

**BIOMEDICAL, IN VIVO AND
IN VITRO DIAGNOSTIC**

**MILLIFLUIDIC DEVICE AS ALTERNATIVE
METHOD TO ANIMAL TESTING**



Daniele Borin, PhD



September 26th 2018

1 / The CEMSlab group

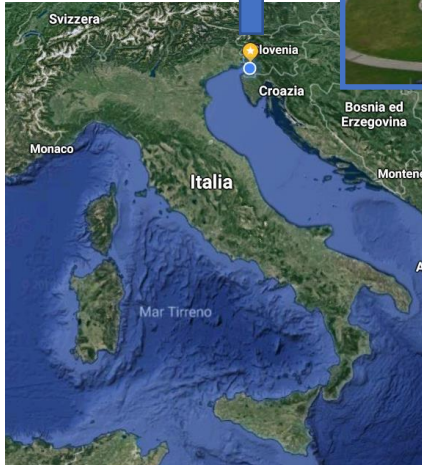
(Cellular Engineering and MicroSystems laboratory)

University of Trieste
Engineering and Architecture Dept.

Head of the group:
Prof. Orfeo Sbaizero, PhD



Trieste, Italy



Members of the group:

- 2 Post docs (1 Chemical Eng., 1 Biologist)
- 2 PhD students (1 Clinical Eng., 1 Nanomaterial Sc.)
- 1 external collaborator (Molecular Biologist)

2 / Main research fields

- Use of atomic force microscopy for mechanical characterization of cells
- Development of “Cell Stretcher” devices
- QCM studies of bacterial biofilms
(BIOSAFE, recently funded by POR-FESR FVG)
- Development of a millifluidic device mimicking biological processes

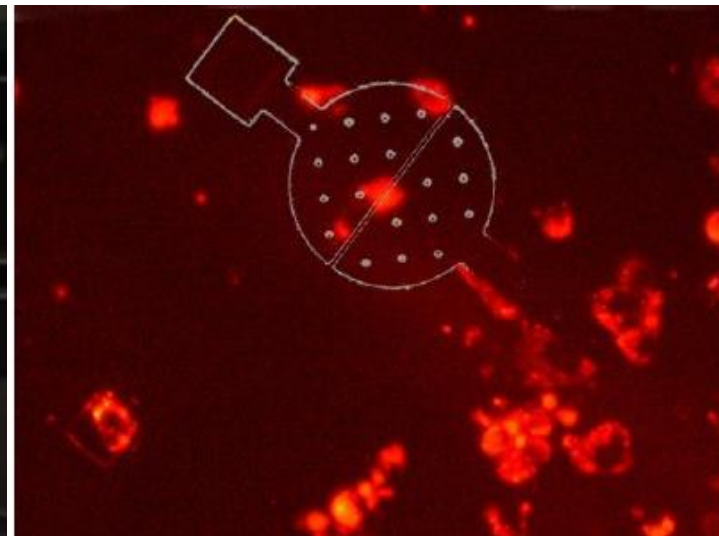
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Cell culture



Single cell



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3 / Aim of the project

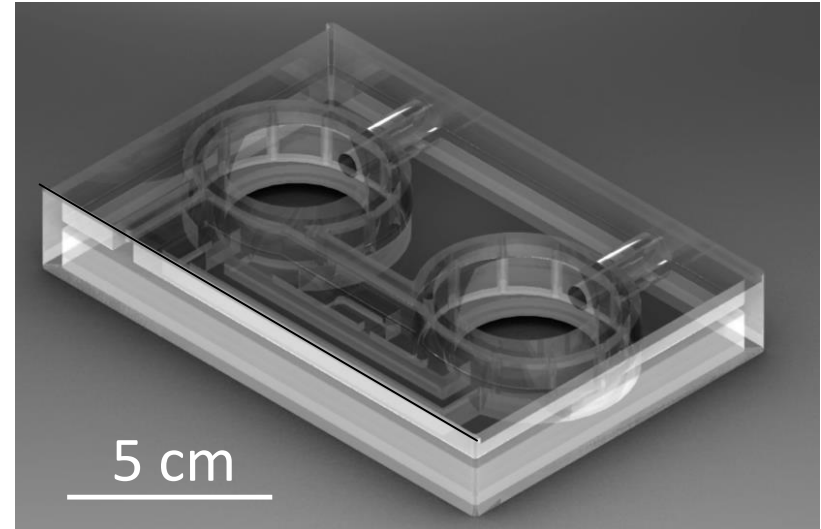
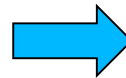
- Need of alternatives to animal testing
 - The “3 R” principle (**Refinement, Reduction, Replacement**)
 - Laws regarding animal testing
- Limits of current methods *in vivo*
 - Ethical issues
 - Large number of animals, complex experiments
- Limits of current methods *in vitro* (static cell cultures)
 - Oversimplified methods

