

## Renal advanced *in vitro* models for nephrotoxicity determination

Monika Sramkova<sup>1</sup>, Kristina Kopecka<sup>1</sup>, Yvonne Kohl<sup>2</sup>, Sarah Spring<sup>3</sup>, Michelle Hesler<sup>2</sup>, Thorsten Knoll<sup>3</sup>, Alena Gabelova<sup>1</sup>

<sup>1</sup>*Cancer Research Institute, Biomedical Research Center, Slovak Academy of Sciences, Dubravska cesta 9, Bratislava, Slovakia.*

<sup>2</sup>*Fraunhofer Institute for Biomedical Engineering IBMT, Department Bioprocessing and Bioanalytics, Joseph-von-Fraunhofer-Weg 1, Sulzbach, Germany*

<sup>3</sup>*Fraunhofer Institute for Biomedical Engineering IBMT, Department Biomedical Microsystems, Joseph-von-Fraunhofer-Weg 1, Sulzbach, Germany*

The natural renal functions, such as detoxification and elimination of xenobiotics along with the homeostatic maintenance, make the kidneys especially susceptible to toxic chemicals including drugs. Hence, the development of sensitive predictive and less expensive high throughput cell-based *in vitro* assays to determine induced nephrotoxicity is an urgent need and a major challenge.

Microfluidic technology offers an alternative platform for *in vitro* toxicity screening of xenobiotics under physiologically-relevant conditions as well as an attractive strategy for enhancing the efficiency of hazard profiling.

In this study, a new microfluidic system was used to evaluate the sensitivity of human renal TH-1 cells to various toxicants. The microfluidic module with a size of a microscopic slide has a microcavity made from silicon nitride (Si<sub>3</sub>N<sub>4</sub>) and is integrated into a fluidic system with tubing, valves, and pump which delivers cell culture medium to the cells under a constant medium flow rate.

The aim of this work was to compare the capacity of human renal proximal tubule epithelial TH-1 cells to attach and proliferate under standard conditions and in fluidic system. In addition, the sensitivity of TH-1 cells to cisplatin, a known nephrotoxic compound, and fluorescent-labeled silica nanoparticles (FITC-SiO<sub>2</sub>NPs) was assessed using the vitality staining (FDA/PI).

We observed no changes in cell morphology and proliferation activity in TH-1 cells growing on the microchip in comparison with the control. Moreover, the module allows a continuous optical characterization and TEER measurement of the cells during cultivation and exposure, thus offering a promising tool for screening of xenobiotics.

### Acknowledgement

The research leading these results has received funding from grant H2020 HISENTS (Grant agreement no. 685817). Kristina Kopecka received STSM Grant (ID 42926) under COST Action CA 17140 "Cancer Nanomedicine from the Bench to the Bedside" supported by COST (European Cooperation in Science and Technology).