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Cell-based biosensors and bioelectronics for health and environment: From poly sensing to deconvoluting complexity and heterogeneity

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Recent decades have witnessed many advances in development of Cell-Based Biosensors (CBBs) for addressing clinical, environmental and toxicological problems. While some could be useful means for diagnosis, prognosis and treatments of lethal diseases such as metastatic cancers or for precision medicine, far too many have not translated into on-site use. Contributing reasons are sensitivity of cells to micro- and nano-environmental alterations that result in noise and distortion from optimum condition, lower specificity of cell-based- compared to nucleic-acid- or antibody-based sensors, and longevity concerns. These CBBs and their integrated bioelectronics, if devised and targeted to address the noted shortcomings, are capable of providing comprehensive functional information and insights into the mechanisms of actions upon cellular interaction with bioactive stimuli (such as bioprobes, drugs, and environmental challenges) or during expression of useful biomarkers. The complexity, heterogeneity, and multi-parameter nature of these processes require development of high-performance and field-ready technologies suitable for handling and analyzing large numbers of heterogeneous samples and providing quantitative ideally digitized, predictive, and integrated readouts from living cells. This study presents technologies that have advanced our understanding, including multi-omics, imaging, and label-specific chemical assays, followed by some examples of missing links for proper tackling of aggressive disease states regardless of the culprits. The promise of polysensing technologies for capturing multiplexed biomarkers and temporal/spatial correlations that would otherwise be missed by static and label-specific measurements on fixed cells or summing of single mode biomarkers sensed by separate equipment or at different times will be discussed.

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3D conducting polymer platforms for electrical control of protein conformation and cell functions

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Fibronectin (Fn) is a prominent extracellular matrix glycoprotein that regulates cell adhesion, migration, differentiation and even pro-angiogenic secretion during processes such as embryonic development and tissue remodeling. Conformational changes of Fn are critically important in guiding these cell functions and have been linked to pathologies ranging from fibrosis to cancer. Fabrication of novel three dimensional (3D) macroporous scaffolds made from poly(3,4-ethylenedioxythiophene) :poly(styrenesulfonate) (PEDOT:PSS) via an ice-templating method is reported. These scaffolds offer tunable pore size and morphology and are electrochemically active. When applying a potential, the scaffolds uptake ions that generate reversible changes in electronic conductivity through their entire volumes, which in turn enable precise control over adsorbed protein (especially Fn) conformation, as assessed by fluorescence resonance energy transfer. Moreover, these scaffolds support the growth of mouse fibroblasts for seven days and show electrical control over both cell adhesion and secretion of vascular endothelial growth factor, a crucial signaling protein involved in angiogenesis (vascularization). Collectively, our data show that we have achieved physiologically-relevant 3D platforms with precise control of cell adhesion and pro-angiogenic secretion over large volumes and long cell culture times. As such, these platforms represent a new tool for biological research with many potential applications in basic research, tissue engineering, and regenerative medicine.

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