# Microfluidic in-vitro Model of Bladder Cancer for Drug Profiling

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*Physiologically relevant in-vitro models are required tools to precisely study cancer progression and to develop efficient therapies. Combining microfluidics and 3D cell culture, this simple platform aims at providing an insightful tool for drug screening.*

Bladder cancer is the fifth most common cancer in Western society, with the global burden predicted to increase significantly in the foreseeable future (383'000 cases worldwide in 2008 [1]). Three quarters of all cases are diagnosed as superficial disease. Whilst half of these cases are cured by simple surgical treatment, about half will develop recurrences. 20-25% of patients develop more aggressive tumors requiring stronger therapies and carrying significantly worse survival rates. Therefore, there is a need to better understand the mechanisms involved in tumor progression and recurrence. The recently identified bladder cancer stem cells are considered to be mediators of resistance to current therapies and therefore represent strong candidates of biological targets for next generation therapies.

The goal of this project is to develop an easy and relevant 3D in-vitro assay in order to evaluate therapies targeting cancer stem cells, thus providing a better diagnostic tool towards personalized medicine.

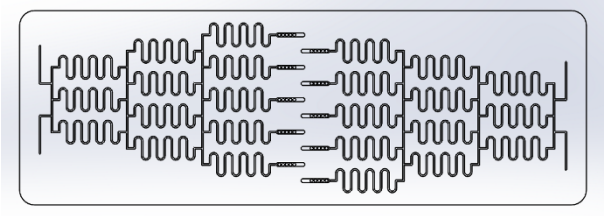

*Figure 1: CAD drawing of the microfluidic chip with a gradient generator and spheroid traps in the center. Dimensions of the chip are 75 × 25 mm.*

Anticancer drug discovery has been hampered by the poor prediction of the preclinical models, leading to a large attrition rate and high costs. In the last 15 years three-dimensional (3D) cell culture systems have shown to provide more accurate physiologically relevant environments compared to their 2D counterparts. However, most studies are using cell aggregates (spheroids) in static conditions, not reflecting physiological conditions where tumors are vascularized.

In this project, CSEM developed a microfluidic chip for drug efficacy screening, combining perfusion and 3D cell culture. The design shown in Figure 1 comprises of a microfluidic gradient generator to facilitate the handling and testing a multiple conditions on the same chip. The chip, made of a thermoplastic, can be connected to a portable pressure-driven perfusion system. At this stage, spheroids were prepared in a different device using the hanging drop technique, and subsequently loaded into the microfluidic chip. In the next iteration of the chip design, spheroids will be formed in the same chip.

Perfusion allows to bring nutrients to the spheroids as well as chemotherapeutical agents to be tested, and reagents to assess their efficacy. Figure 2 (left side) shows a part of the microfluidic chip where spheroids are loaded and perfused.

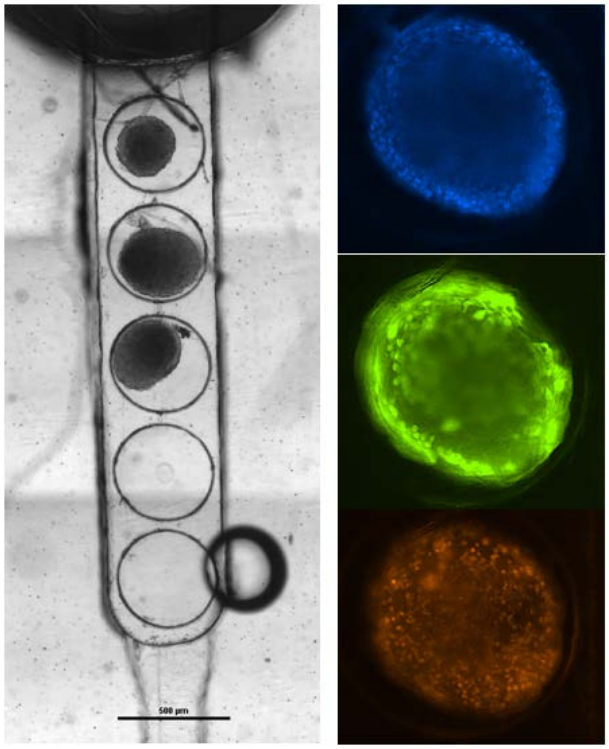


*Figure 2: Microscopic image of the microfluidic chip. Microcavities containing 3 tumor spheroids (left); fluorescence imaging of the spheroid (right), labeled with fluorophores for the cell nuclei (blue), live cells (green) and dead cells (red).*

The right inset of Figure 2 depicts fluorescent staining of a spheroid, providing quantifiable data on the potency of the tested anti-cancer drugs.

The next step will be to use cells extracted from patient biopsy, to eventually allow tailored therapies.

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[1] G. B. Boustead, S. Fowler, R. Swamy, R. Kocklebergh, L. Hounsome, "Stage, grade and pathological characteristics of bladder cancer in the UK", BJU International, 113 (2014), 924.