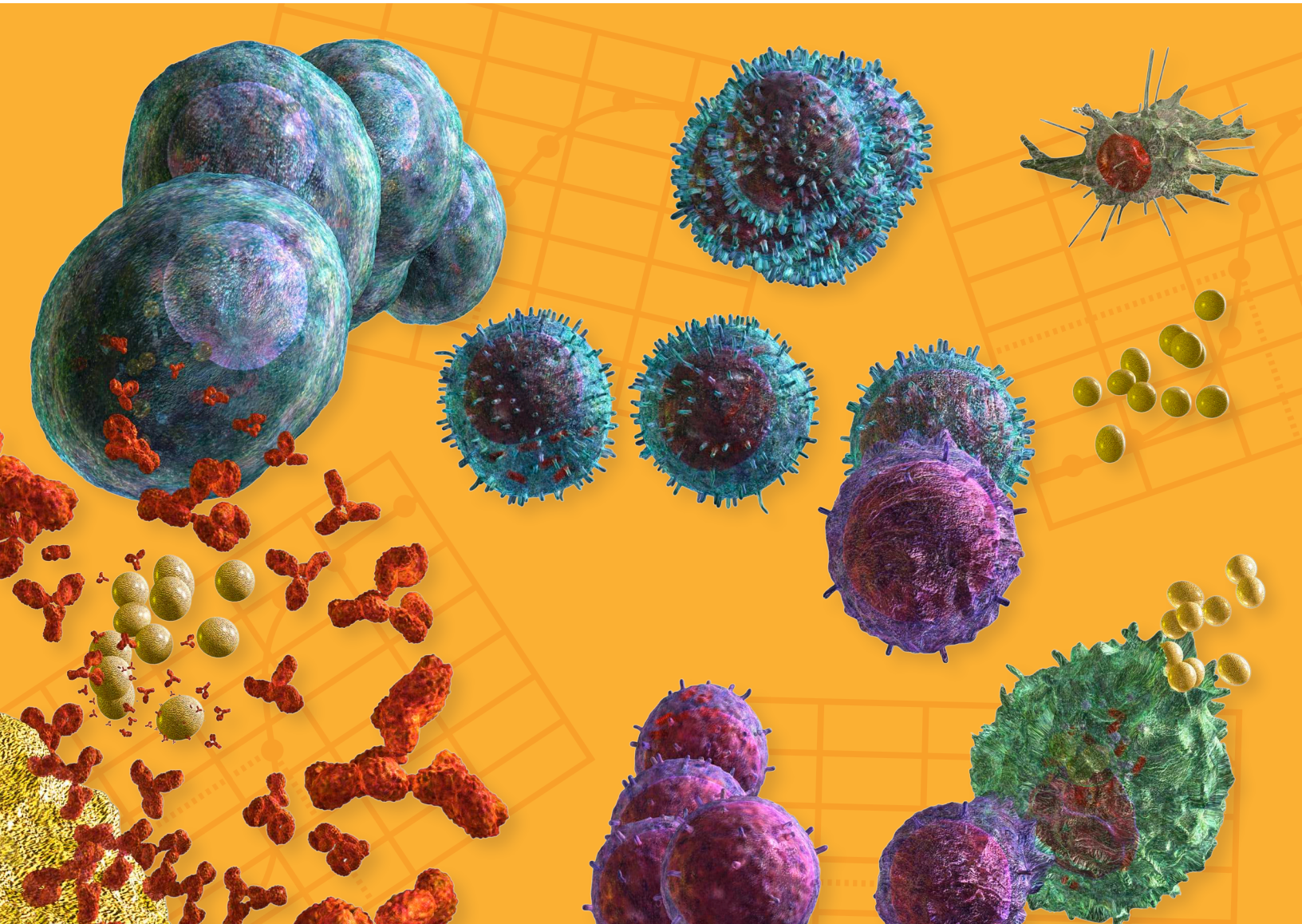
intellicyt
screening solutions for life

High Throughput Flow

Screen Cells and Beads in Suspension with IntelliCyt Systems

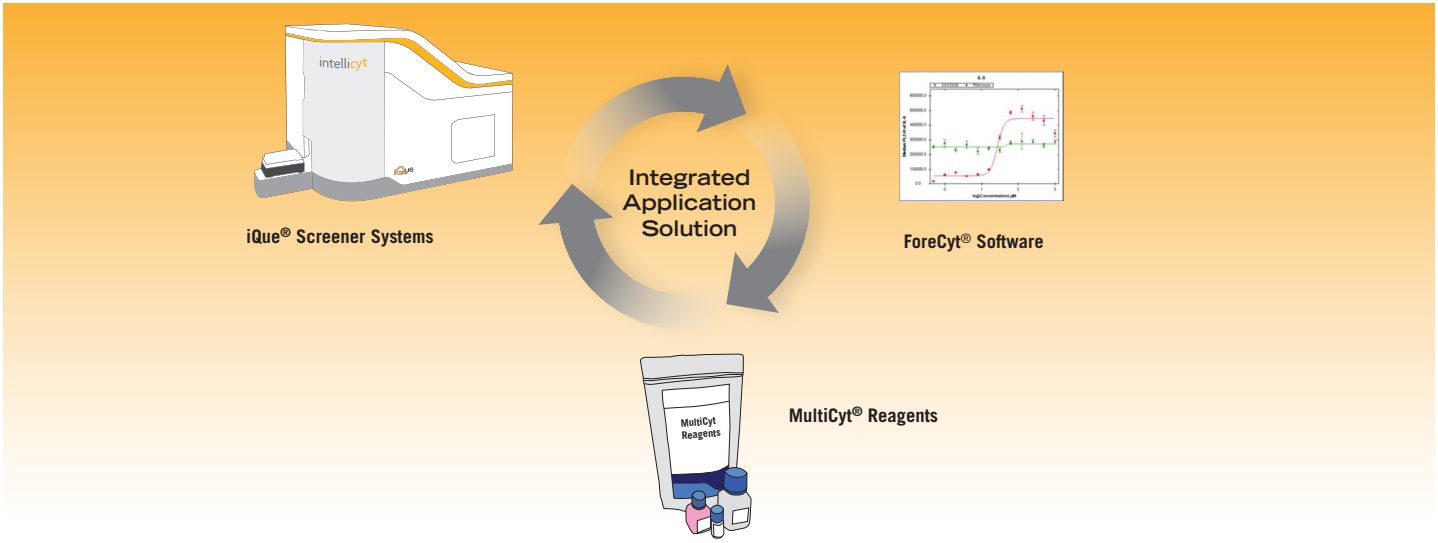


Suspension Screening. Solved.

High-content screening has made multi-parameter cellular assays a routine part of the drug discovery process, greatly improving decision making by offering researchers a rich set of data to advance candidates. However, robust high-content screening has been limited to adherent cells, leaving important therapeutic areas underserved until now. IntelliCyt's iQue® Screener systems provides high-content results at the speed needed for today's screening experiments.

- Increase small-molecule drug discovery productivity by performing high-throughput cell health and cell function phenotypic screens simultaneously.
- Get better information during antibody development studies with simultaneous acquisition of both antigen binding and cross-reactivity data, and screen targets in their natural conformation.

The IntelliCyt Screening Platform



Our fully integrated screening solution consists of instrumentation, software and assay kits that allow researchers to analyze suspension cells with the speed and efficiency required for screening. IntelliCyt's **iQue® Screener and iQue Screener HD,** with 1536-well capability, are high throughput flow instruments that combine rapid sample delivery with information-rich data on a cell-by-cell basis. **ForeCyt® Software** provides plate-centric instrument control and real-time data analysis. Experiment templates ensure the consistent and reliable data analysis required to transform screening data into actionable results. **IntelliCyt Data Manager (iDM)** simplifies data management and enables data sharing between multiple instruments and researchers. **MultiCyt® Reagents** are a family of validated, reagents optimized for a wide variety of cell- and bead-based screening applications.

iQue Screener

HIGHER PRODUCTIVITY

- Screen your libraries in days, not months
- Sample volumes as low as 1 µL reduce reagent costs
- Run 96-well plates in 3 minutes, 384-well plates in 12 minutes, 1536-well plates in 60 minutes (HD)
- Automation-compatible
- Compatible with cells, beads, microbes, and mixtures

