423c Biosensors Incorporating Cell Barrier Architectures for Detecting Biomarkers Indicative of Early Stages of Cancer

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It is well known that early detection of cancer is a key to successful treatment of the disease. Current clinical efforts to detect cancer are hindered because they usually involve complicated invasive procedures. In fact, in some cases, patients with symptoms are often first treated for other ailments and by the time diagnostic tests are performed for cancer, the success of treatment has diminished. Recent research efforts have focused on investigating new biomarkers that are indicative of cancer and developing non-invasive techniques for early screening of these agents. It has been documented in the literature that growth factors and cytokines such as VEGF, IGF-1, BFGF, and TNF are elevated in both plasma and serum of cancer patients and are indicative of metastasis, or spreading of the disease. The focus of this research is to extend the application of a whole-cell based biosensor to the detection of these cytokines and growth factors in blood samples. Briefly, this biosensor consists of a confluent monolayer of human umbilical vein endothelial cells (HUVECs) attached to a cellulose triacetate (CTA) membrane of an ion-selective electrode (ISE). Previous studies regarding this biosensor have shown that when the HUVECs form a confluent monolayer where adjacent cells are connected via tight adherens junctions, ion transport is almost completely inhibited, thereby inhibiting the response of the ISE. When the biosensor is exposed to environmental and physiological toxins that effect cell permeabilty, the response of the biosensor serves as an indirect measurement of the presence of toxin. Previous published studies have shown that the sensor can be used to measure the presence of a model toxin, histamine and we have recently extended this work to the detection of vascular endothelial growth factor (VEGF). Specifically, HUVECs were seeded onto the CTA membrane of an ISE with a seeding density of 2 x 105 cells/ml. The cells were allowed to spread and form a confluent monolayer over the membrane surface for 24 h at 37oC in a humidified incubator with 5% CO2. Following confirmation of a confluent monolayer, the electrode response to a known concentration of K+ ions was measured following treatment for 2 to 10 h with VEGF at concentrations ranging from 100 to 1000 pg/ml. The results showed that the sensor responded to VEGF after approximately 8 - 10 hours of exposure time with a detection limit of approximately 70 pg/ml. In addition, the sensor was also tested for its ability to detect VEGF released from both metastatic and non-metastatic human melanoma cells grown in culture and the concentration measured using the sensor was compared to that obtained using the standard ELISA assay. The results showed that no detectible levels of VEGF were found from normal melanoma cells or from the non-metastatic cancer cells using either the ELISA or the cell-based biosensor. However, VEGF was detected from the metastatic cells and the predicted concentrations from the cell-based biosensor were very close to those obtained from the ELISA assay. Current studies are focusing on the sensor response to other cytokines and growth factors both individually and in combination with VEGF. In addition, other cell-barrier architectures such as epithelial cells are being investigated. Finally, the response of the sensor to serum and plasma samples from both healthy individuals and cancer patients will be discussed. It is hypothesized that a non-specific sensor as described above, will respond to a combination of cytokines released in the blood of cancer patients and hence, will provide a more sensitive measurement that can be used for not only a quick, early screening of metastatic cancers but also used for periodic screening of patients in remission.