



# FlexLab™ GPCR Services

## A Complete Solution for Your GPCR Needs

Millipore's **GPCRProfiler™** service is well-known for providing high-quality cell-based functional  $\text{Ca}^{2+}$  assays for compound screening and profiling. And now we've gone one step further, by providing you full access to our GPCR researchers to support your in-house projects. Our FlexLab GPCR Service offers **access to expertise in GPCR assay development, personalized consultation for assay design and flexible project parameters**—creating a world of possibilities with your vision and our application.

FlexLab GPCR Services provide a variety of custom services spanning project needs from start to finish, including custom receptor cloning, cell line generation, assay development and bulk manufacturing. Put the full force of our experienced GPCR researchers to work for you today.

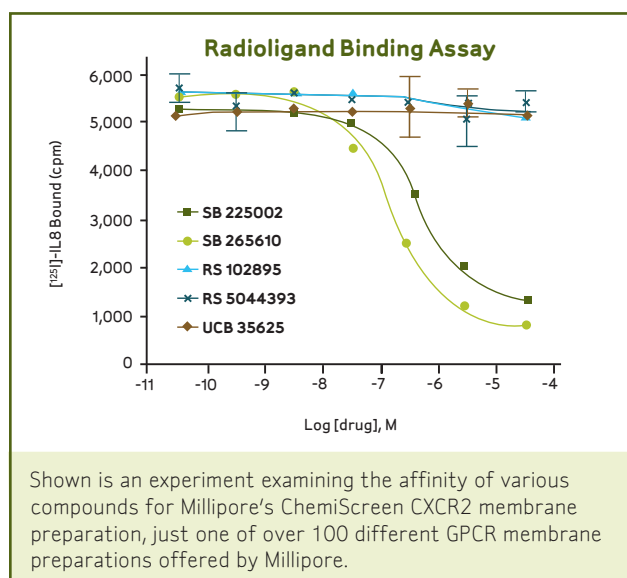
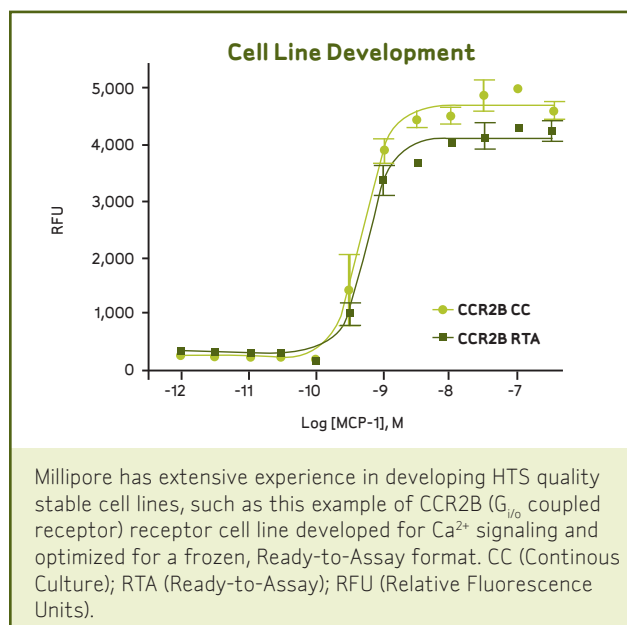


**ADVANCING LIFE SCIENCE TOGETHER™**  
Research. Development. Production.

# GPCR CUSTOM SERVICES

## Cell Line Development

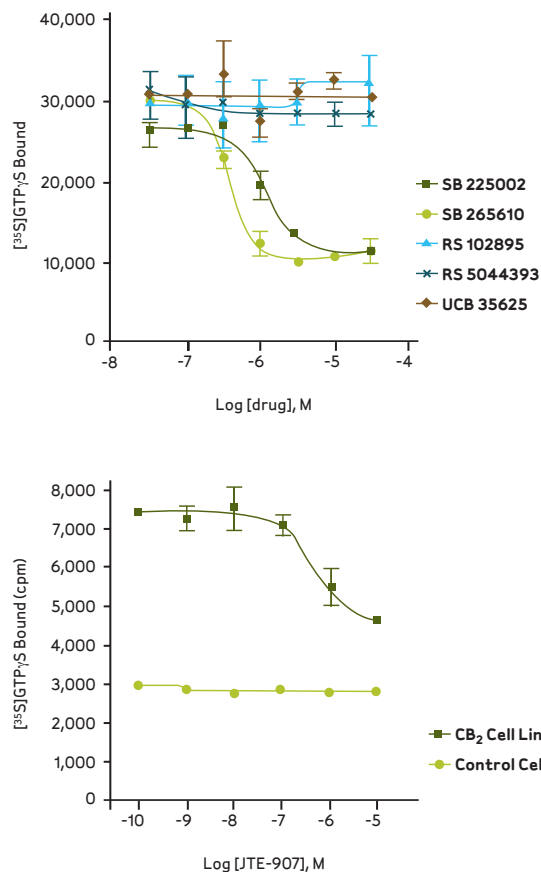
- **Molecular Biology Experience** – cloning and mutagenesis
- **Stable Calcium Optimized GPCR Cell Lines** – cells designed for Ca<sup>2+</sup> flux
  - **Extensive experience:** >140 GPCR cell lines developed
- **Stable GPCR Tailored Cell Lines** – tailored for user-defined assays
- **Ready-to-Assay™ Cells** – cryopreserved cells for immediate assays without laborious tissue culture
  - **Extensive experience:** >40 GPCR Ready-to-Assay cells developed