MORE PHYSIOLOGICAL RELEVANCE

- Perform assays on mixtures of different cell types
- Screen cells in suspension and targets in their natural conformation
- Collect multiple readouts with four fluorescence channels
- Label-free object detection on size and granularity
- Collect bright and dim objects in same sample

MORE ROBUST RESULTS

- 7-decade detection range provides sensitive and reliable results
- Analyze up to 10,000 individual cells per second for better statistics per well

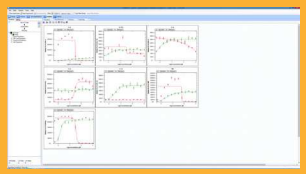
EASIER TO USE

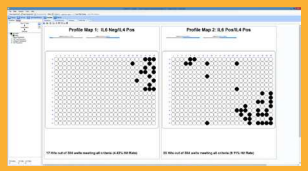
- Interactive profile maps to identify actives
- Seamless report generation including IC50's

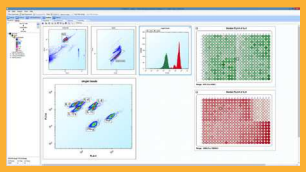
IntelliCyt Customer Applications

- Proliferation
- Cytokine Profiling
- Immunophenotyping
- Apoptosis
- Genotoxicity
- Cell Viability/Cytotoxicity
- Cell Cycle Analysis
- T-Cell Activation
- Autophagy
- Stem Cell Screening
- Biologics/Therapeutic Antibody Screening
- Yeast Library Screening
- Viral Neutralization Assay
- Receptor Internalization
- Transfection and Expression
- Small Molecule Screening
- Cell Signaling
- Solubility Testing
- RNAi

ForeCyt® Software

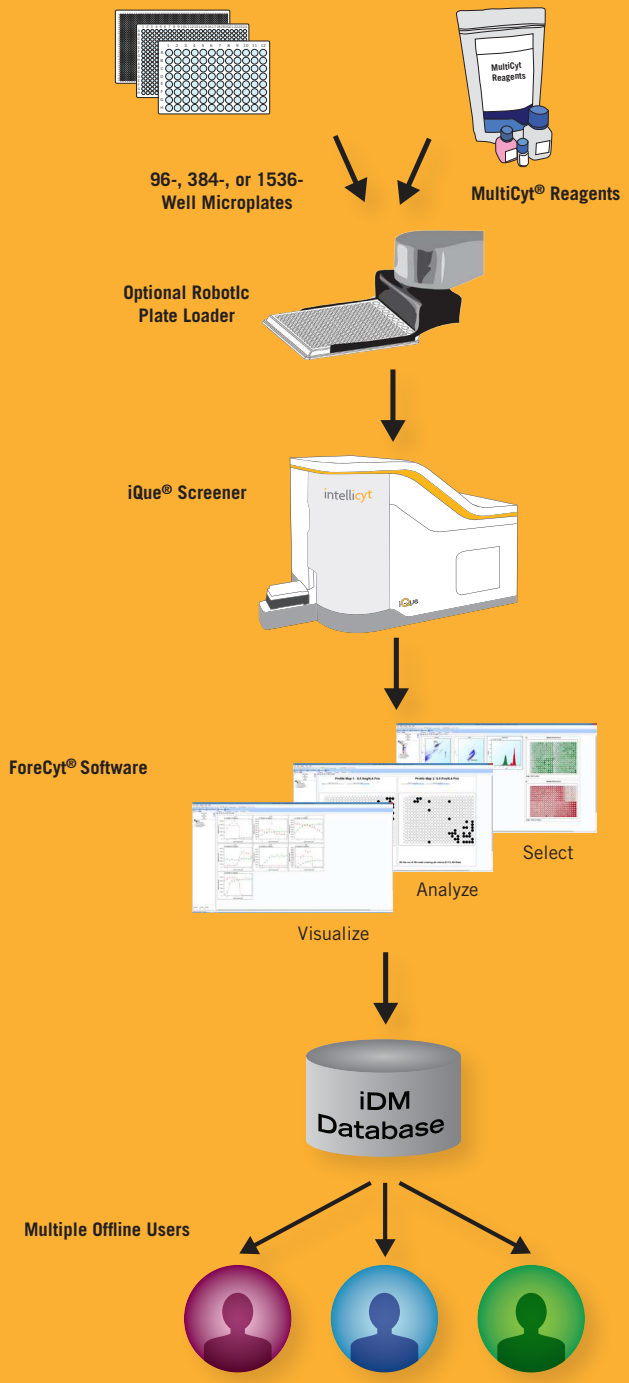






iQue Screener systems use industry leading ForeCyt® Control and Analysis Software. Plate-centric annotation and visualization makes getting the right answers easy. Gates are straight forward to set up, are linked, and update in real time for a truly interactive assay development experience that can be templated and applied to all plates in a run. Real-time data analysis during runs provides visual feedback and automatically performs statistical analysis moments after the run.

