EIS Biochips for studying cell cultures

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Biochips are attracting large interest in cell biology as functional tools to perform quick and extensive cell studies by integrating different functions in a single chip. In this respect, electrochemical impedance spectroscopy (EIS) is an emerging read-out technique since the immobilization/adhesion of cells on biofunctionalized electrodes alters the capacitance C and interfacial electron transfer resistance R_{ET}, which are correlated to cell number, adhesion and cytoskeleton organization [1-5].
Here an EIS Biochip for cell counting is demonstrated. Such device provides an easy tool to study cell attachment, spreading and to perform cell counting and viability tests. Specifically, the chips consist of a PDMS cell culture chamber on interdigitated electrodes. Cr/Au electrodes were fabricated by optical lithography on glass substrates. The PDMS chamber was realized by replica molding from a hard master.
These biochips are very cheap and reusable and represent a robust method to count cells with great sensitivity without detaching/destroying them (a crucial property for further assays such as migration tests and/or cytotoxicity tests):
With such a biochip we are able to count cells from several cell line (B104, HeLa, endothelial cells and others): in particular we report in fig.1 the results of some experiments with HeLa cells. These results show a linear relationship between the number of cells and the impedance measured and demonstrate that our chip is a powerful method for cell counting.
In addiction we have used our biochip to monitor the adhesion between two different cell type, endothelial cells and leukaemia cells. We have evaluated the changes in adhesion as a consequence of an anti-leukaemia drug: SKI606 (fig.2). Ku812 leukaemia cells have a weak adhesion with endothelial cells because of a phosphorilation of β-catenin which in the phosphorilated form is located in the nucleus. SKI 606, a tyrosine-kinase inhibitor, blocks the β-catenin phosphorilation restoring cell adhesion. After the treatment with SKI606 the increase in impedance is bigger than in the control experiment demonstrating a stronger adhesion between the two cell types (fig.2).
The results reveal that our cell chip provides an easy and real-time monitoring tool to study cells and can be very useful in all biology laboratory. Our device is very cheap and reusable and allows us to perform automatic cell counting and other studies saving time and reagents. It joins a great sensitivity and low cost both for fabrication and usage.

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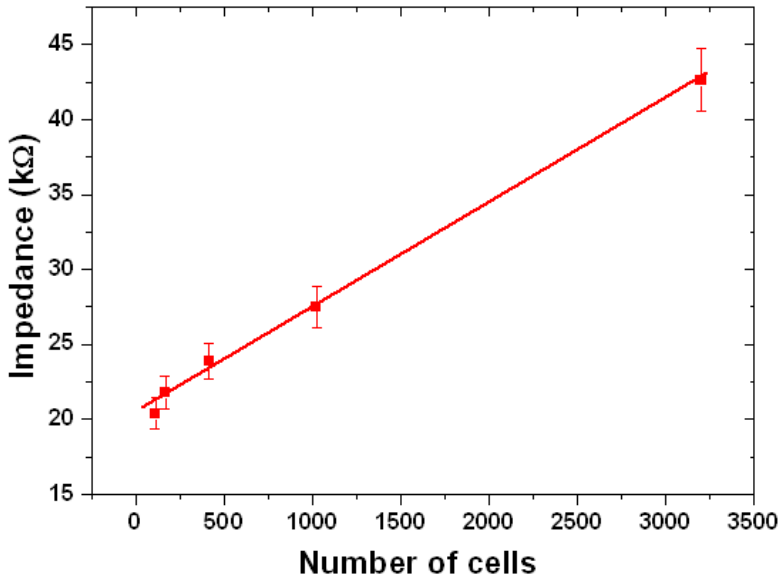

Fig. 1 Cell counting by EIS measurements. The relationship between the number of cells grown upon the device and the impedance values is linear.

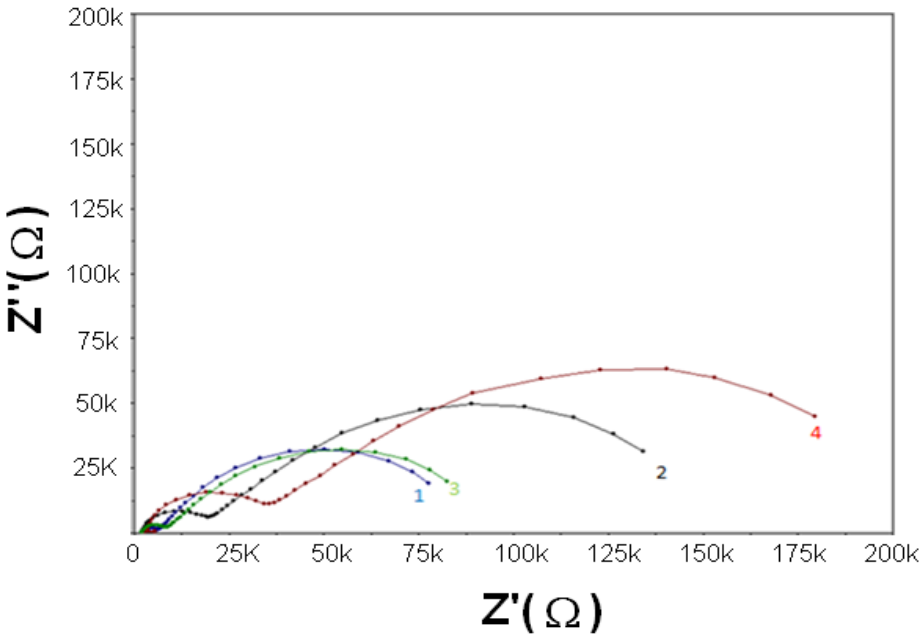

Fig. 2: EIS curves related to a co-culture of endothelial cells and leukaemia cells. The blue curve (1) and the black one (2) are related to a control experiment in which non treated leukaemia cells are seeded on a layer of endothelial cells. The curve 1 is referred to the impedance values measured for the monolayer of endothelial cells, while the curve 2 has been obtained after the addition of the Ku812 (leukaemia cells).
The same experiment has been carried out with leukaemia cells treated with a anti-cancer drug, SKI606, which restores the adhesive properties of lymphocytes. On the layer of endothelial cells (curve 3, green), Ku812 treated for 15 min with SKI606 have been seeded (red curve, 4). As we can see the impedance values after the treatment are bigger than in the control experiment (4 vs 2) demonstrating a stronger adhesion between the two cell type.