4 / Our idea

- Millifluidic device for dynamic cell culture
- External circuitry for medium circulation/gas exchange
- Integrated electrical circuitry for temperature control



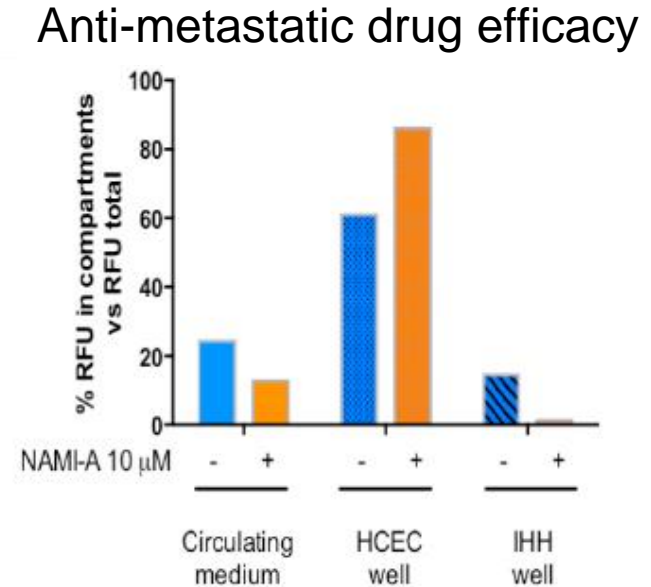
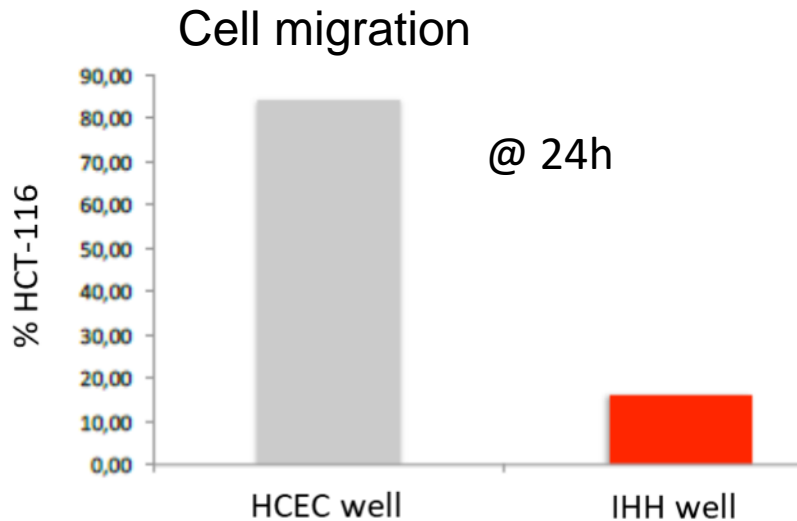
- No need of cell incubators
- Direct coupling with optical/fluorescence microscopes



- Easier monitoring of the experiment evolution
- Possibility to use human-derived cells/tissues

