Anticancer diagnostics and therapies based on lab-on-a-chip

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Lab-on-a-chip laboratory

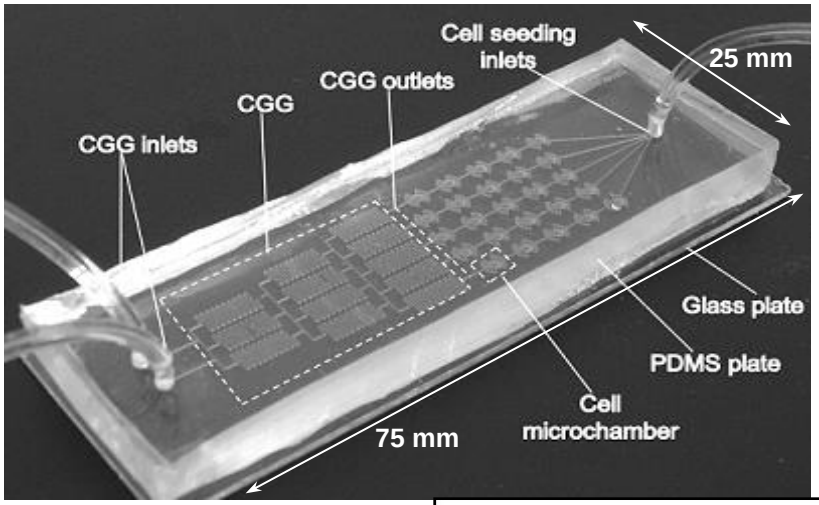
- ✓ Laboratory space: 300 sq.m (technology and metrology)
- ✓ Equipment purchased: 2009-2013
- ✓ Total cost ~1 500 000 €

Technologies

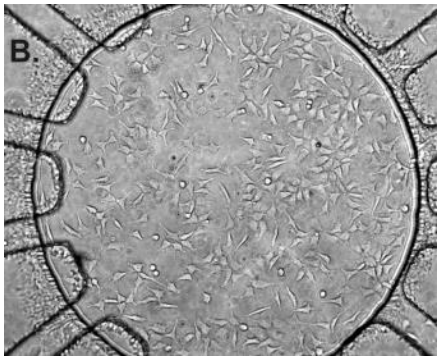
- wet etching of glass
- replica moulding: poly(dimethylsiloxane) PDMS
- micromilling: poly(methyl methacrylate) PMMA
- hybrid: glass/PDMS, ceramics/PDMS

Microfluidic cell culture system for evaluation of cytotoxic effect of anticancer drugs

