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A LTE A Proceedings

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3R Centers in Europe & international – national and local centers

3Rs in education and academia

Advanced safety testing of cosmetics & consumer products and alternatives to animal testing in food safety, nutrition and efficacy

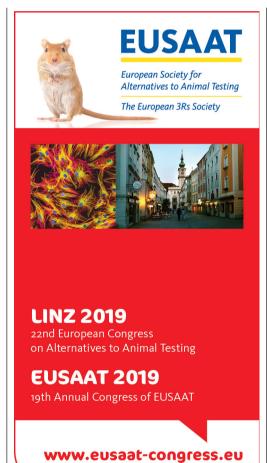
An integrated interdisciplinary approach to animal-free nanomaterial and chemical safety assessment: Results of the in3 project

Biological barriers

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Ecotoxicology

Efficacy and safety testing of drugs, medical devices & biopharmaceutics



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

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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 $\Omega \cdot \text{cm}^2$, and after 24 h TEER was 67.3 ± 17.9 $\Omega \cdot \text{cm}^2$ for control, 67.8 ± 16.4 $\Omega \cdot \text{cm}^2$ for cyclophosphamide, 90.0 ± 20.1 $\Omega \cdot \text{cm}^2$ 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 $40\pm9\%$ 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*.

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