5 / Experiments on the 1st prototype

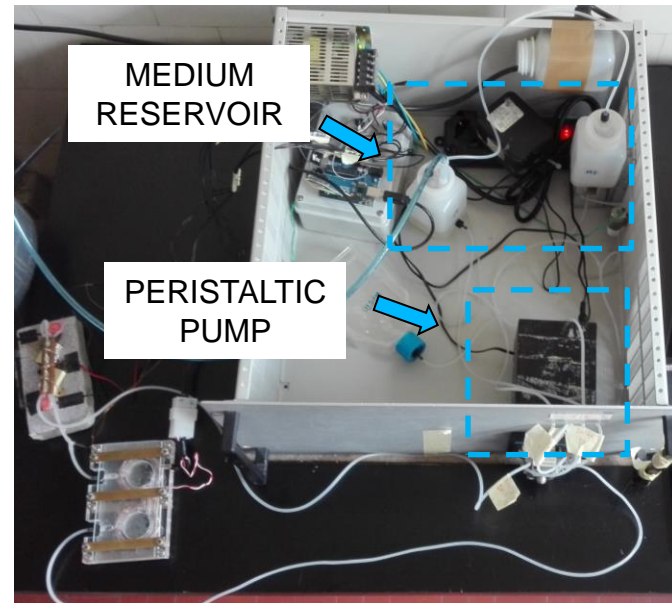
- Metastatic spread of colorectal cancer to the liver*
 - Human colonic epithelial cells (HCEC) } Chamber 1
 - Colorectal carcinoma cells (HCT-116) } Chamber 1
 - Immortalized human hepatocytes (IHH) } Chamber 2



* In collaboration with Prof. G.Sava, Life Science Dept. University of Trieste

6 / Current development

- Improvement of the setup
 - External circulation circuitry



- Validation of the setup in the biological field
 - Sterilization compatible with materials and cells
 - Application to other biological case studies

