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CHARACTERIZING SINGLE SINONASAL SQUAMOUS CELL CARCINOMA USING DI-ELECTROPHORESIS AND ELECTROROTATION

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ABSTRACT

We show the capture and analysis single cells, in particular human sinonasal squamous cell carcinomas (SCC), by the combination of di-electrophoresis (DEP) force and electrorotation, within a microfluidic device. A set of 4 planar polynomial electrodes was employed to perform nDEP trapping of two lines tumor cell with different invasivity, named NC5 and NC7. Once captured at the center of the electrodes set, electrorotation was served to extract the rotational speed's spectra. From the spectra, their electrophysiological properties can be estimated.

KEYWORDS: Sinonasal squamous cell carcinomas, di-electrophoresis, electrorotation, single cell analysis

INTRODUCTION

Cancer cells can be found in various forms, with different physical properties at different stages of malignancy. Metastasis is the main cause of cancer patient death, physical biomarkers discovery is a challenge to develop diagnostic tools. In this context, single cell approach by di-electrophoresis (DEP) and electrorotation, which are electrokinetic phenomena, have demonstrated a potential for tumor cell characterization in lab-on-chip platforms [1]. We investigate and compare two cancer cells at different degrees of malignancy of sinonasal squamous cell carcinomas. The rotational speed's spectra are different for these cells. This spectra indicates the cell dielectric characteristics, such as membrane capacitance, membrane permittivity, cytoplasm conductance and cytoplasm permittivity [1, 2].

THEORY

Di-electrophoresis (DEP) is a force affecting on a polarizable particle in a non-uniform static electric field. DEP drives the particles to move toward high (positive phenomenon) or low electric field area (negative phenomenon) depending on the relative polarizability of the cell and the suspending medium. The time-averaged DEP force is expressed as

$$F_{DEP} = 2\pi r_{cell}^3 \varepsilon_0 \varepsilon_m \text{Re}[f_{CM}(\omega)] \nabla E^2 \quad (1)$$

where r is the radius of cell, ε_0 and ε_m are respectively the relative permittivity of the vacuum and the medium, $\text{Re}[f_{CM}(\omega)]$ is the real part of the Clausius-Mossotti factor, and E is the electric field.

In the case when the cell is suspended in the rotating electric field, the rotational speed is defined as

$$\Omega_{ROT(\omega)} = -\frac{\varepsilon_0 \varepsilon_m E^2}{2\eta} \text{Im}[f_{CM}(\omega)] \quad (2)$$

where η is the dynamic permittivity of the medium and $\text{Im}[f_{CM}(\omega)]$ is the imaginary part of the Clausius-Mossotti factor.

* These authors contributed equally to this work

EXPERIMENT

The two cell lines NC5 and NC7 were cultured in RPMI 1640 (with GlutaMAX + 25mM HEPES) medium, supplemented with 10% of fetal bovine serum and 5% of penicillin. For the experiment, cells were collected by centrifugation, rinsed three times and resuspended in a low conductivity medium ($\sigma = 100mS/m$).

The 4 planar polynomial shape electrodes with a tip-tip spacing of $75\mu m$ was fabricated on a quartz wafer by conventional photolithography technique, which generates DEP force to trap cancer cells, then rotates them by electrorotation force. A thin layer of SU8-2025 was built on the quartz as an open chamber with $25\mu m$ high. A cell suspension of $30\mu L$ was pipetted on the device surface and a coverslip was gently put on to close the chamber.

A voltage with 5V peak-to-peak amplitude is applied on the electrode array, at the frequency 500kHz to trap cells by negative DEP force in the center of the electrodes set. The rotational signal is induced on the set of four voltages, each has 90° phase-shift with the neighbour electrodes, at a fixed 2V amplitude and over a frequency range from 37kHz to 25MHz.

RESULTS AND DISCUSSION

When the cell is submitted in the non-uniform electric field ($5V_{pp}$ and 500kHz), it is captured in the center of the 4 electrodes which is the lowest electric field region by nDEP. After trapping, an electrorotation signal is served to determine the rotational spectra.

Curve fitting between the experimental and theoretical spectra was then performed by the Genetic algorithm in Matlab. The spectra of NC5 and NC7 were indicated in Figure 1. At 210kHz, both NC5 and NC7 cells achieve the maximum speed. However, we observe that NC5 (6.44rps) rotates faster than NC7 (2.93rps).

The electrophysiological properties of NC5, NC7, such as permittivity and conductivity of the membrane and cytoplasm, are estimated from the spectra and noted in Table 1.

Table 1: Estimated the electrophysiological parameters of cell

	$\sigma_{mem}(S/m)$	ϵ_{mem}	$\sigma_{cyto}(S/m)$	ϵ_{cyto}
NC5	2.932×10^{-4}	29.929	0.094	75.248
NC7	2.229×10^{-4}	29.758	0.045	37.021

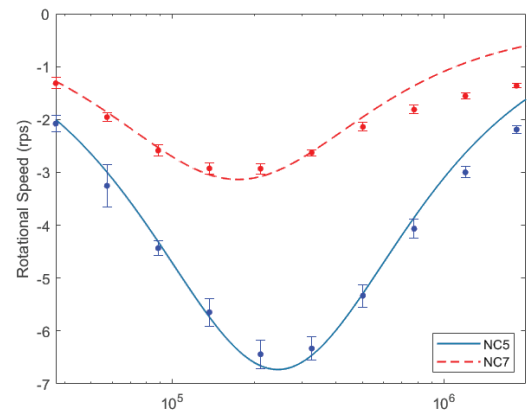


Figure 1: Electrorotation spectra of NC5 and NC7.

CONCLUSION

We characterize the two cancer cells by di-electrophoresis and electrorotation techniques. When the cell is more invasive, it rotates more slowly in the rotating electric field. Furthermore, from the electrorotation spectra, we extract the conductivity and permittivity of the membrane and cytoplasm of the trapped cell.

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