

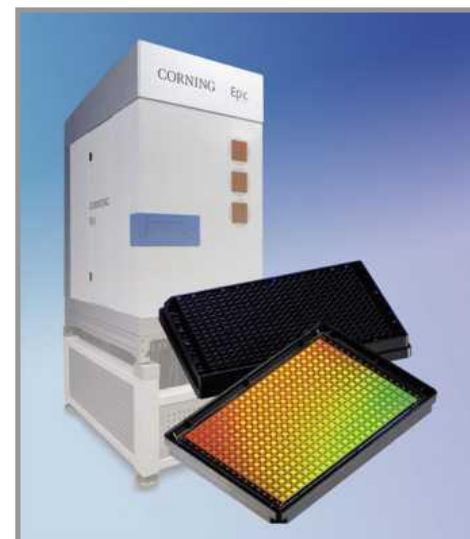
CORNING

Epic[®]
system

Epic[®] Label-Free System

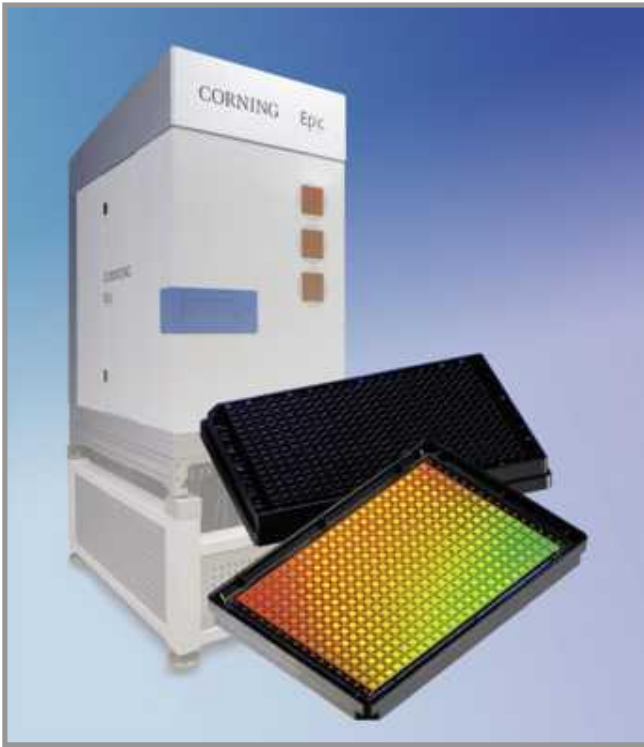
Applicable throughout the drug discovery process

www.corning.com/epic



Menu

The Corning® Epic® System



- Label-free drug discovery system
- High-throughput (40,000 wells/8 hrs)
- Biochemical and cell-based assays
- High sensitivity optical biosensor technology

Epic[®] System Key Attributes

1 Label-Free Detection

- No interference from presence of labels or dyes
- Natural ligand not required
- Novel mechanisms of action (e.g. allosteric binders)

2 High-Throughput

- 40,000 wells in 8 hours
- 384-well microplate format
- Easily integrated with existing automation or stand alone

3 Broad Capability

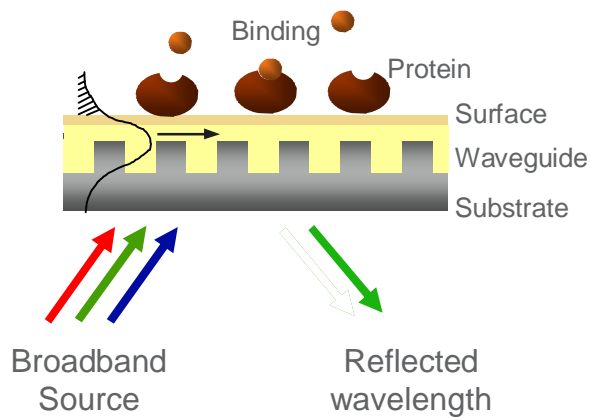
- **Biochemical Assays**
 - (Yes/No binding; affinity; direct bind and functional)
- **Cell-based Assays**
 - End-point and time domain

4 High Sensitivity

- Small molecule binding to protein targets
- Screen with non-engineered cells, including primary cells