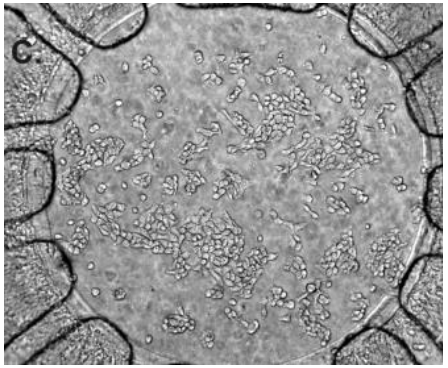
Microfluidic Cell Culture System

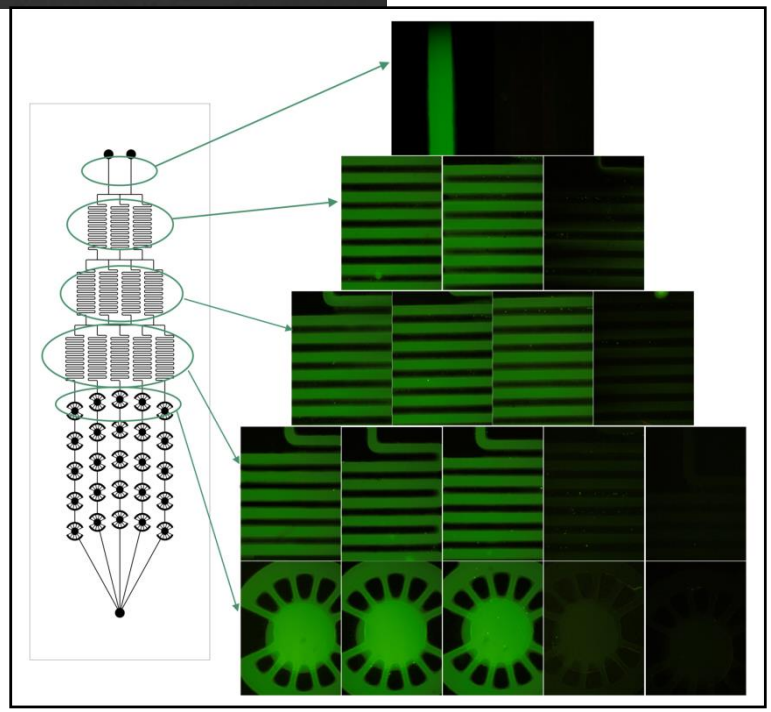


A549

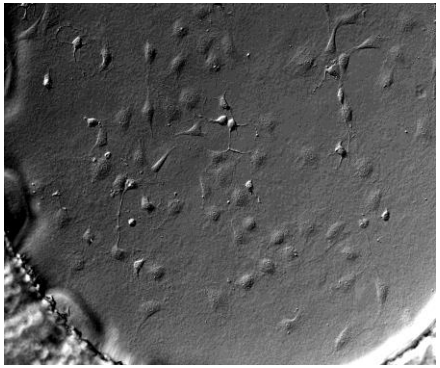


HT29



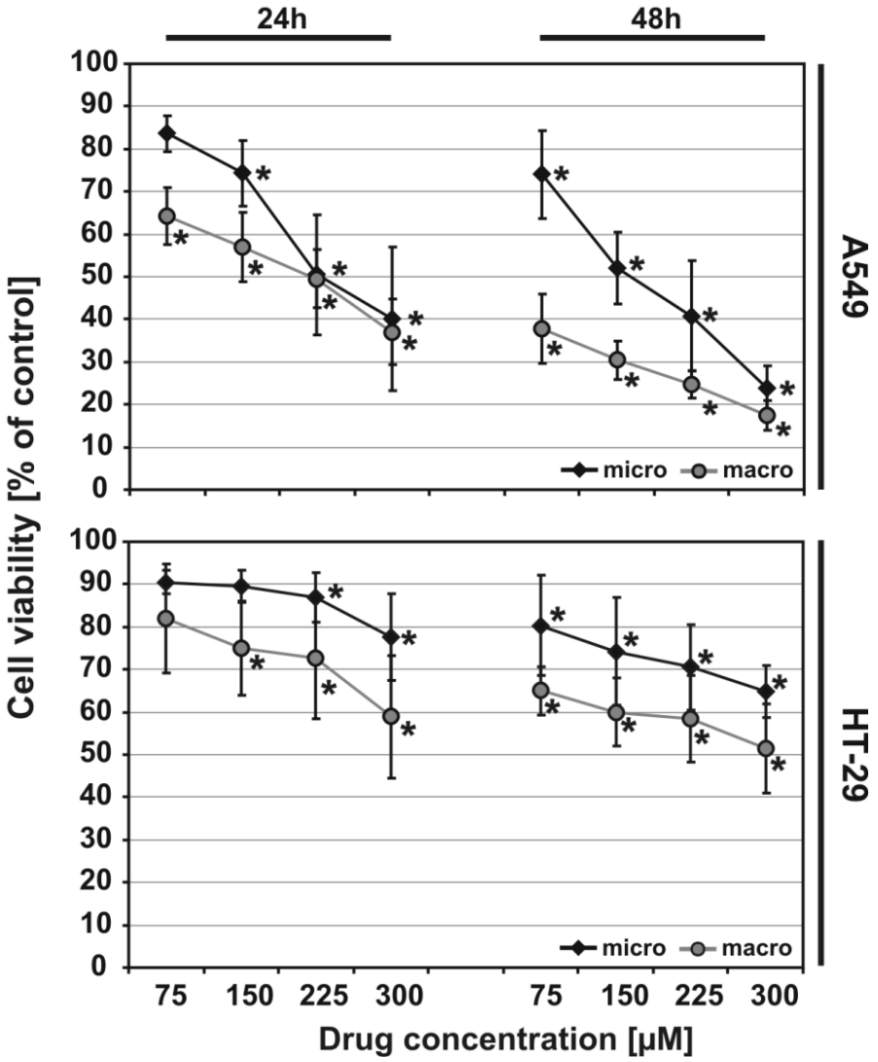


BALB



Ziolkowska K., et al., PDMS/glass microfluidic cell culture system for cytotoxicity tests and cells passage, Sens.Act.B (2010)

