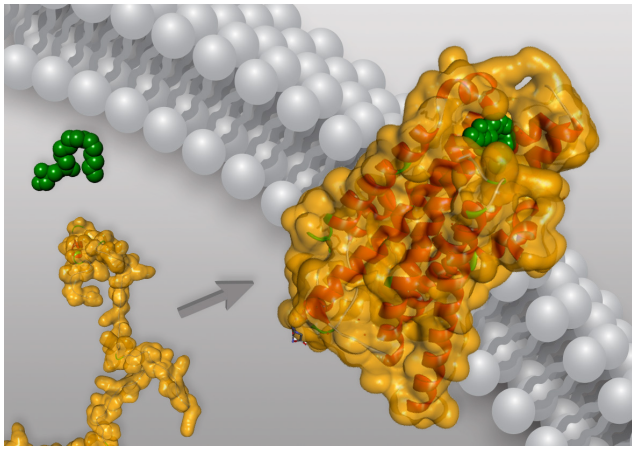
PathHunter®
Pharmacotrafficking Assays

Functionally Rescue Disease Relevant GPCR or Ion Channel Mutants

Transmembrane proteins are translated and folded in the endoplasmic reticulum and then translocated to the cell surface when properly folded. However, defects, such as a mutation, deletion or truncation, can lead to protein misfolding and no trafficking to the surface. This renders the protein non-functional and leads to disease. Compounds called pharmacochaperones provide a way to rescue these misfolded proteins. PathHunter cell-based pharmacotrafficking assays provide a simple, quantitative screening and profiling tool for the discovery and characterization of pharmacochaperones that correct protein misfolding related diseases.



PathHunter Pharmacotrafficking Assay Advantages

- Detect trafficking and functionally restored GPCRs or ion channels
- Simple, rapid cell-based assay with a 1-step addition protocol
- Identify and rank potential antagonists, agonists and allosterics
- Directly measure pharmacotrafficking using standard plate reader

PathHunter Pharmacotrafficking Assays*

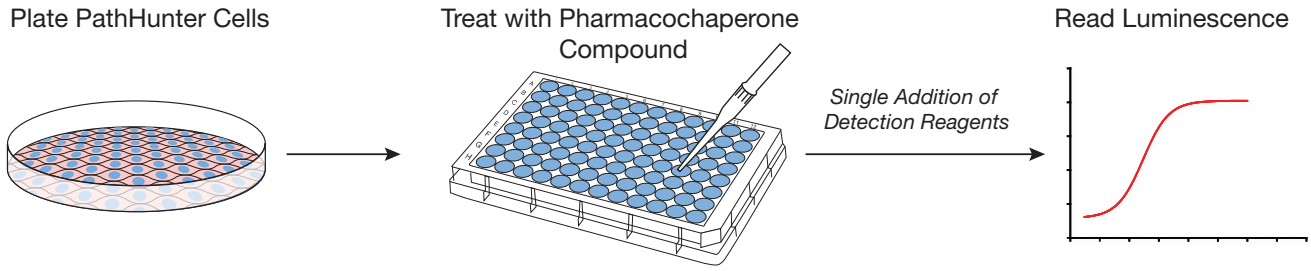
Cell-line Target	Description	Class	Disease Relevance
AVPR2 (S167T)	Vasopressin receptor 2	GPCR	Nephrogenic diabetes insipidus
CFTR-ΔF508	Cystic fibrosis transmembrane conductance regulator	Ion Channel	Cystic fibrosis
KCNH2 (G601S)	HERG1 Potassium voltage-gated channel, subfamily H (eag-related), member 2	Ion Channel	Long QT syndrome (cardiac arrhythmias)
MC4R (T162I)	Melanocortin 4 receptor	GPCR	Obesity
mRHO (P23H)	Rhodopsin	GPCR	Retinitis pigmentosa
SMO (W535L)	Smoothened frizzled family receptor	GPCR	Basal skin cell carcinomas

* Adrenergic receptor β2 (ADRB2 (W158A) GPCR) is also available as an off-target control cell-line.

For pricing information, ordering, and an up to date assay list, visit discoverx.com/pharmacotrafficking

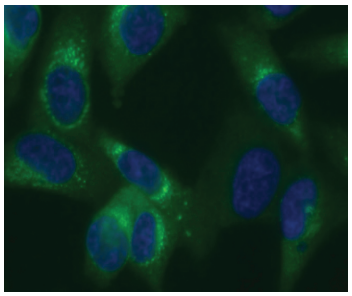
PathHunter® Pharmacotrafficking Assay Highlights & Data

Simple Assays Using a 1-step Protocol

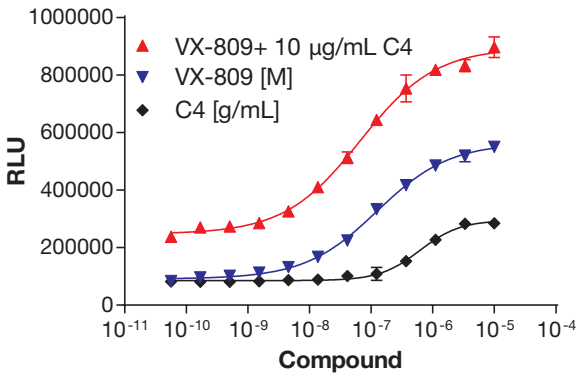


Quantitative Results with Expected Pharmacology and Localization

CFTR-ΔF508 Immunostaining



CFTR-ΔF508 Pharmacotrafficking Assay



Analysis of a mutant form of the ion channel cystic fibrosis transmembrane conductance regulator (CFTR) containing a single point deletion CFTR-ΔF508 was conducted. This common deletion in cystic fibrosis patients causes the protein to misfold, thus preventing efficient trafficking and leading to ER retention (immunofluorescence image, left). Using the PathHunter CFTR-ΔF508 Pharmacotrafficking assay with a combination of 2 compounds, C4 and VX-809, stabilizes the mutant receptor, allowing for proper trafficking. Dual treatment results in elevated signal (right, red curve) indicating an additive effect, which is the expected behavior of the combination of the two compounds.

Learn more about PathHunter Pharmacotrafficking Assays at discoverx.com/pharmacotrafficking

w discoverx.com usa 1.866.448.4864 eu +44.121.260.6142 e info@discoverx.com