Microsystems to evaluate the effectiveness of cancer therapy

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Miniaturization has started to play an important role in medical sciences, pharmacology and tissue engineering. Miniaturized versions of bioassays offer many advantages such as small consumption of solvents, reagents and cells, which is critical for valuable, available in limited volume, samples and for high-throughput screening. Moreover, they provide short reaction times, portability, low cost, low power consumption, versatility in design that leads to further integration with other miniaturized devices. Besides, the scale of microchannels corresponds well with the native cellular microenvironment, so microfluidic devices are especially suitable for biological applications particularly at the cellular level.

We developed microsystems, which enable: cell culture, passage process, cytotoxicity tests and evaluation of photodynamic therapy (PDT) procedures. In Fig. 1 and Fig. 2 are shown two different hybrid microfluidic systems, dedicated for cytotoxicity tests and PDT procedures in sequence. Hydrophilic glass surface and gas permeable poly(dimethylsiloxane) - PDMS were used to fabricate microdevices. Both of fabricated microdevices consist of culture microchambers (a diameter of 1 mm and a depth of 30 μm), and microchannels (a width of 100 μm and a depth of 50 μm) creating also concentration gradient generator (CGG). Culture chambers were etched in the sodium glass, the concentration gradient generator with microchannels network were replica molded in the PDMS. The geometry of microdevices enables to test different concentrations of tested compounds in a single assay. Moreover, the microsystem for the evaluation of the effectiveness of photodynamic therapy procedures (Fig. 2) contains two identical microstructures on a single chip, so the microchip can be used for examination simultaneously various cell lines (carcinoma and normal) or various photosensitizers.

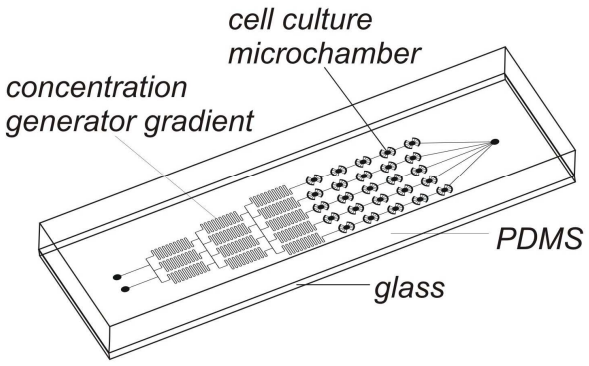

Fig.1 The geometry of microfluidic system integrated with the concentration gradient generator dedicated for cytotoxicity tests.

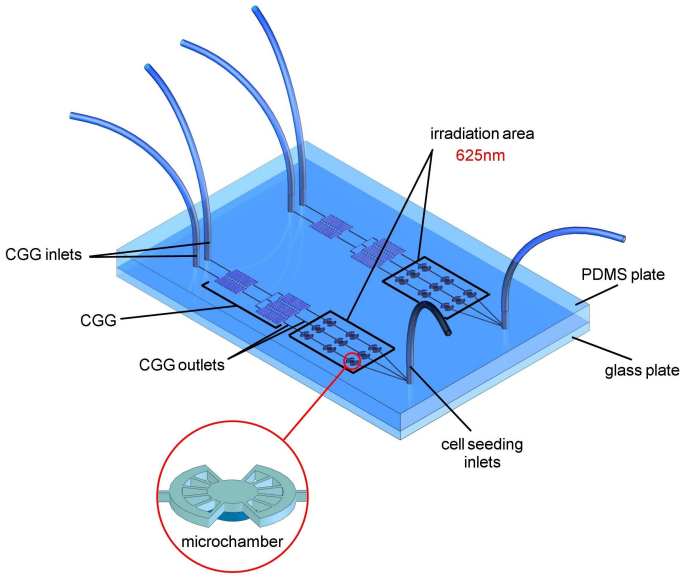

Fig. 2 The geometry of microfluidic system dedicated to evaluation of photodynamic therapy (PDT) procedures.