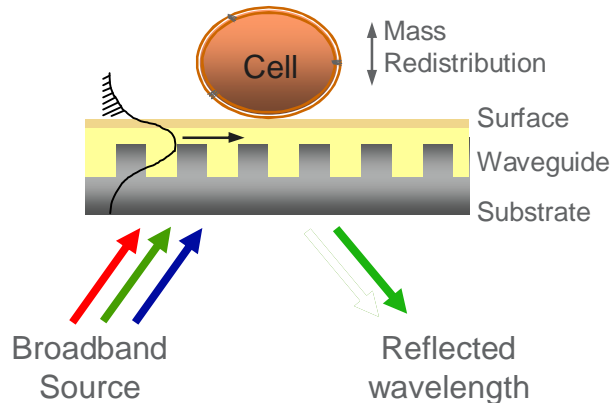
Epic[®] uses an optical biosensor to measure very small changes in index (mass)

Biochemical Assays



Biochemical binding events cause index of refraction changes, resulting in a wavelength shift

Cell-Based Assays

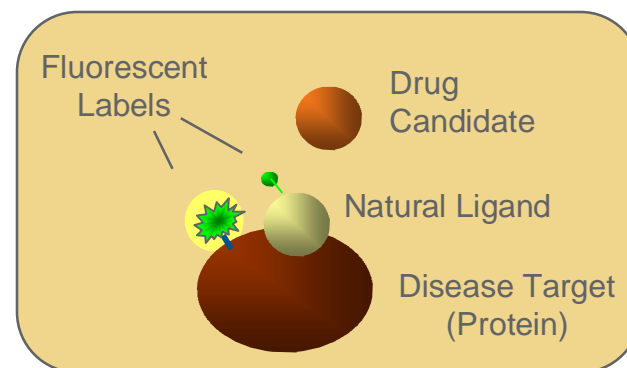


Dynamic mass redistribution within a cell causes index of refraction changes, resulting in a wavelength shift

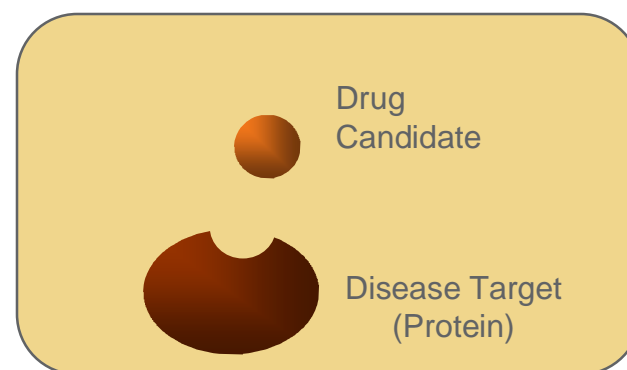
Label-free biochemical assays eliminate artifacts of labels and enable new opportunities

- Labels have many undesirable artifacts in drug screening applications
 - False positives create unnecessary work
 - False negatives are unknown
 - Additional time and expense of implementing labeling strategy
 - Autofluorescent compounds
- Label-free technology enables new opportunities
 - Screen orphan targets
 - Identify compounds with novel mechanisms of action
 - Orthogonal to many HTS assays

Conventional Technology



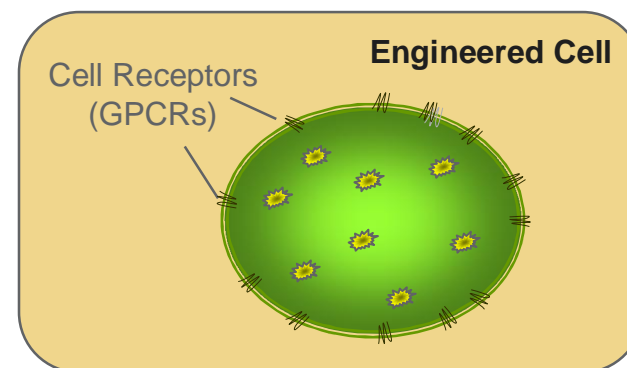
Label-Free Technology



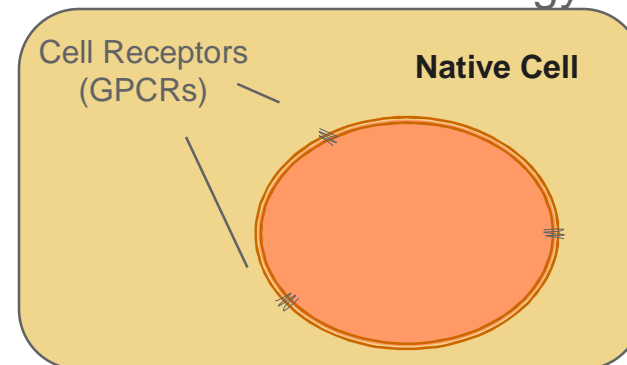
Epic[®] cell assays have additional benefits

