Evaluation of Electric Cell-substrate Impedance Sensing (ECIS) for the Detection of Biological and Chemical Toxins

by

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ABSTRACT

Electric Cell-substrate Impedance Sensing (ECIS) is a function-based biosensor that can detect in real-time, and with high sensitivity a wide range of toxicants by measuring the activity of a cell monolayer cultured on electrodes. This instrument measures the impedance of the monolayer at a range of frequencies, which is subsequently separated into its two components: resistance and capacitance. Resistance data provides information on cell-cell and cell-substrate adhesions, and capacitance data is indicative of confluence of the monolayer. Through analysis of both of these continuously measured parameters, it is possible to rapidly detect the toxicity of any hazardous compounds. In comparison to structure-based approaches which depend on specific enzyme reactions or antibody binding to determine cell viability, proliferation or damage, function-based sensing takes advantage of non-specificity to detect toxicity.

Within the scope of this project, we have focused on the detection of both biological and chemical agents that are known or suspected to have cytotoxic effects. Recent events concerning the development of biological warfare agents motivated our investigation of the effects of enteropathogenic bacteria and synthesized toxins. In particular, the cytotoxicity of *Bacillus cereus*, a stimulant for the highly lethal *Bacillus anthracis*, and the cholera toxin of *Vibrio cholera* were evaluated using the ECIS system. Additionally, the development of industrial and medical technologies incorporating nanomaterials has elicited concerns about safety during the commercialization process. Thus, the cellular response during exposure to a range of dosages of both silver and copper nanoparticles was monitored with ECIS. Subsequent analysis of the collected data also provided greater information on the dose-dependence of signal decay. Lastly, immunofluorescent microscopy was used to not only visually confirm that the ECIS signal accurately reflected cell morphological changes, but also to qualitatively evaluate structural alterations (cell-cell adhesions and cytoskeleton) after toxin exposure.

Here, we show that the combined use of structure- and function-based sensing approaches allows for both quantitative and qualitative evaluation of the cellular response to several biological and chemical toxicants.