STUDY EFFECTS OF ONCOGENE ON IN-PLANE ELASTICITY OF ALVEOLAR EPITHELIAL CELLS USING ELECTROFLUIDIC PRESSURE SENSOR-EMBEDDED MICROFLUIDIC DEVICE

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In this paper, we construct a microfluidic device with an embedded pressure sensor to study the in-plane direction elasticity of adenocarcinomic human alveolar epithelial (A549) cells layer with different oncogene, multiple copies in T-cell malignancy (MCT-1), expression levels [1]. The pressure sensor is constructed based on electrofluidic circuits, ionic liquid-filled microfluidic channel networks. The device consists of three polydimethylsiloxane (PDMS) layers: a top cell culture chamber layer, a middle sensing membrane layer and a bottom electrofluidic circuit layer as shown in Figure 1(a). On the top layer, a cell culture chamber with a single inlet and a single outlet is designed to culture cells for the measurement. On the bottom ionic liquid-filled circuit layer, four identical electrofluidic resistors [2] designed and arranged as a Wheatstone bridge circuit as shown in Figure 1(b). An elastic sensing membrane is sandwiched between the top and bottom layers. When the sensing membrane is deformed by pressure application, the geometries of the electofluidic channel will be changed, and the characteristic of the electrofluidic circuit will also be changed accordingly. The change will further vary the output voltage signal from the circuit. When the cells are seeded on the top of the sensing membrane, the cell-adhered membrane can be modeled as a two-layer composite plate. To quantitatively estimate the in-plane elasticity of a layer of cells, we derive a theoretical model based on first order shear deformation theory of plate (FSDT) [3-4] and basic circuit theories to estimate the cell elasticity from the sensor sensitivity variation. For comparison, we use the atomic force microscope (AFM) to measure the out-of-plane elasticity and thickness of the A549 cell layers. The average measured thickness of A549 cells is 1.11μm. With the measured pressure sensor output signals and the sensing membrane geometries and mechanical properties, we can calculate the relationship between the Young's modulus of the cells layer and the sensitivity ratio. The ratio is obtained from the same device with and without the cells cultured in it (Figure 2). In the experiments, A549-control cells (A549-C) and A549 cells with MCT-1 oncogene overexpression (A549-M) [5] are used to investigate their in-plane elasticities. Figure 3 shows the bright field phase images of the A549 cells cultured in the microfluidic devices during the experiment. Figure 4 (a) and Figure 4 (b) show the typical time-lapsed sensitivity variation of the devices cultured A549-C and A549-M cells, respectively. According to the Figure 2, we can estimate the in-plane elasticity of A549-C and A540-M cells layers. Figure 5 shows comparison of the average in-plane elasticities of the A549-C and A549-M cells measured using the developed microfluidic devices. The results show that the average in-plane elasticities of A549-C and A549-M are 10.51 MPa and 20.87 MPa (n=3), respectively. The result demonstrates that the device can successfully measure the in-plane elasticity of the cells, and the elasticity increases when MCT-1 oncogene overexpressed in the A549 cells. With the demonstrated capability, the developed device shows its great potential for study of cell physical properties with different gene expression.

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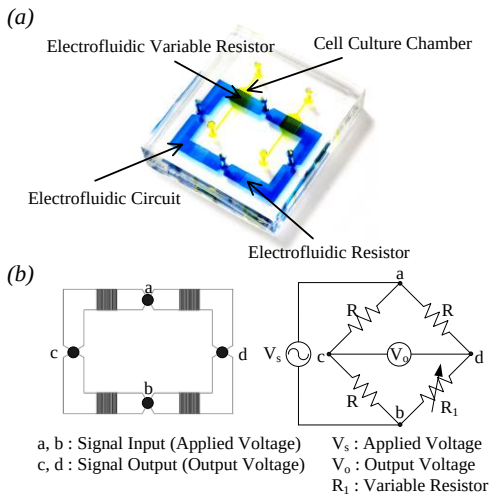

Figure 1: (a) The pressure sensor embedded microfluidic device (b) the bottom layer electofluidic circuit channel layout and the equivalent Wheatstone bridge circuit.