- Biologically relevant assays with primary or endogenously expressed cells
- Avoid time, expense, and/or license fees associated with engineered cells
- Integrated measure of cellular response, which is pathway unbiased
- Response profile indicative of cellular pathway

Conventional Technology



Label-Free Technology



Epic[®] Can Address the Majority of Key Screening Targets

HTS Drug Screening by Target Class

Target Class	'06 Screening (% of wells)
GPCRs	29.1%
Kinases	23.9%
Other Enzymes	11.1%
Ion Channels	8.0%
Protease	5.3%
Nuclear receptors	4.2%
Protein-Protein	2.2%
Phosphatase	1.9%
Transporters	1.7%
Protein peptide	1.3%
Helicase	0.9%
Polymerase	0.8%
Protein-DNA/RNA	0.4%*
Other	9.2%
Total	100.0%

GPCRs

- **GSK**: 2k and 10k compound screens
- **Amgen**: Profiling and pathway analysis
- **Astra Zeneca**: human neutrophils
- **Corning**: LOPAC studies for screening robustness

Viral Infection

- **Johns Hopkins University**: Influenza virus
- **Cornell University**: Rhinovirus

Kinase

- **Boehringer Ingelheim** and **Schering AG**

Proteases

- Examples from **Novartis**, **Gilead**, and **Astra Zeneca**

Protein/Peptide and Protein/protein

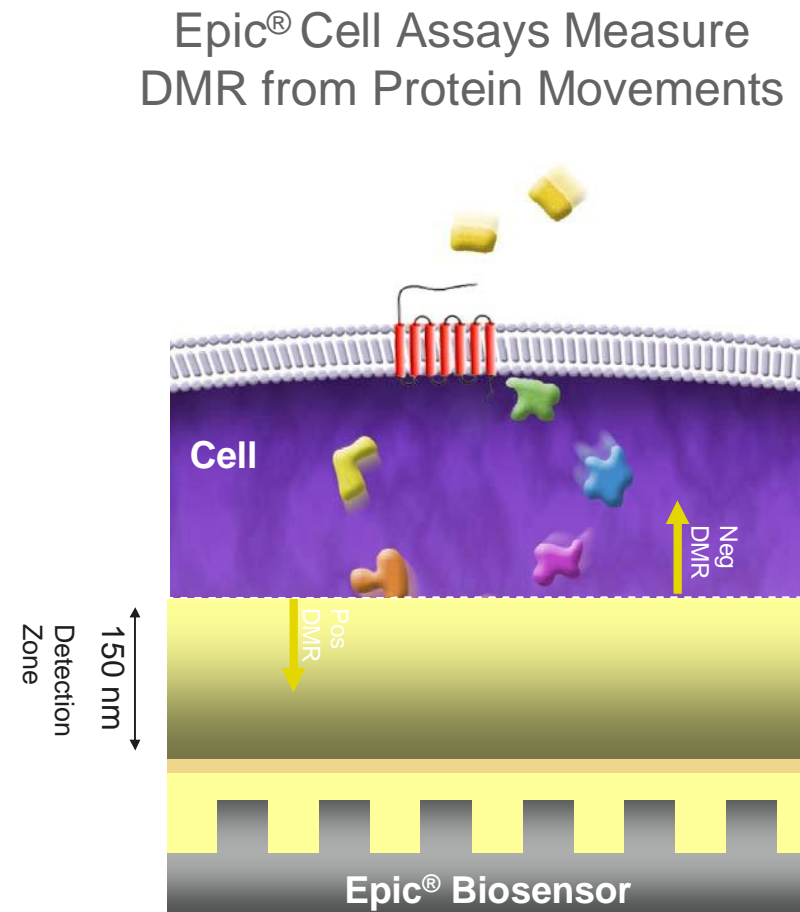
- Example from **Johns Hopkins** and major pharma

Nuclear Receptor

- Example from **Novartis**

Epic[®] Cell Assays measure integrated cellular response

- Cellular response is the result of a series of biochemical interactions within a cell
- These interactions involve protein movements within a cell that are tightly regulated and highly specific
- Mass movement (mainly proteins) in the detection zone is measured with the Epic[®] optical biosensor
- We refer to this as dynamic mass redistribution (DMR), which is an integrated measure of cell response