The IntelliCyt Screening Workflow

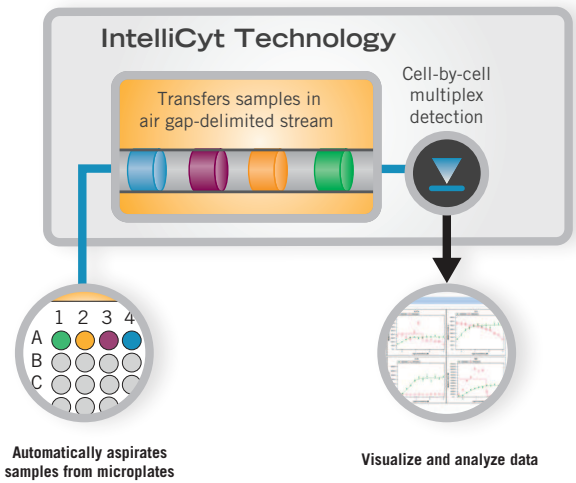


Solution Screening

Cells are labeled using MultiCyt reagents or specific customer protocols and then aliquoted into 96-, 384-, or 1536-well plates. The plates are automatically or manually loaded into the iQue system, and as little as 1 µL is sampled from each well. Up to six measurements for each cell are taken and automatically entered into the iDM database. Users can then access the data in the lab or at their desk and quickly analyze results.

How Does it Work?

A continuous sample stream is sent by the system to the detectors which collects multiple readouts from every object. The systems' unique sampling method transfers cells or other contents from microplate wells to the detectors in a continuous, air gap-delimited stream. The resulting assays take minutes, not hours, and plate-level results are generated for each output.



Antibody Screening in Biologics Discovery

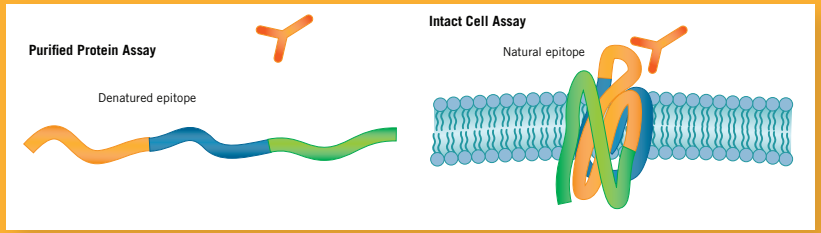
The creation of novel biologics-based drugs for diseases from cancer to arthritis is one of the hottest areas in drug discovery. ELISA, FMAT, and Flow Cytometry have been widely used to screen for therapeutic antibodies generated from hybridoma and phage display methods but each technology suffers from limitations:

- ELISA lacks multiplexing capabilities, incorporates numerous wash steps that introduce variability, and can destroy important epitopes during antigen immobilization
- FMAT has limited multiplexing capabilities, lacks sensitivity for low binding, and is no longer supported
- Flow Cytometry is relatively slow, complex to set up and use, and requires large sample volumes

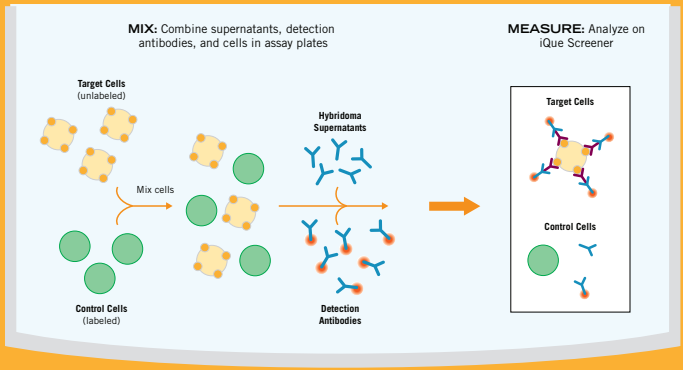
The IntelliCyt Solution

- Processes plates 5 to 30 times faster than flow cytometry, in 96-, 384-, and 1536-well plates
- Improves epitope presentation by measuring individual cells expressing conformationally intact antigens
- Provides no-wash formats that reduce workflow steps and variability
- Multiplexes to assess binding specificity and cross-reactivity from multiple cell lines in the same well

