MDS Sciex

Experience the new nature of drug discovery

Now...

CELLKEY™

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NOW simplify and accelerate the drug discovery process

The CellKey™ System is a label-free, universal, functional cell-based assay technology that allows the measurement and analysis of receptor activation in live cells. Measurements are made in real time and are attainable from both endogenous and transfected receptor types.

Key attributes of the CellKey™ System include:

- **Bio-relevant measurements**
  Reliably and consistently measure endogenous receptors
- **Label-free**
  No requirement for tags, dyes or specialized reagents
- **Unique kinetic response data**
  Response profiles equate to receptor mediated signal transduction pathways
- **Universal**
  One platform to measure G protein-coupled receptors (GPCRs) and tyrosine kinase receptors (TKRs)
- **Minimal assay development**
  No reliance on artificial markers such as promiscuous G proteins, arrestins, and reporter gene constructs
- **Ease of use**
  Complete turnkey system that is both intuitive and flexible to use

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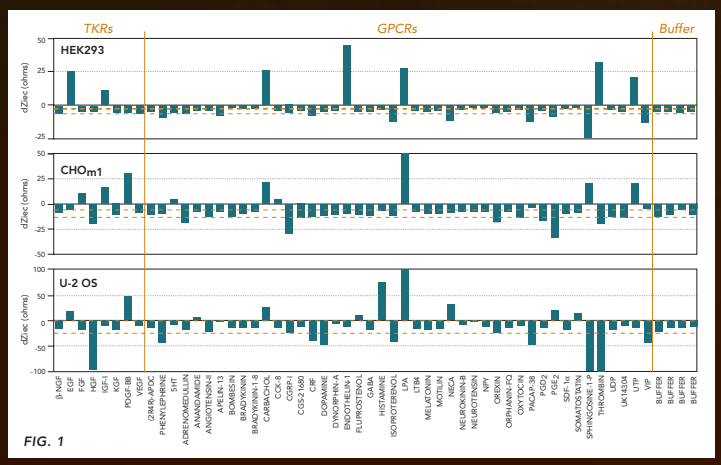
NOW the one solution for many applications

With the CellKey™ platform, perform a range of applications that provide unique, bio-relevant response data for faster, more informed decisions. Assay implementation is simple and the system enables the comprehensive study of all receptors within adherent or non-adherent cell lines and primary cells.

Receptor Panning

An innovative and easy to use application — with one protocol analyze GPCRs and TKRs simultaneously by adding a panel of receptor ligands to cells with the CellKey™ System integrated 96-well fluidics.



- Catalog all types of functionally active endogenous receptors in any given cell line
- Screen a panel of cell lines for functional activity of a specific receptor target
- Choose the most appropriate bio-relevant cell context for secondary screening

FIG. 1 *Receptor Panning — CellKey™ responses identify functional endogenous receptors in cells commonly used in drug discovery, HEK293, CHO_{m1}, and U-2 OS. The change in impedance (Ziec) is plotted in each graph, with a hit set at three standard deviations above and below the buffer mean, as represented by the dotted orange lines.*

Signal Pathway Identification

A universal assay to monitor activation of different classes of known and orphan receptors and differentiate between their signaling mechanisms.

- Equate characteristic CellKey™ response profiles to different receptor signaling pathways
- Cluster responses into discrete groups that represent common receptor coupling mechanisms
- Monitor mechanism of action & off-target effects of lead compounds

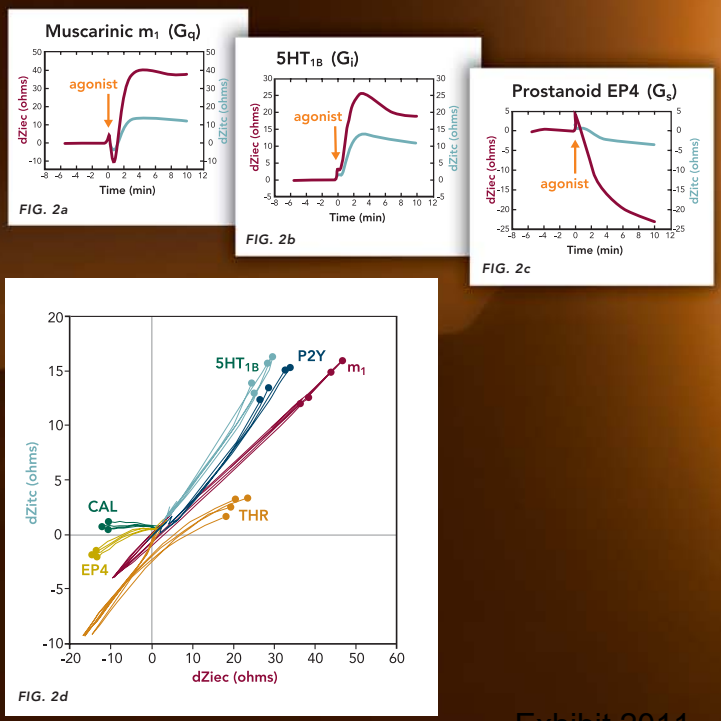


FIG. 2a–d *Graphs illustrate the characteristic response profiles for Gq-, Gi-, and Gs-coupled GPCR-mediated response profiles in CHO_{m1} cells (Fig. 2a–c). This data is further displayed in a 2D representation over time (Fig. 2d). Orange and red lines indicate G_qGPCR responses; light and dark blue lines indicate the G_iGPCR responses; and light and dark green lines indicate G_sGPCR responses.*

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Signal Pathway Deconvolution

Deconvolute receptor mediated signal transduction and obtain a more detailed interpretation of the mechanism of action of lead compounds.