Epic[®] Cell Assays Have Broad Applicability

GPCRs

- **GPR41/43:** U. Bonn (Evi Kostenis)
- **Dopamine:** Profiling/pathway analysis (Paul Lee)
- **Muscarinic:** Astra Zeneca (Martin Coldwell)
- **Serotonin:** Roche (Ralph Garippa)
- **> 50 receptors demonstrated**
- **> 30 cell types demonstrated**

Ion Channels

- **Slack K⁺ channel:** Yale (Len Kaczmarek)
- **hERG:** Corning
- **Kir6.2/SUR2 K⁺_{ATP} channel:** Corning
- **Others:** to be published

Primary Cells

- **Keratinocytes:** U. Bonn (Evi Kostenis)
- **Neutrophils:** AstraZeneca (Martin Coldwell)
- **Others:** to be published

Viral Infection

- **Influenza:** Johns Hopkins U. (Min Li)
- **Rhinovirus:** Cornell University (Moonsoo Jin)

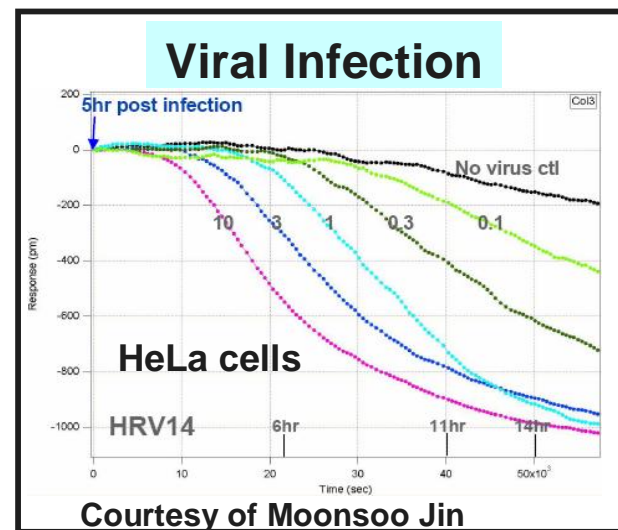
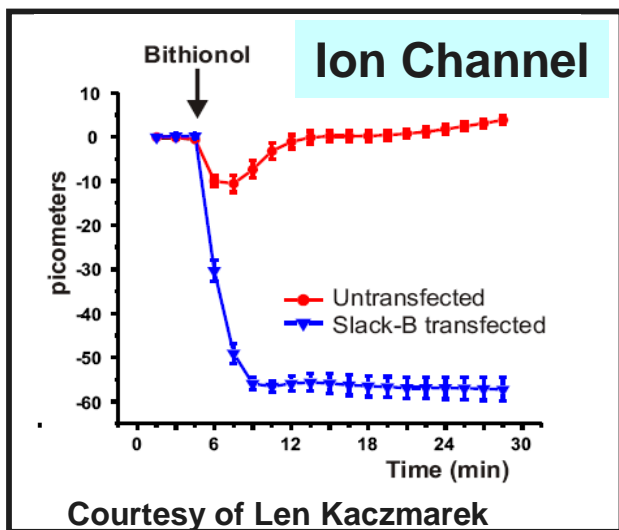
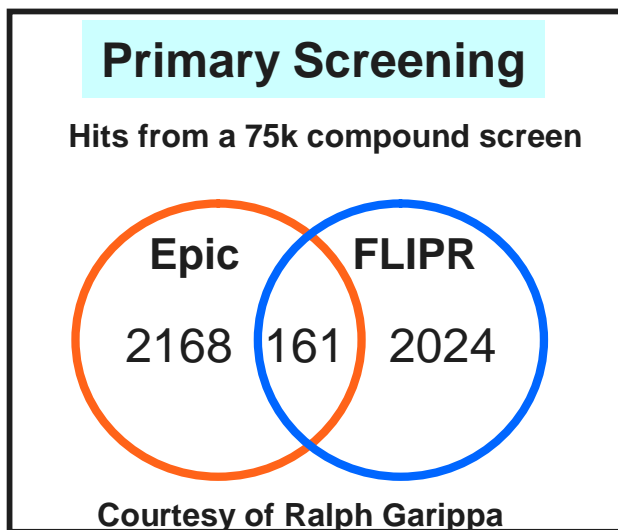
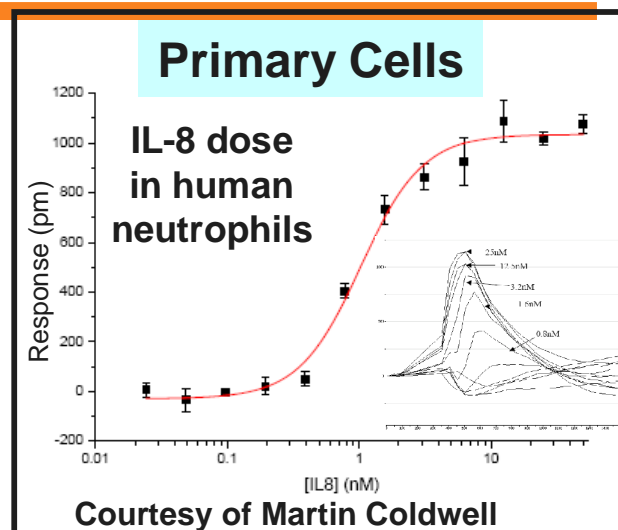
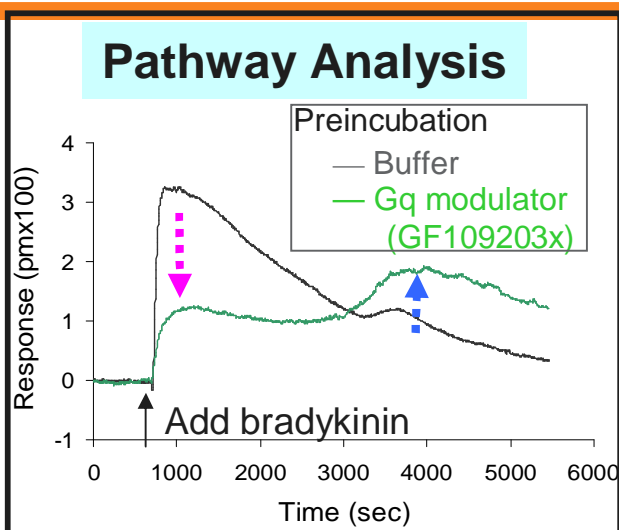
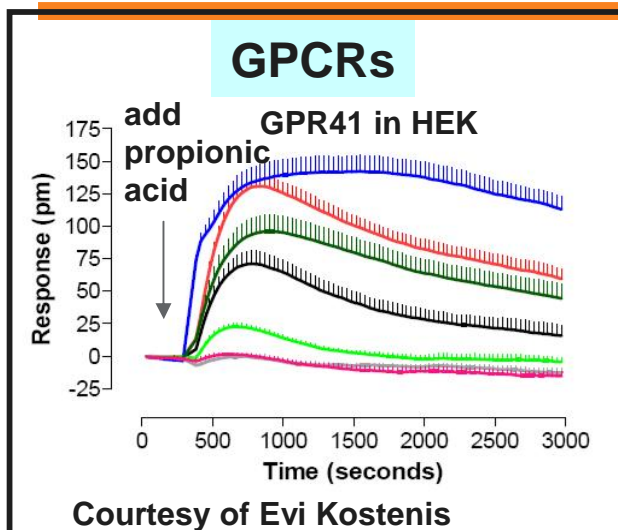
High-Throughput Screens

- **AstraZeneca:** 100k compound antagonist screen (Martin Coldwell)
- **Roche:** 75k compound agonist screen (Ralph Garippa)
- **J&J:** 100k compound agonist screen (Hong Xin)