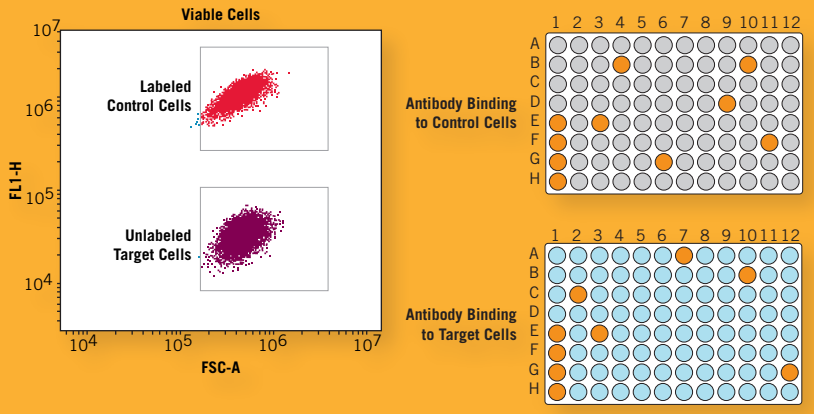
Screening Antigens in Their Natural Conformation



Intact cell-based assays allow screening of antibodies to conformational epitopes that may not be available in ELISA and other purified protein assays, in which the antigens are often unfolded and denatured during the purification process.



Target cells (unlabeled) and control cells (dye labeled) are mixed together and distributed into assay plate wells. Test antibodies from a hybridoma library are then added and incubated with a red fluorescent detection antibody so that non-specific binders (bound to control cells) are distinguishable from specific binders (bound to target cells).

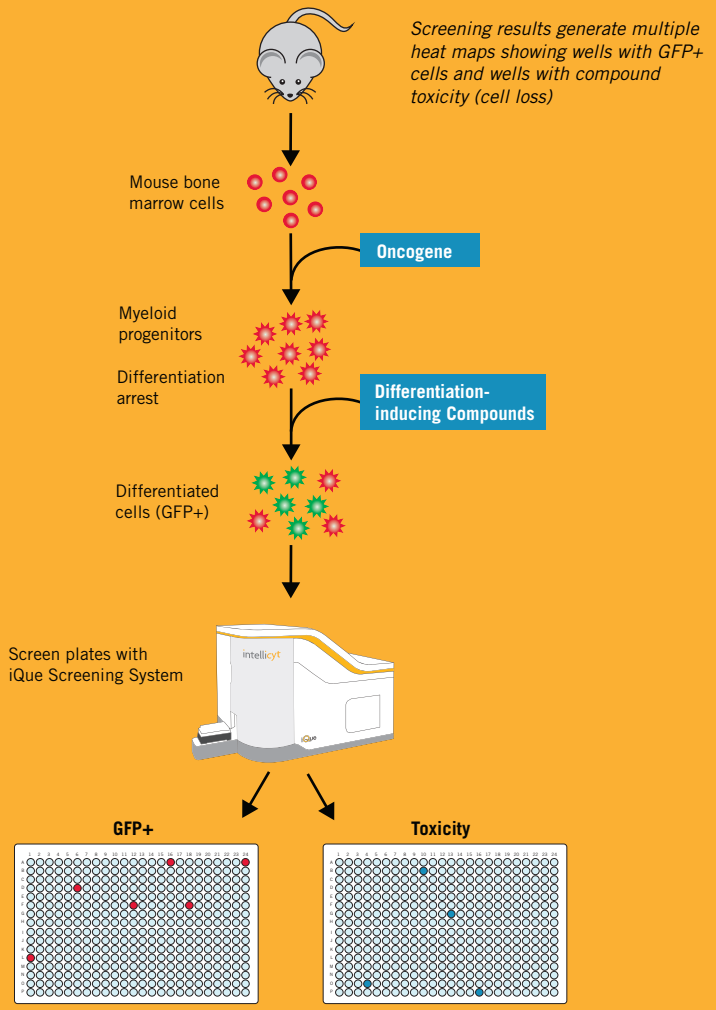


Comparing the antibody binding heat maps generated for the two populations allows supernatants that exhibit specific binding to be identified.