5-fluorouracil cytotoxicity tests in MCCS



- toxic effect of 5-FU was higher for A549 than for HT-29 cells for both after 24 and 48h
- toxic effect of 5-FU was time dependent
- for both cell lines the number of dead cells was increasing with higher concentration of 5-FU
- the discrepancy between two systems was observed

Jedrych E., et al., Evaluation of cytotoxic effect of 5-fluorouracil on human carcinoma cells in microfluidic system, Sens.Act.B, (2011).

Photodynamic therapy

Photodynamic therapy

photosensitizer

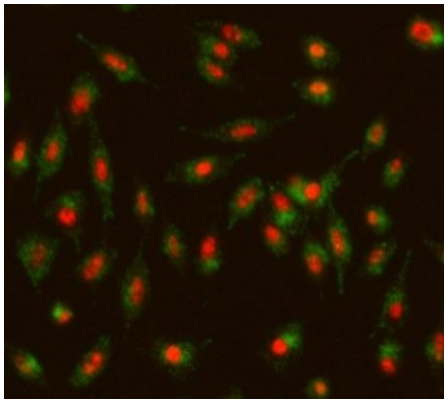
✚

irradiation

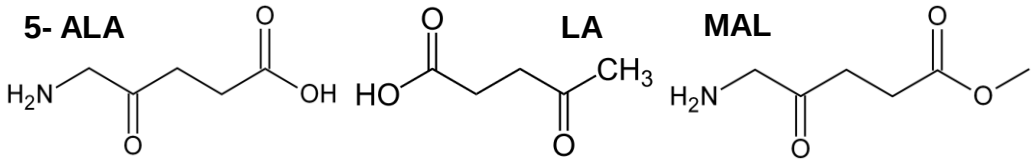
✚

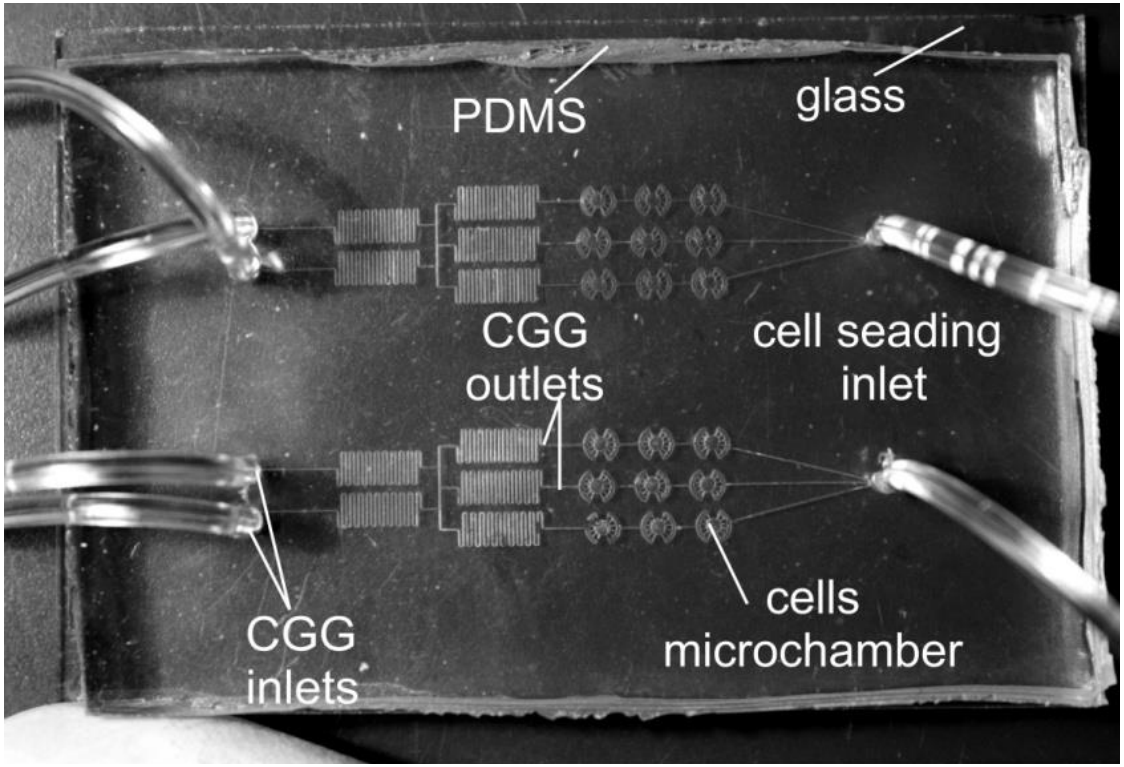
intracellular oxygen

Cells dead
(necrosis, apoptosis)