- Measure and analyze downstream signaling events triggered by receptor activation
- Monitor the effects of a panel of signal pathway modulators on the characteristics of CellKey™ response profiles

FIG. 3 *Specific components of G_q-, G_i-coupled or TKR responses are differentially blocked by treatment of HeLa cells with various signaling pathway inhibitors prior to receptor activation with receptor specific agonists.*

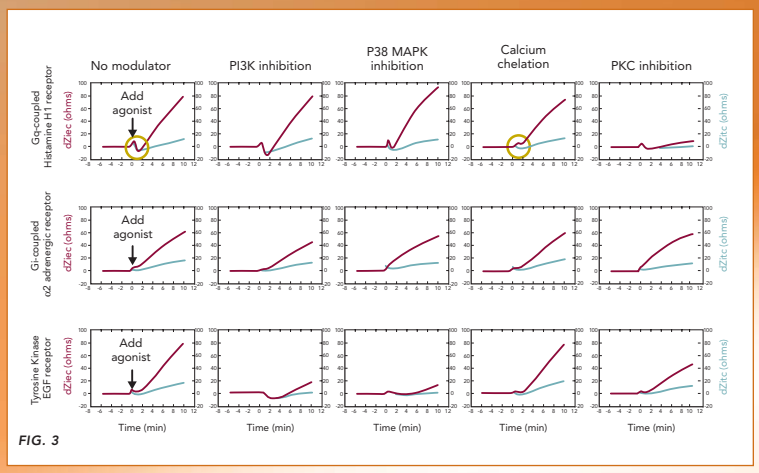


FIG. 3

Hit Identification and Pharmacological Profiling

A single platform to conduct a pharmacological evaluation of ligands across a spectrum of receptors and cell types irrespective of coupling mechanism.

- Confirm hits from primary screen with ease regardless of receptor target
- Determine potency and efficacy of agonists and antagonists
- Analyze data to provide receptor selectivity analysis and Schild analysis for receptor antagonists

FIG. 4 *CHO cells endogenously expressing the $5HT_{1B}$ receptor are treated with increasing concentrations of the antagonist Methiothepin. CellKey™ data is used to perform Schild analysis that demonstrates competitive antagonism of the agonist, 5HT.*

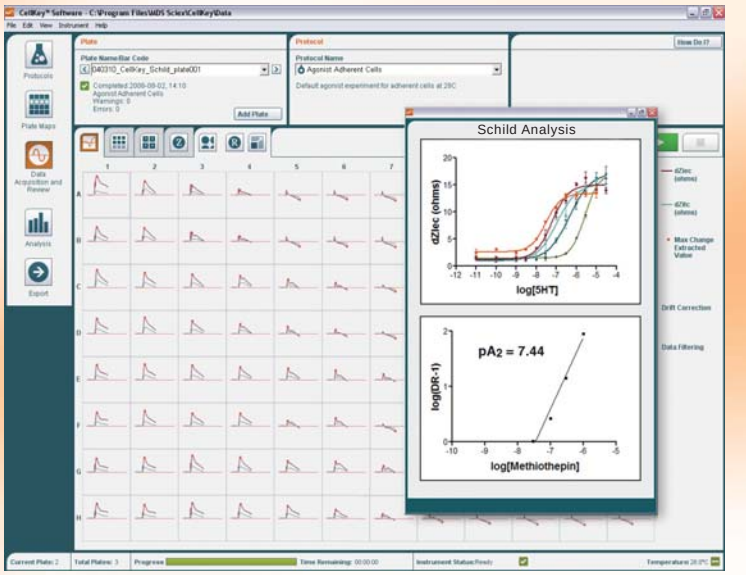
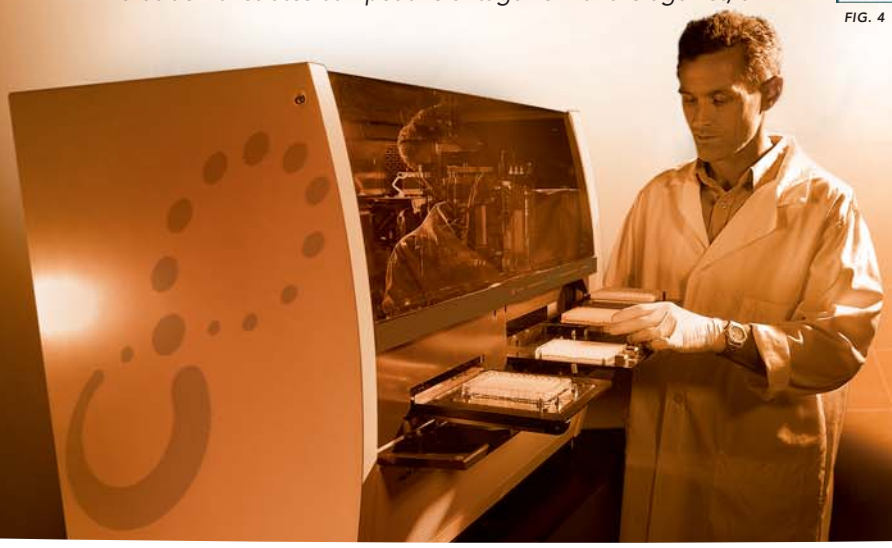


