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Microplates with Integrated Oxygen Sensors for Kinetic Cell Respiration Measurement and Cytotoxicity Testing in Primary and Secondary Cell Lines

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Abstract:

This paper presents a cytotoxicity and cell respiration assay that is nondestructive and kinetic. It makes use of 96-well microplates integrated with oxygen sensors. The oxygen signal monitored on-line gives an indication of the cell viability. We show its application for suspension cell lines (Chinese hamster ovary and HL60 cells) as well as adherent (Caco2 cells) and primary (rat hepatocytes) cells using well-known cytotoxic compounds (sodium azide, diclofenac, clozapine, sodium dodecyl sulfate, 2-thiouracil, tamoxifen, and tranlycypromine). The 50% lethality concentration (LC_{50}) obtained from the assay is compared with the standard 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H tetrazolium bromide endpoint assay. The cells can be grown directly in the plates, and the assay requires no further reagents or processing. The cells can be harvested for further analysis, if required. The on-line dynamic measurement allows the calculation of LC_{50} as a function of exposure time. LC_{50} was shown to decrease with time in HL60 cells. The dynamics of this process was considerably different for the three compounds sodium dodecyl sulfate, tamoxifen, and diclofenac, indicating a large potential of application of this method for cell death studies. The assay system can be applied to almost any cell-based systems with little adaptation. The assay is robust, flexible, and applicable for medium- to high-throughput systems requiring only minimal handling and no additional agent.