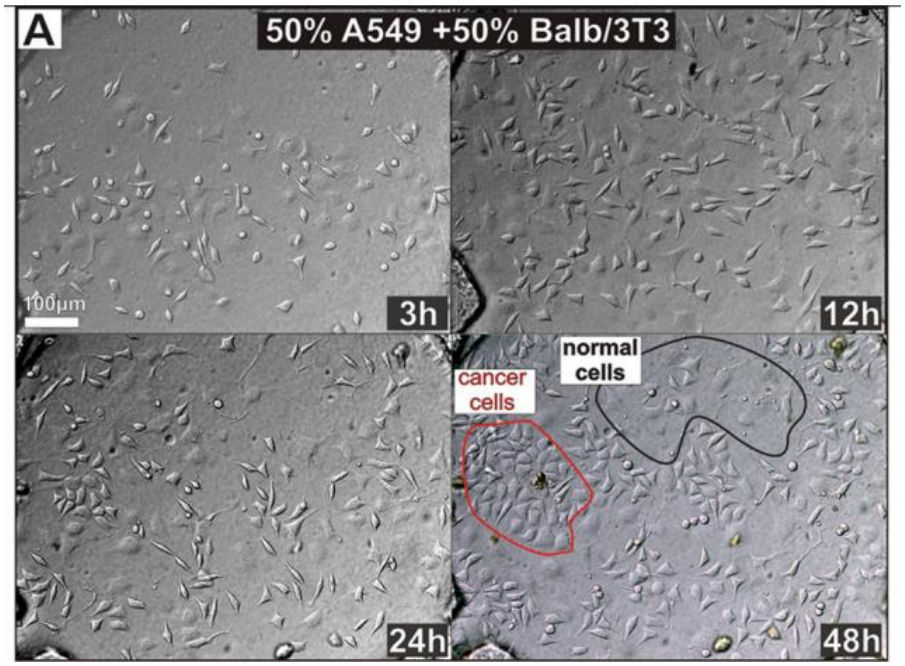
Microdevice geometry



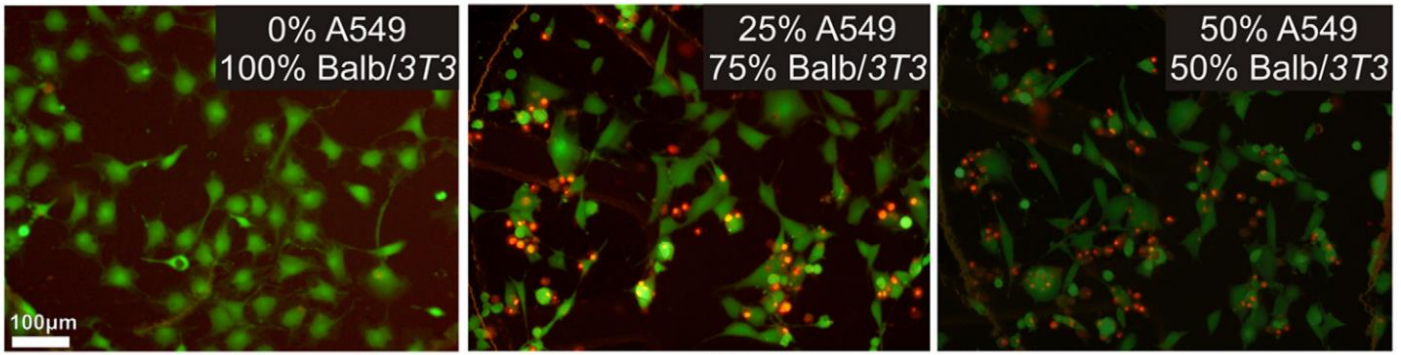


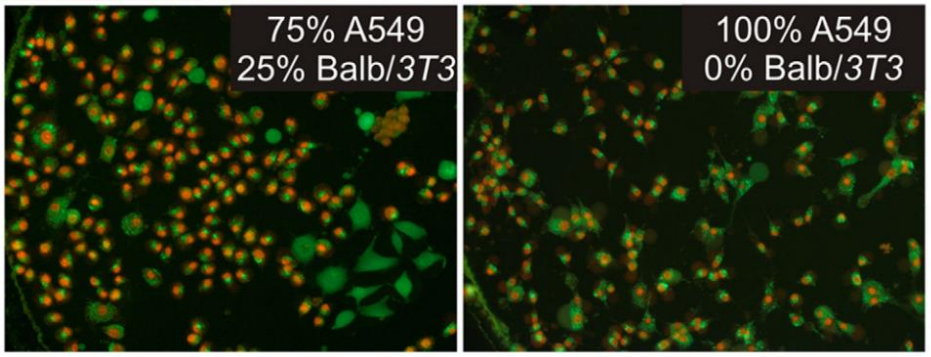
Jedrych E., et al. Evaluation of photodynamic therapy (PDT) procedures using microfluidic system, Anal. Chim. Acta (2010)

Jedrych E., et al. Multi-function microsystem for cells migration analysis and evaluation of photodynamic therapy procedure in coculture, Biomicrofluidics,(2012)



