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Monitoring drug-induced cytotoxicity and hepatotoxicity using impedance

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A number of different cell-based assays for cytotoxic effects of drugs exist including the lactate dehydrogenase (LDH) leakage assay, the neutral red assay, protein measurement and methyl tetrazolium (MTT) assay. We describe the development and optimization of a cell-based assay for cytotoxicity using impedance measurements. This assay is sensitive and provides reproducible results for safety pharmacology, toxicity screens of adherent, proliferating or non-proliferating cells. Changes in the impedance signal indicate effects on cell contractility, cell morphology and proliferation. One advantage of this technique over standard cytotoxicity assays is that continual monitoring of the development of cytotoxicity is possible. We show the effect of reference compounds on the impedance signal of CHO cells, hepatocyte-like cells and human induced pluripotent stem cell derived cardiomyocytes (hiPS-CMs). In addition, we show hepatotoxic effects of paracetamol and recovery from hepatotoxicity after short exposure to the drug. This method provides a viable alternative to standard cell-based cytotoxic screening assays for drug induced liver injury (DILI) as well as cytotoxicity of cells and stem cells.