Key System Features for Cell Assays

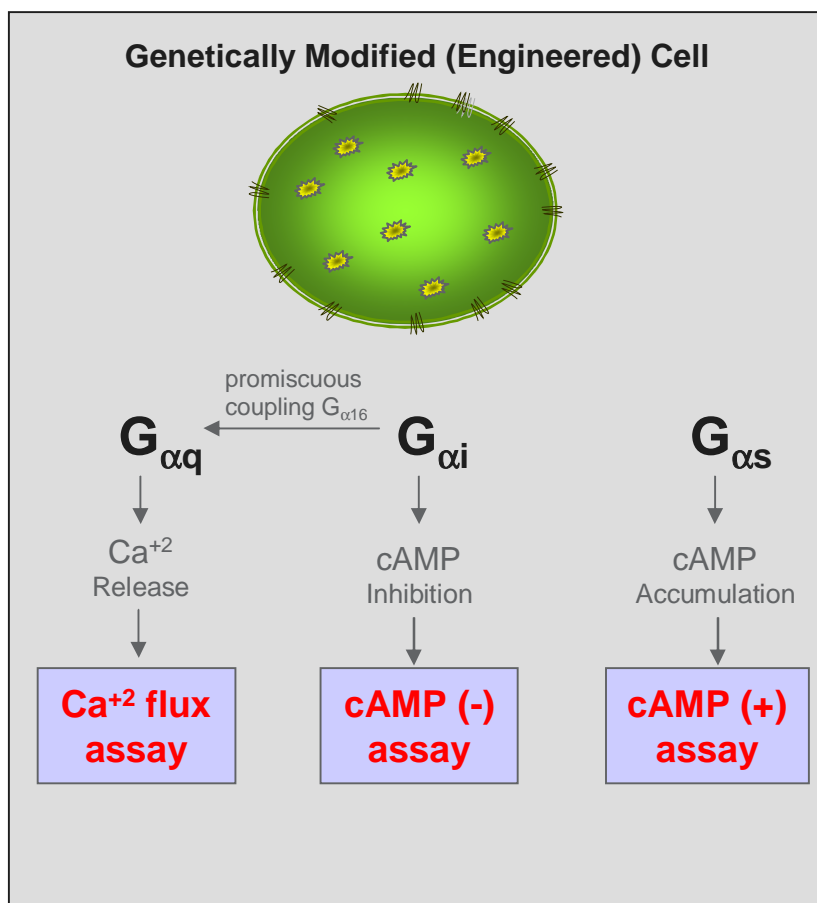
- **Temperature Control**
- **384-well Format**
- **High Sensitivity**

