Chemical-Free and Reusable Cellular Analysis:
Electrochemical Impedance Spectroscopy with a Transparent ITO Culture Chip

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ABSTRACT

To advance innovative green technology in studying cytology, this study developed an electrochemical impedance spectroscopic (EIS) system with an indium tin oxide (ITO) culture chip module. This paper also demonstrates typical examples of solution effects and B16-F10 cell culture. Results indicate that higher concentrations of saline or albumin had lower impedance. From impedance data, cell proliferation and decline could be elucidated. The impedance soon decreased when Triton X-100 was applied to kill cells. Furthermore, the implemented transparent ITO culture chip module is experiment-friendly to perform optical inspections. The proposed green EIS system which is advantage of chemical-free and reusability can be widely applied to cytology studies in the future.

Keywords: *B16-F10 (Murine Melanoma Cell Line), Cell, Chip, Impedance, Indium Tin Oxide*

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INTRODUCTION

The cell is the smallest functional basic unit of life that is classified as an organism, and is often called the building block of life. All organisms such as bacteria, protozoans, plants, and animals are composed of one or more cells. Cells contain the hereditary information that is essential for regulating cell functions and for transferring genetic codes onto the next generation. Cytology studies are fundamental for the products of biotechnology. A number of major applications of cytology research, such as in enzymes, synthetic hormones, immunobiologicals (monoclonal antibodies, interleukins, lymphokines), vaccines, and anticancer agents have been developed and applied.

In vitro cell-based screening method is an efficient and economic approach prior to examining animal models. Various cell proliferation assays have been developed to investigate cell growth regulation in response to biomaterials, chemicals, nutrients, drugs, cytokines, and growth factors (Yliperttula, 2008). The different manners of detecting effects on cell proliferation include trypan blue exclusion assay, intracellular enzyme release, metabolic activities of cells, DNA staining dye, ATP level, and radiolabeled thymidine uptake (Harvey & Cree, 2010). Although these mentioned methods are convenient and well established for evaluating cell proliferation, concerns regarding cytotoxicity and environmental hazards caused by chemicals utilized in the experiments are present.

Most DNA exposure methods incorporate chemicals into double-strain DNA and measure fluorescence intensity correlated with the amount of DNA to determine the number of cells, such as the method of employing Hoechst 33258 (Chen, 2007). Hoechst 33258 can cause acute toxicity through oral intake, dermal contact, respiratory inhalation, as well as mutagenesis. Radiolabeled thymidine uptake is another efficient approach to monitor cell proliferation; however, radioactive materials can endanger health, the environment, and cause genetic mutation. MTT assay is a good example for testing the metabolic activities of cells (Zhao, 2008). MTT produces a yellowish solution that is converted into dark blue water-insoluble MTT formazan by mitochondrial dehydrogenases of living cells. The blue crystals are solubilized with organic solvent such as dimethyl sulfoxide, which is an eco-unfavorable reagent. To decrease the amount of chemicals and protect the environment, a novel technology, electrochemical impedance spectroscopy (EIS), has been developed for cellular analysis in a non-invasive and non-noxious manner compared to conventional chemical assays.

EIS using microelectrode arrays has gained much attention as a promising, label free, fast, and real-time method for cellular analysis (Opp, 2009). The electric cell-substrate impedance sensing (ECIS; Applied BioPhysics, Troy, NY, USA) and real time cell electronic sensing (RT-CES; Roche Applied Sciences, Basel, Switzerland) systems are two typical examples. Those systems are widely applied in measuring cell proliferation (Zudaire, 2007), attachment and spreading (Charrier, 2007; Liu, 2007), motility (Chen, 2008; Jiang, 2008; Jiang, 2009), toxicology (Opp, 2009; Van der Schalie, 2006), barrier function (Low, 2009; Nahari, 2007), wounding, and migration (Sapper, 2006; Saxena, 2007). There has been a drastic increase in the number of scientific publications on ECIS, RT-CES and other EIS systems listed in the ISI-Web of Knowledge database over the past decade. Currently, commercial sensing chips are opaque due to the chip substrate and the gold electrical route. However, transparent chips for optically related examination are sometimes required to have simultaneous optical images and electrical impedance data to elucidate some complicated cellular behaviors.

This study developed a green EIS system with transparent indium-tin oxide (ITO) glass chips. More importantly, the transparent ITO culture chip module is experiment-friendly, and numerous conventional optical inspections can be conducted on this chip. B16F10 cell is demonstrated to be cultured on this ITO glass chip. The cell proliferation of this cell culture is monitored continuously during the incubation

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