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Microsensor arrays for the measurement of acute cellular responses to stimulation

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Near real time quasi-continuous measurements of low molecular weight signalling molecules and markers of metabolism enable quantitative characterisation of acute cellular responses to stimulants such as drugs, growth factors or pathogens. In combination with well-characterised intracellular pathway blockers and conventional cell biology, the mechanisms of early stage cellular responses can be quantitatively established. Whilst longer term responses are well-characterised from gene expression studies, immunohistochemistry and Western blotting, the initial cellular responses and their dynamics remain understudied. Electrochemical methods hold out the possibility of non-destructive repeated measurements provided the sensor chemistry can still function in the complex matrix and that typical healthy behaviour of the cells can be observed in the presence of the sensors. We have produced microfabricated sensor arrays comprised six or eight working electrodes as platform technology. Choice of operating potential allows selective quantification of O¬2, H2O2, and NO and, with further modification, pH, glucose and lactate. Key to getting meaningful biomedical results is quantitative data demonstration that valid electroanalytical results are achievable in the presence of surface active cell culture components. We have developed standardised protocols for quantifying the effects of medium of mass transport and electrode kinetics and, in combination with classical cell biology these have enabled rational biodevice development. Methods for the determination of nitric oxide release, O2 concentration, O2 consumption and pH will be presented along with the results of biomedical application these in two principal areas: (1) the early stages of angiogenesis, the growth of new blood vessels, a critical process in both wound healing and metastatic disease in cancer and (2) acute responses of macrophages to anthrax protective antigen, a key early stage in the development of the disease

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