Multichannel Series Piezoelectric Quartz Crystal Cell Sensor for Real Time and Quantitative Monitoring of the Living Cell and Assessment of Cytotoxicity

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ABSTRACT:

A new multichannel series piezoelectric quartz crystal (MSPQC) cell sensor for real time monitoring of living cells *in vitro* was reported in this paper. The constructed sensor was used successfully to monitor adhesion, spreading, proliferation, and apoptosis of MG63 osteosarcoma cells and investigate the effects of different concentrations of cobalt chloride on MG63 cells. Quantitative real time and dynamic cell analyses data were conducted using the MSPQC cell sensor. Compared with methods such as fluorescence- staining and morphology observation by microscopy, the MSPQC cell sensor is a non-invasive, label- free, simple, cheap, and capable of online monitoring. It can automatically record the growth status of cells and quantitatively evaluate cell proliferation and the apoptotic response to drugs. It will be a valuable detection and analysis tool for the acquisition of cellular level information and is anticipated to have application in the field of cell biology research or cytotoxicity testing in the future.

SUPPORTING INFORMATION AVAILABLE

Table 1. The comparison between the frequency shifts of calculated by theoretical model and obtained by sensor.

Time	ΔR_{cell} (Ω)	ΔC_{cell} ($\times 10^{-12}$F)	ΔF_{theory} (Hz)	ΔF_{sensor} (Hz)	**error**
0h	0	0	0	0	0
16h	83.3	0.51	151.48	158	-4.8%
32h	138.1	2.27	183.62	192	-3.2%
48h	206.4	6.05	298.33	284	+3.7%
64h	211.3	6.58	419.96	432	-2.6%
80h	197.7	6.22	396.47	412	-1.2%

To verify the validity of the theoretical model, we measured and calculated the cell adhesion resistance and capacitance at different time points using the impedance analyzer. These parameters were substituted into the derived equations to calculate the theoretical value of frequency shift (ΔF_{theory}), which was then compared with the frequency shift obtained from the sensor (ΔF_{sensor}). The results showed that the theoretical and experimental values were consistent with each other within the range of error. Please refer to Table 1. ΔC_{cell} and ΔR_{cell} were the changes of the cell adhesion capacitance and resistance, respectively.

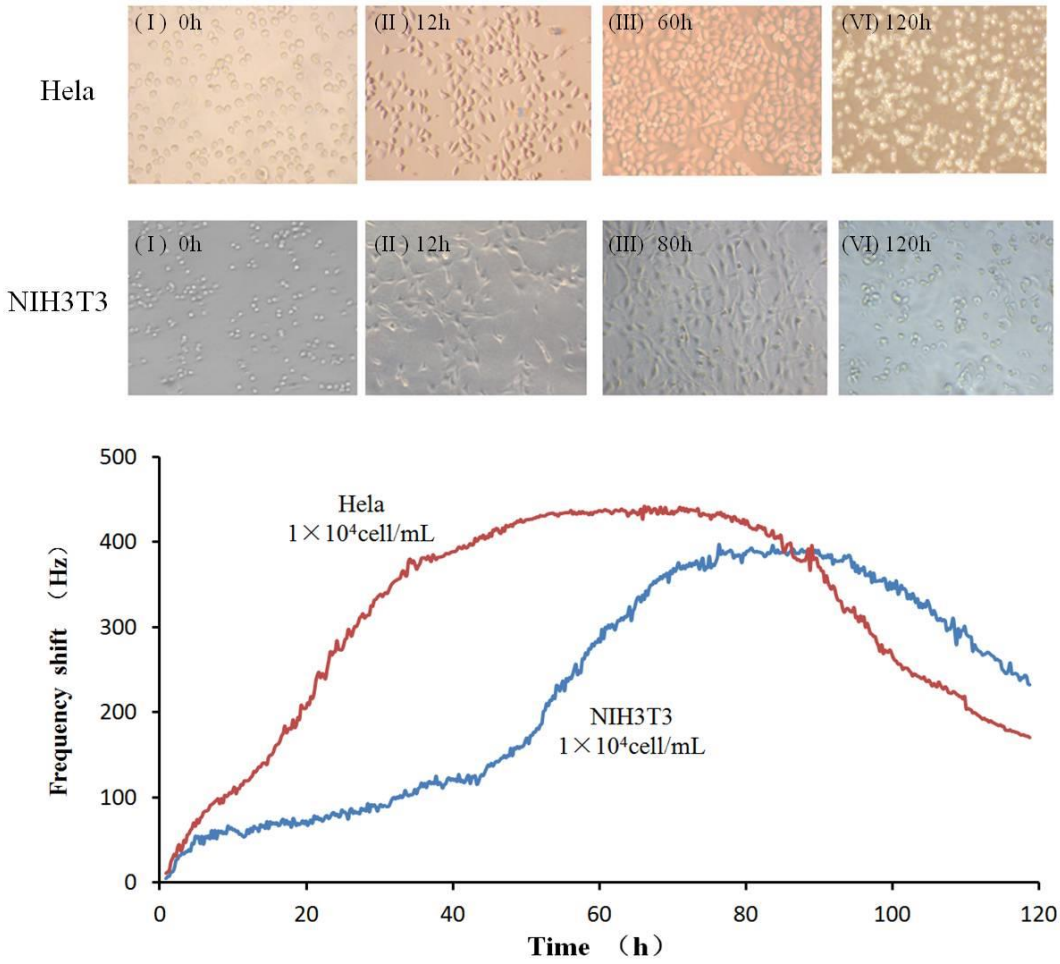

Figure 1*. The frequency shift response and photomicrograph of Hela and NIH3T3 cells inoculated on the ITO electrode at different time points.

The frequency shift response of Hela cells increased rapidly after seeding, and soon reached the plateau, which was consistent with the oblate shape of Hela cell and the early arrival of proliferation phase observed by the microscope. The frequency shift response of NIH3T3 cells increased slowly after seeding, consistent with that NIH3T3 cells appeared slender shape and relatively longer spreading phase. After 48h, NIH3T3 cells begun to proliferate, so the frequency shift rising significantly. In the decrease phase of the frequency shift, apoptosis took place in both kinds of cells, as

showed in Figure 1*. The results confirmed the sensor’s performance.