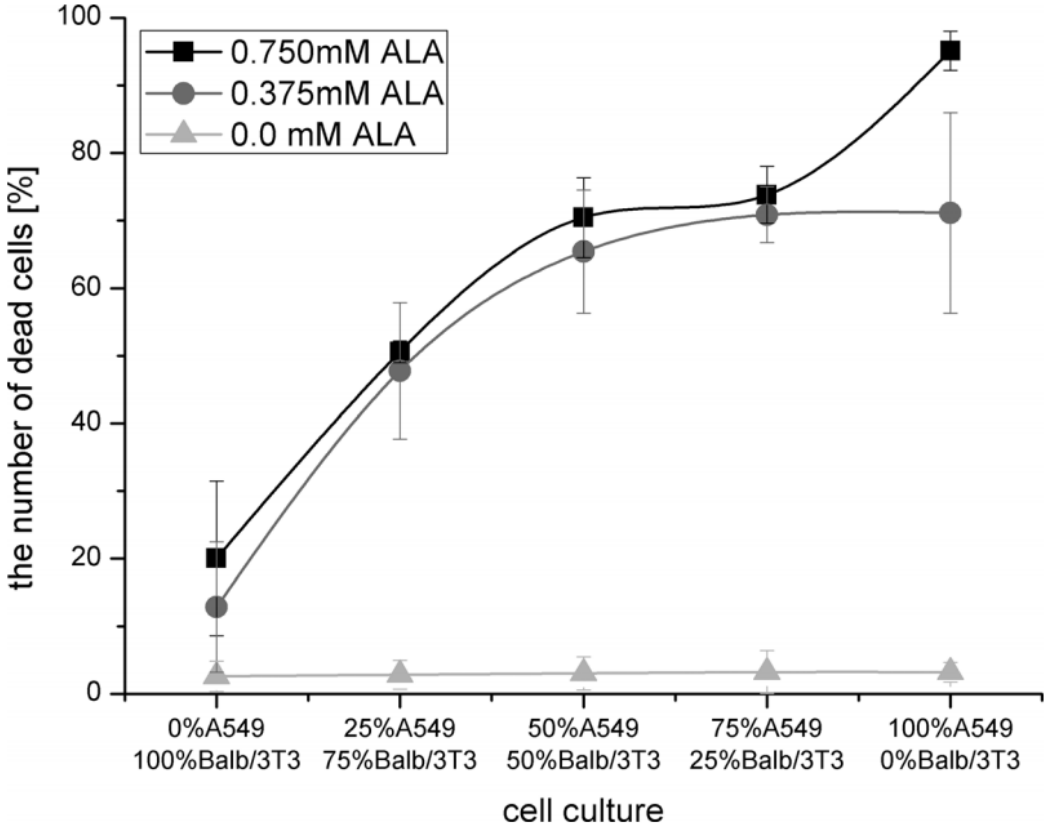
normal and cancer cells





viability assay
after PDT

Viability assay after PDT



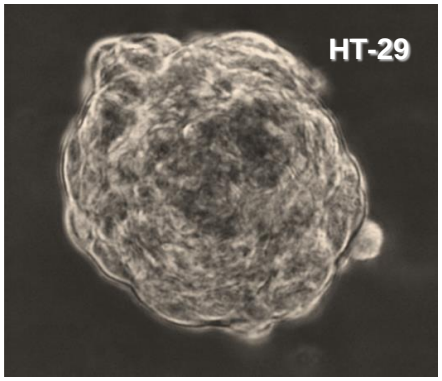
- after 4 hours of incubation with different concentrations ALA proper growth and proliferation of the cells was observed
- tested concentrations of ALA did not have toxic effects on the cells