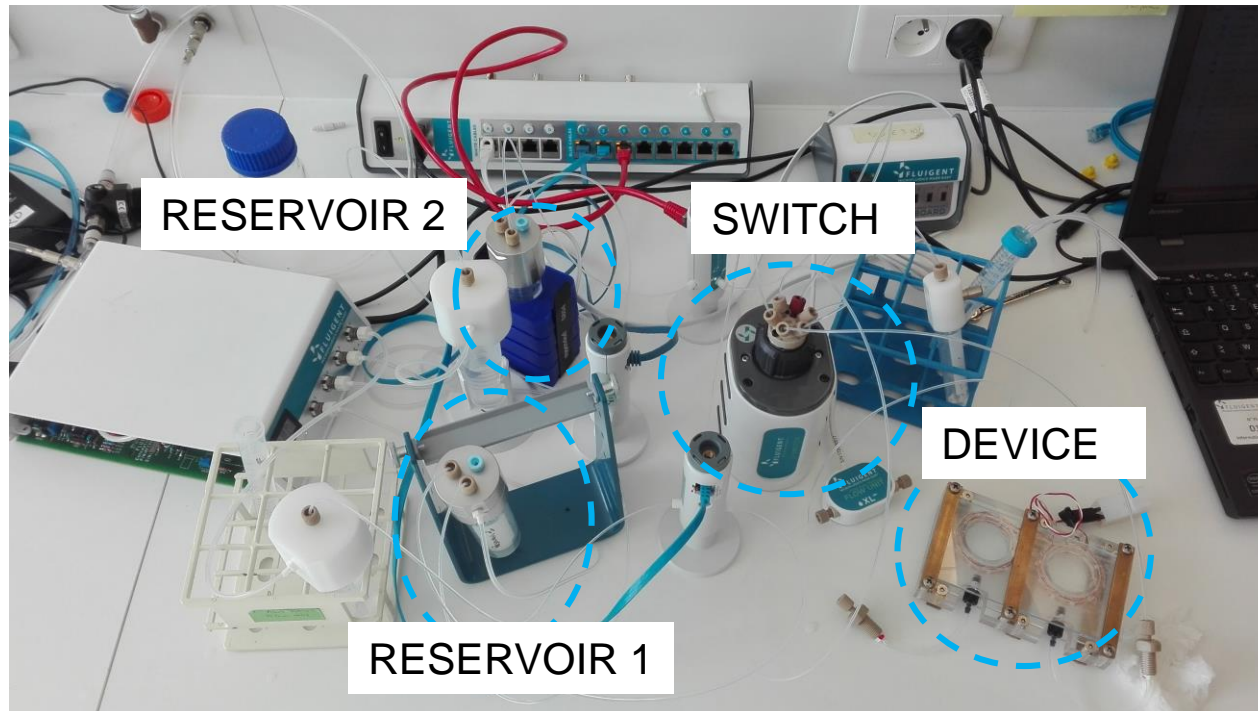
7 / The partnership



- Fluigent SA (Paris, France):
 - Global leader in pressure-driven flow pumps and microfluidic components
- MTTlab srl (Trieste, Italy):
 - Preclinical CRO providing biomedical, biotechnological and pharmaceutical testing services for biotech industry



8 / Circulation system improvement



- ✓ Reduction of circulating medium (-65%) and contamination issues
- ✓ Fully automated and programmable control (long time experiments)
- ✓ Integration of components in a single unit

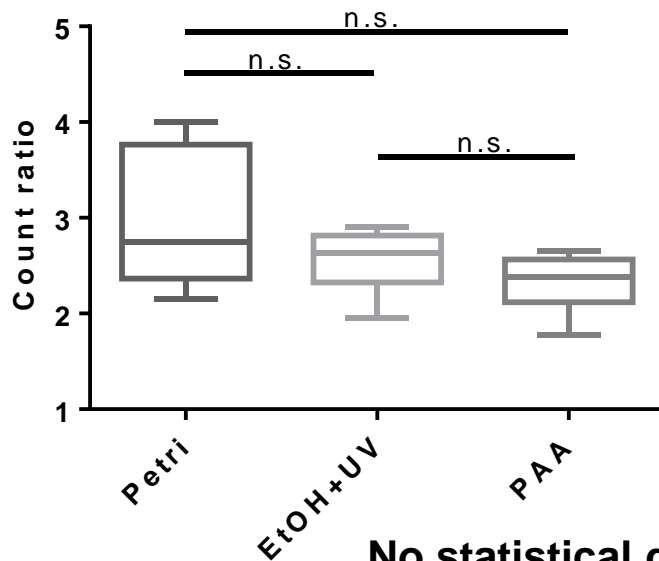
9 / Sterilization protocol

- Commercial sterilizer developing peracetic acid (PAA, FDA approved)
 - No damage on the device components
 - Compatibility of sterilized components with cell growth

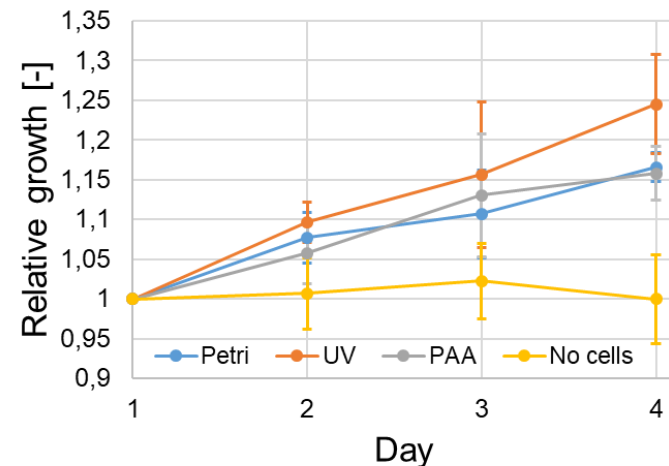


MTTlab
Expand your research

NIH 3T3 fibroblasts
Count ratio day2/day1



Primary neonatal mice fibroblasts
Cell proliferation using alamarBlue™



No statistical difference among controls and PAA treated substrates

10 / Take home message

- Advantages:
 - Easy platform for dynamic biological experiments
 - Real time monitoring
 - Automatic control of the experimental setup
 - No cell incubators
- Further tests ongoing for validation in the biological field

11 / Contacts

Prof. Orfeo Sbaizero, PhD
sbaizero@units.it

Daniele Borin, PhD
dborin@units.it

THANK YOU FOR YOUR ATTENTION