FIG. 4



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NOW a new label-free technology for cell based assays

Upon receptor stimulation, a cascade of signal transduction events occur that lead to cellular changes that include

- Changes in cell adherence
- Cell shape and volume
- Cell-cell interactions

At the heart of the CellKey™ System is a technology based on cellular dielectric spectroscopy (CDS), a non-invasive, impedance based, label-free measurement approach.

Cells expressing the receptor of interest are seeded in the CellKey™ Standard 96W microtiter plate which contains electrodes patterned in each well. Throughout the assay, small voltages are applied to these electrodes. At low frequencies, the voltages induce extracellular currents (iec) that pass around the cells that sit on the electrodes, while at high frequencies, transcellular currents (itc) penetrate the cells.

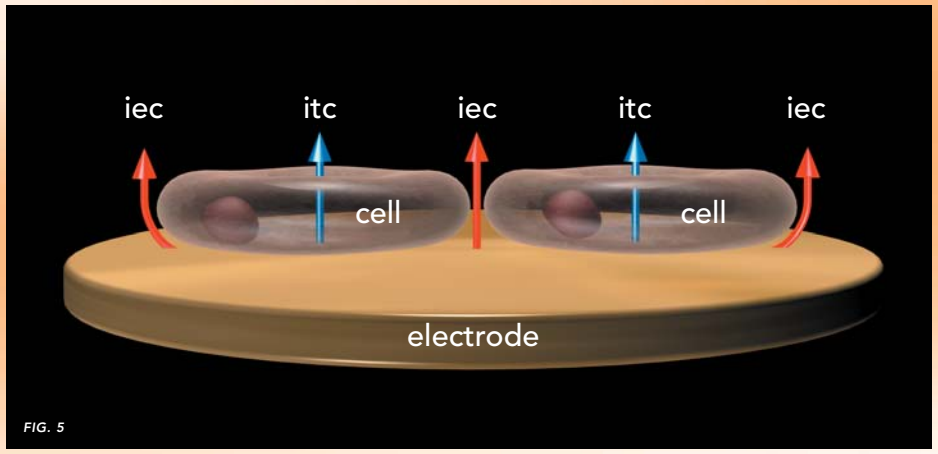

FIG. 5 *A subsection of a single well, displaying cells sitting on a portion of the electrode with current flowing around and through the cells.*

These currents are affected by the cellular changes that take place following receptor stimulation. This affects the magnitude and characteristics of the signal that the CellKey™ System measures, leading to the unique response profiles, as represented in Fig. 2a–c, that are central to the universality and flexibility of the system.

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CellKey™ Instrument Specifications

The CellKey™ System integrates a proprietary impedance measurement system, custom 96-well microtiter plates, on-board 96-well fluidics, environmental control, and custom acquisition and analysis software in a full solutions package.

Measurement principles	Impedance
Measurement frequency range	1 kHz–10 MHz
Assay type	Homogenous, cell-based
Measurement modes	
Simultaneous fluid addition and read	Endpoint or kinetic measurements
Update rate	
96-well	2 or 10 second update rate
Microplate formats	
CellKey™ Standard 96W microtiter plate	96-well Sciex proprietary cell plate
Compound plate	96-well and 384-well compound plates and reservoirs
Fluidics	
Format	96-well pipettor head
Dispense speed	Adjustable
Pipettor height	Adjustable
Compound mixing capability	Yes
Dispense volume	0–200 µL
Temperature Range	
Analysis range	17–37 °C (depending on ambient)
Ambient range	15–30 °C
Physical Attributes	
Benchtop	Yes
Dimensions	HxWxD = 700 mm x 850 mm x 580 mm / 28 in x 33 in x 23 in
Weight	128 kg / 282 lbs
Deck positions	Four
Read position	One
Compound plate positions	Two
Tip-loading position	One
Electrical	
Power consumption	630 W
Line voltage and frequency	100–120 / 200–240 V (self-adjusting) 50 / 60 Hz
PC	Included
Processor	Dual
LCD monitor size	19-inch

Ordering Information

CellKey™ System	1019185
CellKey™ Standard 96W microtiter plates	1019176

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Science advancing health

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