Screening for Compounds that Induce Myeloid Progenitor Cell Differentiation

A small molecule screen was developed to identify compounds that overcome differentiation arrest in primary myeloid progenitor cells. Cell lines were derived from a transgenic mouse expressing GFP under control of the lysozyme promoter: differentiated cells express GFP (GFP+), undifferentiated cells do not (GFP–).

Simultaneous measurements of cell viability, cell number, and green fluorescence were made. By measuring forward scatter, side scatter, and cell number for each well, toxic compounds were identified by measuring forward and side scatter and by cell counts, concurrent with identifying GFP+ cells.



Phenotypic Screening in Small Molecule Discovery

Screening for cellular phenotypes that represent the outcome of multiple biological events in more relevant cell types has become routine with the advent of high content screening methods (i.e., high content imaging). Combining phenotypic screening and target- based screening where appropriate provides an expanded toolbox and more holistic approach to disease-targeting in the drug discovery community. However, High Content Imaging suffers from certain limitations:

- HCI is optimized for adherent cells, not suspension cells and their physiology
- HCI cannot measure secreted or released cell materials
- HCI has limitations measuring dim and bright objects in the same well
- HCI has a relatively low sampling rate, so large sample sizes take a long time

The IntelliCyt Solution

- Provides a high content complement to imaging for suspended cells, beads, microbes, and mixtures
- Measures suspension cells in their natural state, preserving relevant physiology (i.e., primary cells)
- Analyzes cells and beads one at a time (high sensitivity) at high sampling rate to reduce time
- Multiplexes populations of bright and dim objects in the same well

Multiplexed Cell Health Assays

Moving cell health toxicity testing earlier in the drug discovery process enables earlier identification of potentially undesirable outcomes prior to expensive and time-consuming *in vivo* testing. High-throughput *in vitro* testing for targets using non-adherent cell lines is especially challenging because traditional microplate-based methods require cells to be fixed to the plate surface, poorly serving many oncology- and immunology-related targets. IntelliCyt's systems analyze the health of thousands of cells per second in solution — each one individually. The iQue Screener, software and application-specific kits are optimized and validated to identify and characterize cell health and function.

