Proceedings of ASME 2010 First Global Congress on NanoEngineering for Medicine and Biology
NEMB2010
February 7-10, 2010 Houston, TX, USA

NEMB2010-13256

ELECTRICAL IMPEDANCE SPECTROSCOPY MICROSYSTEM AS A TOOL FOR CANCER CELL ANALYSIS

Hyun Soo Kim[1], Younghak Cho[1, 2], A. Bruno Frazier[3], Zhuo (G). Chen[4], Dong Moon Shin[4], and Arum Han[1,5]
[1]Department of Electrical and Computer Engineering, Texas A&M University, College Station, TX, USA
[2]School of Mechanical Design & Automation Engineering, Seoul National University of Technology, Seoul, Korea
[3]School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, USA
[4]Winship Cancer Institute, Emory University, Atlanta, GA, USA
[5]Department of Biomedical Engineering, Texas A&M University, College Station, TX, USA

Email for a corresponding author: arum.han@ece.tamu.edu

Conventional methods for diagnosing and analyzing cancer cells are based on histology, genetic analysis, and protein analysis. Specific genotypes or proteins have been used as biomarkers in identifying cancer cells with specific phenotypes. Despite recent advances in cancer research, quantifying the heterogeneous tumor cell populations has been one of the main challenges in cancer diagnosis and prognosis [1]. The heterogeneous population of cells in the same tissues at different tumor development stages makes analyzing genetic alteration in tumors complicated. Methods conventionally used to study the heterogeneity of cancer cells are based on bulk analysis requiring large number of cells for assay. The resultant measurements are an average from multiple cells. As a result, any single protein or biomarker assay is not capable of determining the cellular heterogeneity of tumor [2]. To overcome such challenges, technologies capable of conducting reliable and high throughput sample analysis with single cell resolution is crucial.

Microfluidic based systems are capable of controlling and analyzing small amount of samples with extremely high accuracy and throughput. A large number of microsystem platforms for cancer analyses have been developed in the past decade, mainly focusing on microsystems for cancer cell sorting and detecting specific biomarkers [3]. Such microdevices can provide many advantages such as shorter analysis time, less sample/reagent consumption, and the capability to integrate cell sorting/analysis with various other functionalities.

Electrical impedance spectroscopy (EIS) is a technique that can be used for characterizing cells or distinguishing pathological cells from normal cells by measuring the electrical impedance of the target in the frequency domain [4]. Due to the non-invasive nature of this method, it is suitable for analyzing biological samples. Recent progress in lab-on-a-chip technologies enabled microfabricated EIS system to detect and analyze biological samples at single cell level [5]. The single cell approach has many advantages over bulk cell analysis. It can provide more accurate information, does not require time-consuming cell preparation process for uniform cell population, and can also be used to quantify heterogeneous cell populations from a mixture.

Here, we present a micro-EIS (μEIS) system for analyzing cancer cells with single cell resolution. This device has a total of 16 impedance analysis sites on a glass substrate (5 x 7.5 mm), with each analysis site composed of a horizontal single-cell trap, an integrated pair of electrodes, and a trapping channel perpendicular to the cell flow channel. By applying suction through this trapping channel, a single cell flowing through the cell flow channel can be captured into the trap. Once a cell is trapped, the impedance can be measured using the integrated electrode pair. This developed μ EIS system was successfully used to obtain the electrical impedance spectra (50 kHz – 2 MHz) of head and neck cancer cells with different metastatic potential, demonstrating the potential of the μEIS system as a tool for quantifying cancer heterogeneity [6].

REFERENCES

[1] G.H. Heppner, “Tumor heterogeneity”, *Cancer Research*, vol. 44, pp. 2259–2265, 1984.
[2] J.A. Ludwig, J.N. Weinstein, “Biomarkers in cancer staging, prognosis and treatment selection”, *Nature Reviews Cancer,* vol. 5, pp. 845–856, 2005.
[3] Maluf, N. & Williams, K. An Introduction to Microelectromechanical Systems Engineering. (Artech House, Inc., 2004).
[4] J. Morucci, M.E. Valentinuzzi, B. Rigaud, C.J. Felice, N. Chauveau, P. Marsili, “Bioelectrical Impedance Techniques in Medicine. Part I Bioimpedance Measurement”, *Critical Reviews in Biomedical Engineering*, vol. 24, pp. 257–351, 1996.
[5] A. Han, L. Yang, A.B. Frazier, “Quantification of the heterogeneity in breast cancer cell lines using whole-cell impedance spectroscopy”, *Clin. Cancer Res.*, vol. 13, pp. 139-143, 2007.
[6] Y. H. Cho, H. S. Kim, A. B. Frazier, Z. Chen, D. M. Shin, and A. Han, “Whole-Cell Impedance Analysis for Highly and Poorly Metastatic Cancer Cells”, Journal of Microelectromechanical Systems, 18, pp. 808-817, 2009.

