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### Rapid profiling of multiple toxicity indicators using a laser scanning imaging cytometer

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A major problem for the pharmaceutical industry is the failure of promising drug candidates very late in the testing phases. Often, there are unpredicted side-effects and toxicity issues which limit or prevent a candidate molecule being taken to market. Any testing regimes that can identify toxic molecules and exclude them from the screening programs as early as possible will lead to significant time and cost savings. Here we describe a method which rapidly provides four measures of toxicity in every cell in every well of a microtitre plate. A scan time of 15 minutes per 384 well plate for whole well scans which includes both data acquisition and analysis time on the acumen® eX3 makes this system amenable to primary screening. HepG2 cells were treated with either vehicle control or compound and assay readouts relative to control wells were: total cell number, mitochondrial health, dead cell staining and nuclear condensation. A range of drugs displayed different toxicity profiles and modes of toxicity. This multiplexed approach, which measures completely different cellular effects, maximizes the ability to detect toxic molecules and would be readily applicable to toxicity screening in ADMET labs.

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### Homogeneous binding assay for hybridoma screening: comparison of two laser scanning systems

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Monoclonal antibody therapy represents one of the most rapidly expanding and exciting segments of the pharmaceutical industry today. This has placed unprecedented demands on the antibody discovery process that has traditionally relied on assay formats such as ELISA and flow cytometry.

In this study, we compare a mirrorball® high sensitivity microplate cytometer (TTP LabTech) with the ABI 8200 system (Applied Biosystems, FMAT®) for a homogeneous (no wash) homogenous binding assay. mirrorball is a new bench top laser scanning system that rapidly and simultaneously acquires and processes data from the whole well to provide simple readouts for antibody binding.

The combination of mirrorball and no-wash assay protocols allows researchers to screen antibody supernatants with minimal reagent additions, no wash steps and achieve excellent sensitivity with only 5-10 microlitres of sample. Using the mirrorball's unique ability to scan simultaneously with up to three lasers, it is also possible to multiplex antigens, for example target antigen and counter-screen.

In this poster, we demonstrate a direct comparison of these systems for a representative hybridoma screen.

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### Assessment of chromosomal size variation in CHO cells

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Chinese hamster ovary (CHO) cells are widely used for the production of recombinant proteins. Currently, the pharmaceutical industry relies on stable CHO cell clones for therapeutic protein production. Most of the currently used methods to analyze clonality and stability in recombinant cell lines only take into consideration the cellular phenotype. However, few methods are available to study clonality and genomic stability in recombinant cell populations. Here we present a relatively simple, cost-effective method based on digital image processing to analyze metaphase chromosome length. The method was applied to parental and recombinant CHO cells. Metaphase chromosome spreads were prepared from growth-arrested cells and visualized with a confocal microscope after fluorescence staining. An ImageJ plugin was then used to sort the chromosomes by size. In studies of seven different CHO cell lines (20 metaphase spreads for each cell line), we noticed that the average chromosome number was not homogenous and each cell line had a specific chromosomal length pattern. This pattern can be used to identify the CHO cell lines and to assess the degree of homo- or heterogeneity in clonal populations.