- 24 hours after PDT procedures, viability test confirmed that the toxic effect of the cell was depended on the ALA concentration

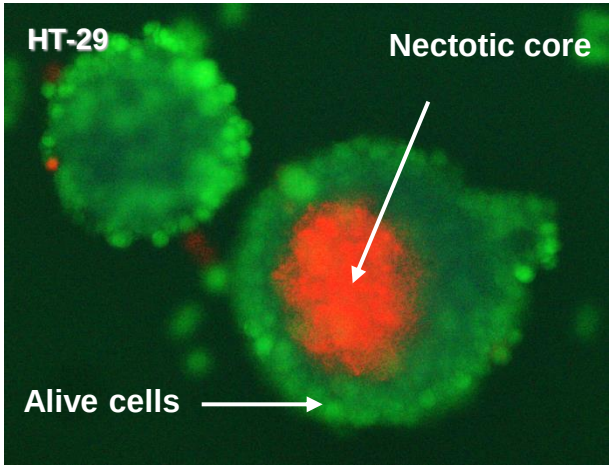
Tumor spheroids

Multicellular tumor spheroids (MTS)
advanced 3D tumor model

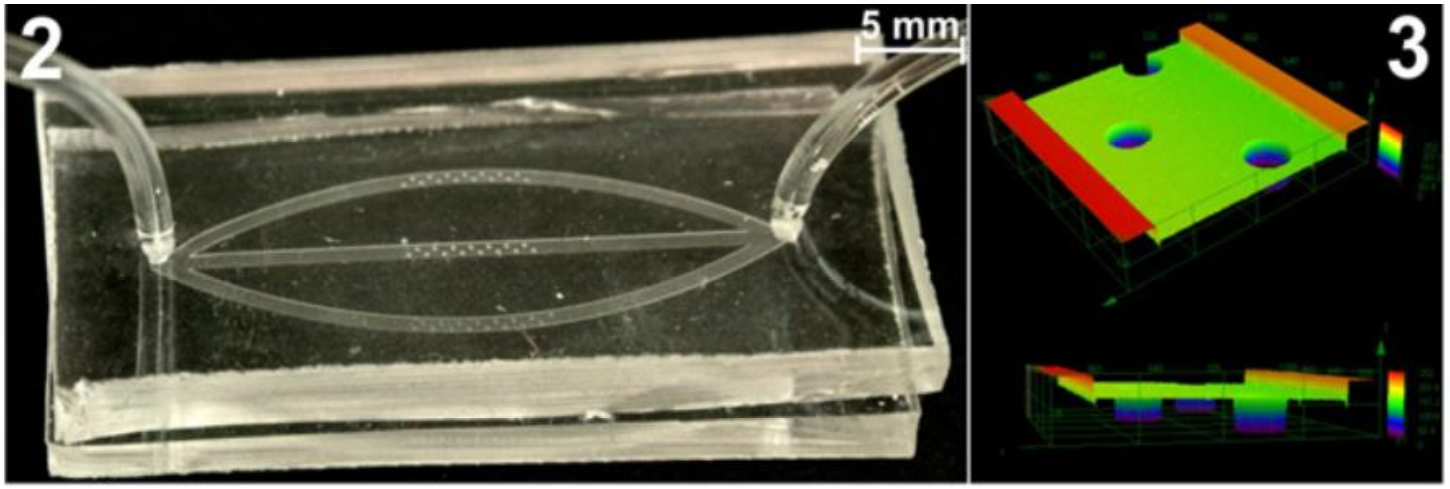
Spherical multicellular aggregates with interesting properties:

