ml), doxorubicin (50 µg/ml), cyclophosphamide (150 µg/ml), or all three drugs were added to the cells for 1 hour. Control cells were cultured in the presence of 0.05% DMSO. The impedance spectrum was measured before and 1 and 24 hours after the addition of the drug. The concentration of the drug was determined by HPLC-MS/MS. Cell viability was assessed using the CellTiter-Blue Assay.

Results

After 1 h incubation with drugs, TEER decreased in experiment and control groups from an average of 90 to 25 $\Omega \cdot cm^2$, and after 24 h TEER was 67.3 ±17.9 $\Omega \cdot cm^2$ for control, 67.8 ±16.4 $\Omega \cdot cm^2$ for cyclophosphamide, 90.0 ±20.1 $\Omega \cdot cm^2$ for 5-fluorouracil, and decreased to the background for doxorubicin and drug mixture. Cell viability did not differ significantly between the control, 5-fluorouracil, and cyclophosphamide, but decreased to 40 ±9% of the control when exposed to doxorubicin and drug mixture. The placenta-on-a-chip model transported the drugs from the apical to the basolateral side.

Conclusion

The developed placenta-on-a-chip model is suitable for assessing the transport and toxicity of xenobiotics *in vitro*.

This work is supported by the Ministry of Science and Higher Education of the Russian Federation, project: 14.588.21.0007, unique id: RFMEFI58817X0007.

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Submission declaration:

Conflicts of interest: The corresponding author declares that there is no conflict of interest with the authors.

Statement on ethics vote: No ethics vote is required.