An integrated microfluidic system for gastrointestinal tract analogue for prodrug screening with on-line monitoring

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Keywords Microfluidic analogue, Prodrug, Cancer

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Context The classic ways to induce selection pressure for cell cultures is injecting different doses of active agent into microtiter plate, flow-through cell or chemostat. Using microfluidics the necessary features of 3D restrictions, surfaces and controlled flow of many liquids in channels are achieved for conditions approaching in-vivo. The compartmentalized microfluidic analogue of a mammalian body will also lead to a decreased number of animal tests which clearly benefits the huge medical industry pursuing the ways to reduce this type of thus far necessary element. Based on IIS's [1] and also others' [2-3] experience mammalian cells can be placed to an interactive microfluidic system.

Objectives and Methods As PDMS microfluidic device is capable of mimicking a functional body, this study pursues for two-flow on-line monitoring and characterization of prodrugs never tested in a microfluidic analogue. In this work a microfluidic device was built to mimic human body circulation for studying action of a lung cancer drug on the viability of lung cancer cells (A549). In this device the prodrug was aimed to be introduced to the system via thin membrane (intestinal cells), metabolized to actual drug in liver (area with liver cells) and transferred then to the lungs (area with lung cancer cells) via heart (micropump).

Initial tests showed that HEPG2 could not be used in the experiments, as it was less resistant to Tegafur drug than A549 target cancer cells. Therefore primary HEP was chosen for main experiments.

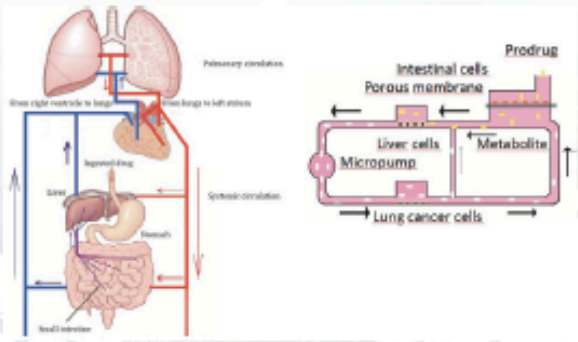

Fig. 1 The approach used in this work consisting of human body (left) that is mimicked by the analogue (right).

Results Within the 48-hour time frame it was difficult to see the effect of Tegafur and Uracil on the target A549 cells in the microfluidic device. The staining method used in the work revealed only few dead cells and many improvements for experimental conditions was suggested.

References and Publications

[1] Kimura H. et al., Lab on a chip 8, pp. 741-746, 2008

[2] Mahler G. J. et al., Biotechnology and Bioengineering 104, pp. 193-205, 2009

[3] Jong HS. et al., Lab on a chip 10, pp. 446-455, 2010