- Intercellular interactions and connections (desmosomes)
- Cytoskeleton structure like *in vivo*
- Extracellular matrix
- Concentration gradients of substances inside spheroids





Microsystem - design



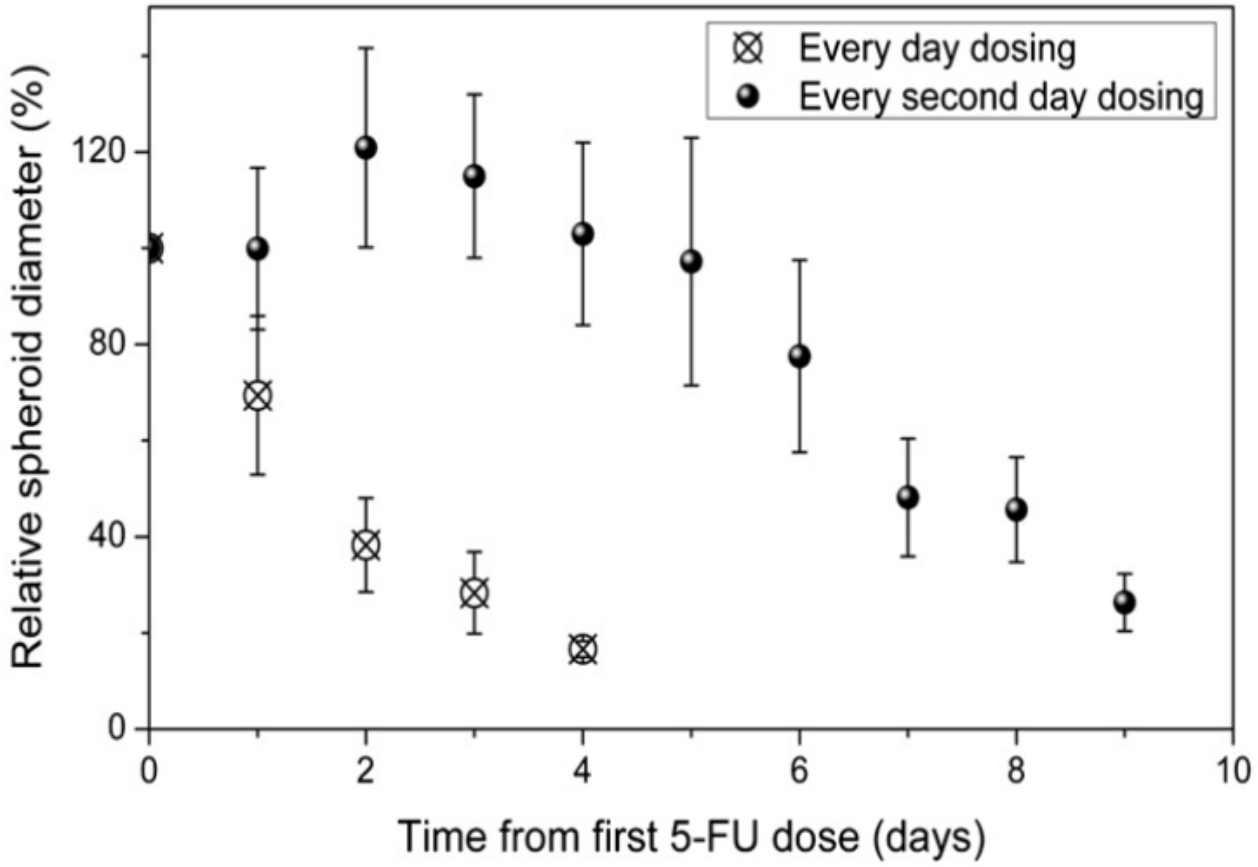
Fabricated microdevice

- Microwells – a diameter of 200μm, a depth of 150μm
  compatible with a single spheroid size
- Microchannels 1mm x 50 μm
- 3D structure of microchannels

