Microfluidic device for spheroid culture and anticancer drug testing with electrochemotherapy

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In the search for new drug delivery strategies, relevant in vitro tumor models are needed, as part of the process of reducing preclinical trials. They also to offer the possibility to design patient-specific medicines [1]. 3D aggregates called spheroids have been identified as a good tumor model, able to reproduce cell-cell interaction. We have developed a microfluidic device (Fig.1b) allowing spheroid culture inside agarose hydrogel microwells (Fig.1a) [2], and their monitoring with both electrical bioimpedance and high-content microscopy. This hydrogel is chemically bonded to a glass slide acting as an electrode and integrated into a microfluidic chamber enabling medium exchange and drug injection (Fig.1b). A first application of the device has recently been published [3]. HT29 colorectal cancer cell spheroids were treated with electrochemotherapy (ECT), a physical method based on a pulsed electric field to enhance drug intake in cells. Preliminary results also showed it was possible to monitor spheroid growth by measuring the evolution of bioimpedance Z with coplanar interdigitated electrodes, but with more precision and reliability when the conductivity inside the chamber is reduced from 1.3 S/m (high σ, culture medium) to 0.03 S/m (low σ, Hepes buffer) (Fig.1c). A device with two chambers, one with medium only for control (Z_0) and one with spheroids (Z_S), was used for this experiment (Fig.1d), and the cell index $CI = \frac{|Z_0|-|Z_S|}{|Z_0|}$ was measured (Fig.1e). The impact of a surfactant to permeabilize cells (TritonX-100) on the growth curve could also be monitored in less than an hour. Taking advantage of the electrodes, we intend to monitor the effect of ECT on spheroids with bioimpedance in future work.

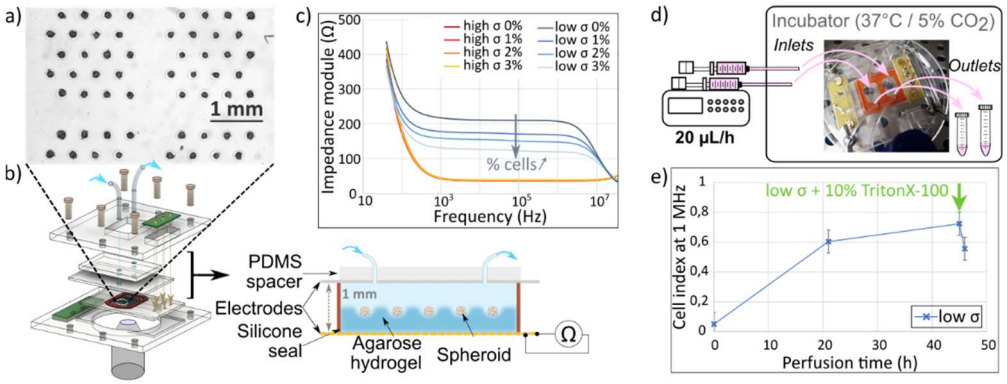

Figure 1: (a) Microscope image (2.5X) of spheroids after 3 days of culture. (b) Exploded view of the CAD of the microsystem and side view of the microfluidic chamber. (c) Impedance measure on cell suspensions in high and low conductivity mediums. (d) Picture of the microsystem during culture under perfusion (20 µL/h) with two chambers. (e) Spheroid growth monitoring with bioimpedance in Hepes buffer and impact of TritonX-100.

References

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