Representative Epic Cell Assay Data

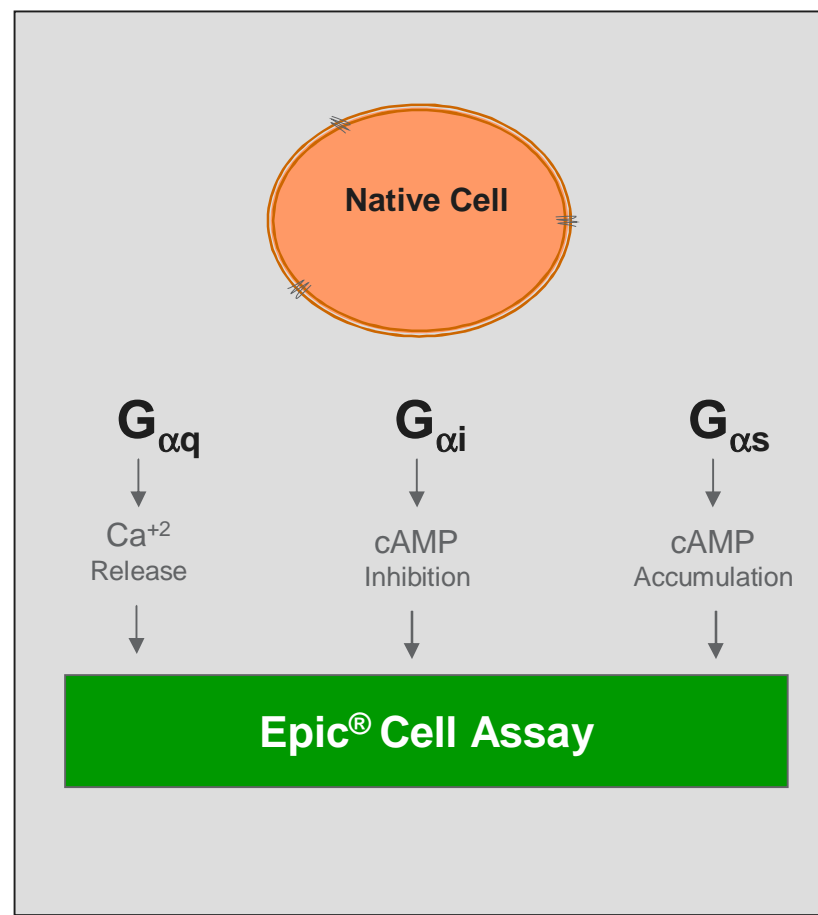


Epic[®] cell assays can detect multiple signaling pathways

Conventional Screening Assays



Epic[®] Label Free Assays

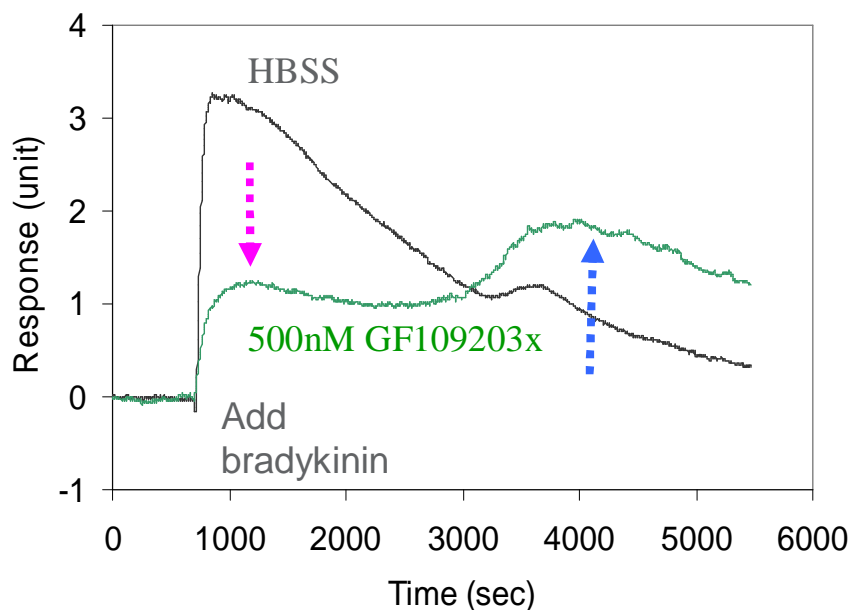


Identification of Pathway Modulators

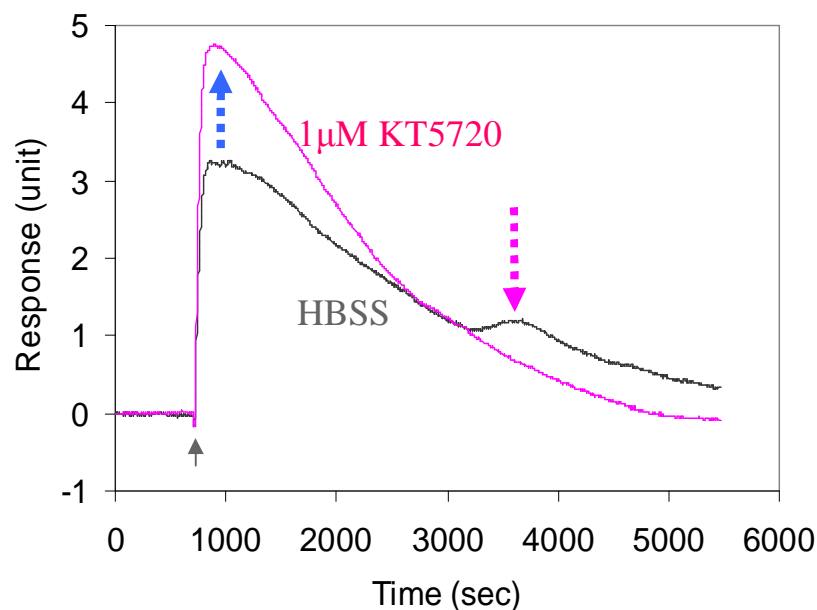
Endogenous Bradykinin B₂ Receptor in A431 Cells

- ∅ B₂ receptor in A431 uses dual signaling pathways: G_s and G_q.
- ∅ The G_s and G_q signaling can cross-regulate each other.

G_q pathway modulators



G_s pathway modulators



1 unit = 100pm

Fang, Y., et al. (2005) *FEBS Lett.*, 579, 6365-6374

Your Resources for Epic[®] System



Contact information:

Björn Kull, PhD
Senior Scientist
Actar AB
Bjorn.Kull@Actar.se
08-524 84801



Contact information:
Corning Epic[®] Team

Account Manager
Joanne Woodward
WoodwardJ2@Corning.com
Mobile: +44 (0) 7788 645 292

Field Applications Scientists
Maria Torvinen and Denis To Van
Torvinenm@Corning.com
Mobile: +49 (0)170 586 1038
Tovand@corning.com