K. Ziolkowska et al. Long-term three-dimensional cell culture and anticancer drug activity evaluation in a microfluidic chip, Biosensors and Bioelectronics (2013)

Effect of dosing regimen on spheroid sizes

- results for 5-FU, concentration of 5 mM



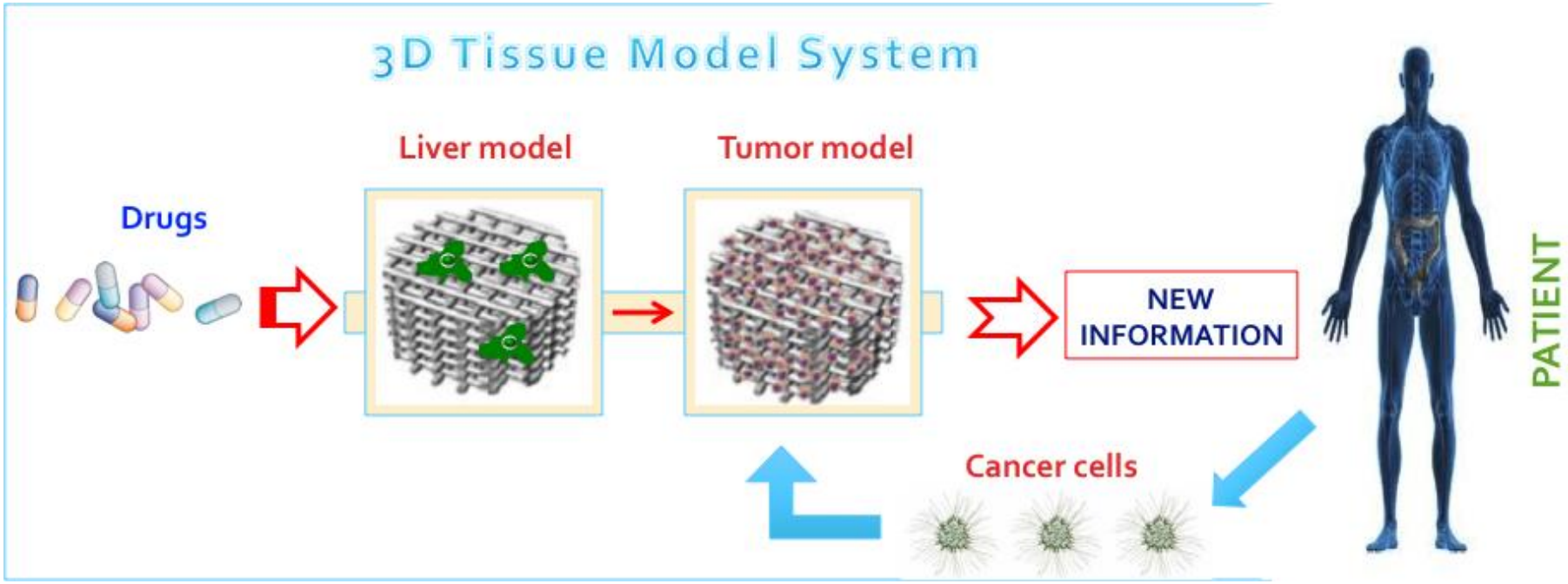
Applications of lab-on-a-chip

- cytotoxicity tests
- multidrug analysis
- drug dosing procedures
- photodynamic therapy
- cells' migration
- 3D spheroids' degradation

✓good correlation between micro- and macroscale experiments

✓personalised therapy

Current works: organ-on-a-chip



Preliminary results - based on 3D scafold:

- ✓ liver-on-a-chip
- ✓ heart-on-a-chip

Thank you for your attention!