In fabricated microsystems different cell lines were cultured. A549 human lung carcinoma cells and HT-29 human colon adenocarcinoma cell line were successfully cultured in the microdevice for several days (Fig.3). The growth and proliferation was possible due to development of: (I) sterility, (II) cell seeding in microsystem, (III) medium dosage protocols.

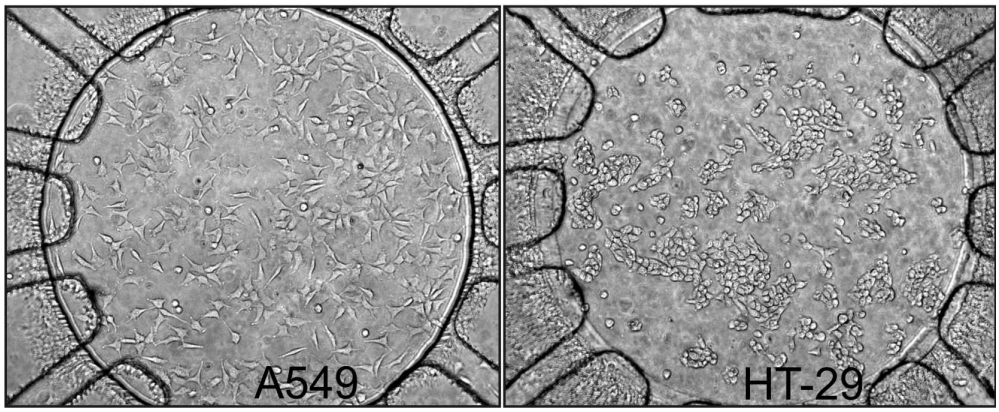

Fig. 3 Cell culture of A549 human lung carcinoma cells and HT-29 human colon adenocarcinoma cell line

In designed microsystems, after 5 days, when cells reached the confluence state in the microchambers, cells' passage was performed according to the procedure applied for standard scale cell culture. The passage process was based on partial cells' flushing with trypsin EDTA-solution. After passage good cells' adhesion and the ability to further growth was observed. The passage process assures long-term cell culture in microsystem. Moreover, it is possible to test in microscale, how passage numbers influence on alterations in cell morphology, response to stimuli, growth rates, protein expression and cell analysis. The

developed microsystems enable also performance cytotoxic experiments. We have started investigation of influence of cytostatic drugs (for example 5-fluorouracyl, oxaliplatyna).

A hybrid PDMS/glass microfluidic system (Fig. 2) was used for evaluation of the efficiency of photodynamic therapy with 5-aminolevulinic acid (ALA) as a precursor. The viability of the A549 cells (Fig. 4) was determined 24 hours after PDT procedure (irradiation with light which induced a photosentitizer accumulated in carcinoma cells, $\lambda = 625$ nm). This results confirmed the possibility of perform the photodynamic therapy process *in vitro* in microscale and the possibility of assess its effectiveness.

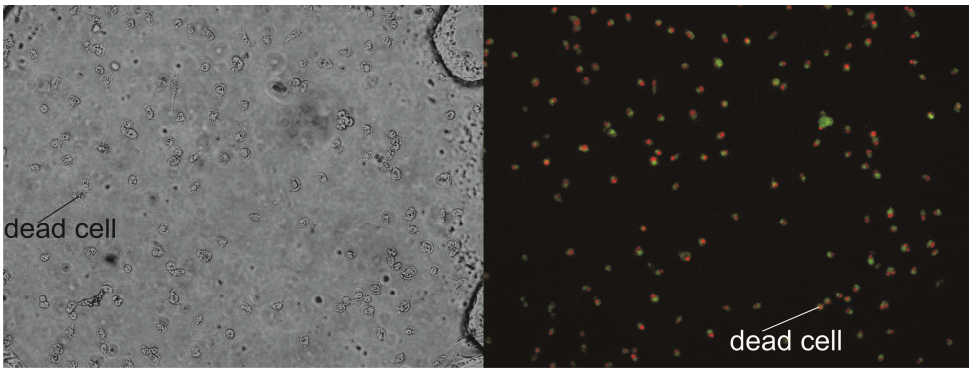

Fig. 4 The microchamber with A549 cells after PDT procedure.