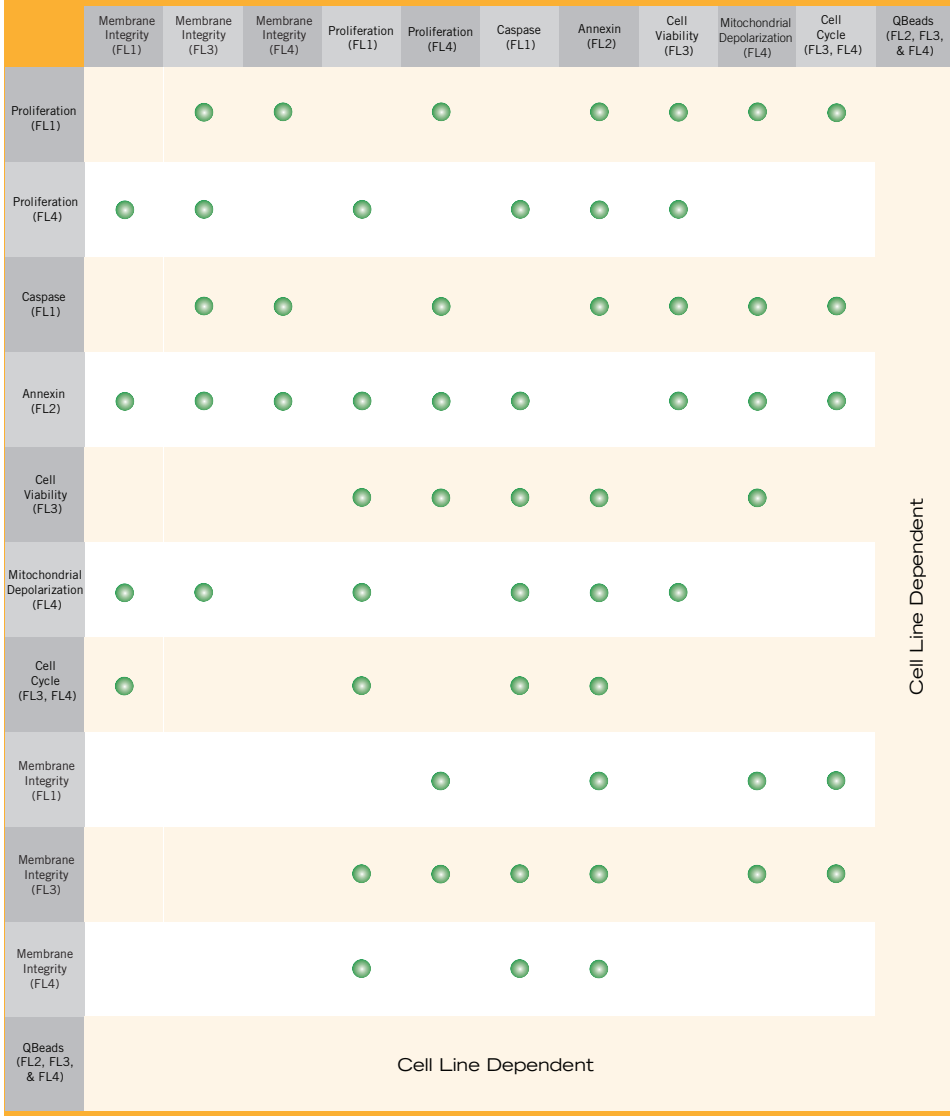
More Robust Apoptosis Results

The no-wash MultiCyt® 4-Plex Apoptosis Screening Kit monitors Caspase 3, Annexin V, mitochondrial depolarization and viability to deliver better correlation between endpoints and more complete apoptotic profiles. Complex mixtures of cells can also be monitored for differential effects.

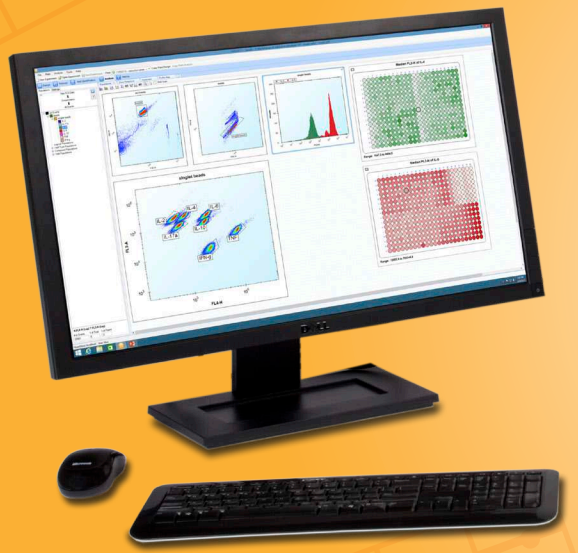
Easier Cell Cycle Assays

The MultiCyt® Cell Cycle Screening Kit is a mix-and-read solution for performing high throughput screens for modulators of the cell cycle. Its unique DNA intercalating dye enables profiling of the G0/G1, S and G2/M phases of the cell cycle without the need for cell fixation, permeabilization, RNase treatment or washing.

MultiCyt Reagents
Profile Cell Health & Monitor Cell Function



MultiCyt® cell health reagents can monitor a variety of endpoints simultaneously including proliferation, membrane integrity, and apoptosis. Dyes have been selected to provide multiplexed results of different endpoints or the same endpoint in a mixed population of cells in the same well. MultiCyt dyes can also be multiplexed with QBeads™ PlexScreen beads to profile cell health and secreted proteins. With MultiCyt dyes and QBeads™ DevScreen beads, cell health can be profiled simultaneously with custom analytes. All dyes use no-wash protocols for robust low-volume assays.



"I don't think you can really grasp the potential of this machine until you own one."

— Research Fellow, Antibody Discovery Group

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