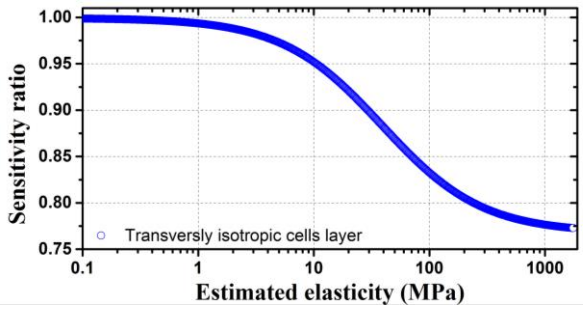

Figure 2: The relationship between the estimated in-plane elasticity and the sensitivities ratio of the pressure sensor with and without cell cultured on the membrane

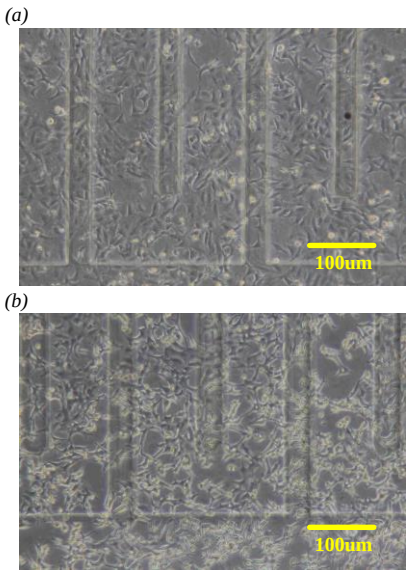

Figure 3: (a) Image of microfluidic pressure sensor device seeding A549-C on top of the sensing membrane (b) Image of microfluidic pressure sensor device seeding A549-C on top of the sensing membrane.

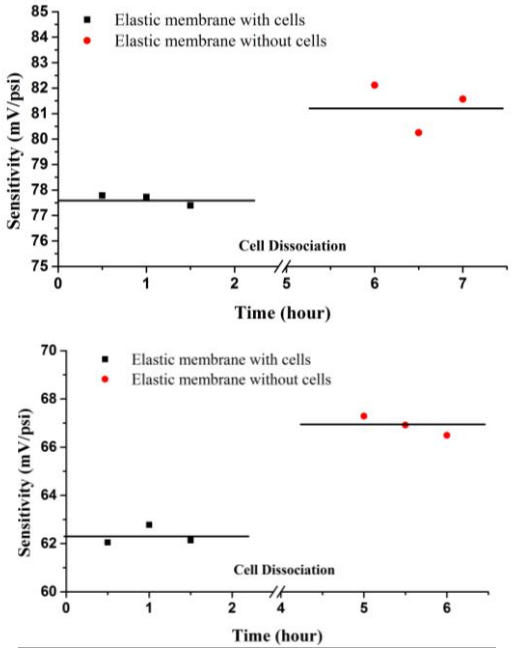

Figure 4: Experiment results of pressure sensor sensitivity variation during a set of measurements (a) seeding A549-C on top of the sensing membrane (b) seeding A549-M on top of the sensing membrane

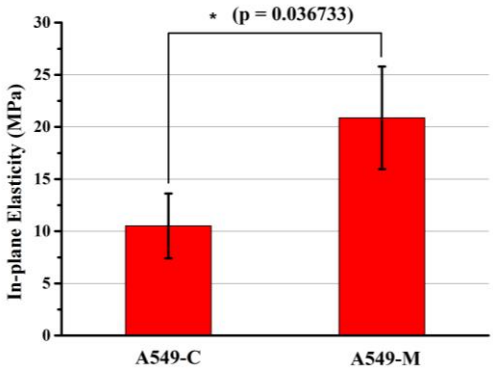

Figure 5: Average in-plane elasticity of A549-C and A549-M cell layers measured using the developed microfluidic device. Data are expressed as mean ± sd (n=3).

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