## Custom Assays

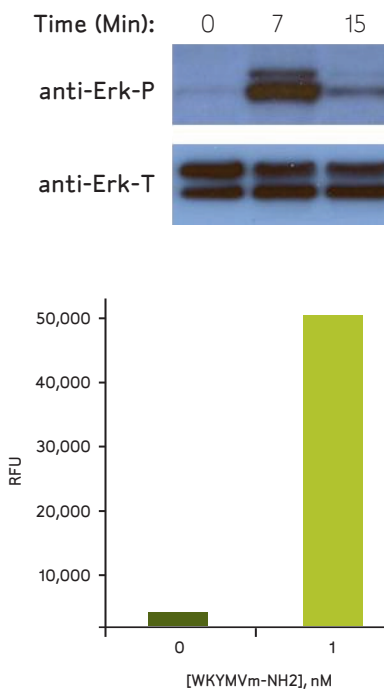
- **Radioligand Binding** – when knowledge about a compounds affinity is a must
  - **Saturation** (K<sub>d</sub> & B<sub>max</sub>)
  - **Competition**
    - Screening
    - Dose response (K<sub>i</sub> determination)
  - **Extensive experience:** >110 GPCR membrane preps developed
- **Primary Functional and Inverse Agonist Assays**
  - **GTPγS** – well suited for further investigation of G<sub>i/o</sub>-coupled receptors
    - Screening
    - Dose Response
  - **PI hydrolysis** – well suited for in depth knowledge of G<sub>q/11</sub>-coupled receptors or for Millipore's ChemiScreen™ Calcium-Optimized GPCR cell lines.
    - Screening
    - Dose Response
  - **cAMP** – well suited for examining G<sub>s</sub> and G<sub>i/o</sub>-coupled receptors
    - Screening
    - Dose Response
- **Secondary Assays** – for confirmation of hits in downstream or whole cell response assays
  - **Erk phosphorylation** – common signaling event downstream of GPCRs
    - Dose Response
  - **Chemotaxis & Cell Migration** – for GPCRs involved in chemotactic responses
    - Dose Response
- **Bulk Manufacturing** – for high volume use of existing Millipore GPCR products or your reagents developed in-house.
  - **Membrane preparations**
  - **Ready-to-Assay Cells**
  - **Ready-to-Assay Pre-Plated Membranes**
  - **HTS quantities**

### Primary Functional & Inverse Agonist Assays



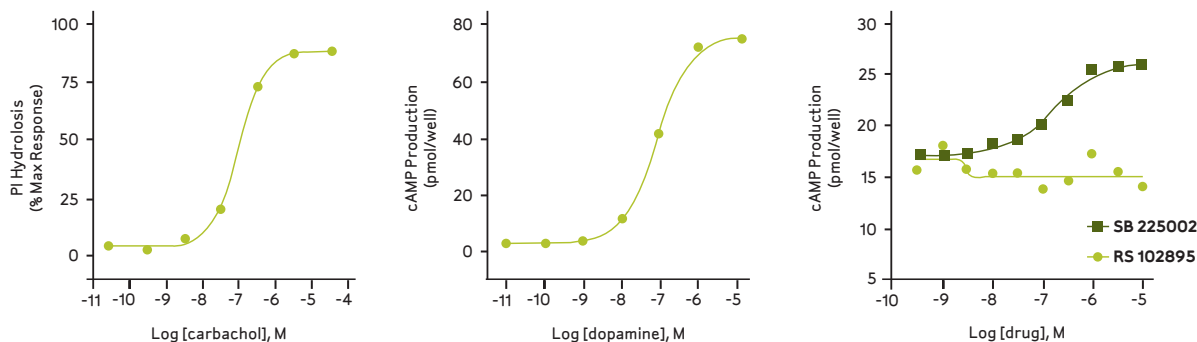
Functional activity of compounds can be monitored by GTP $\gamma$ S assays utilizing ChemiScreen GPCR membranes expressing G<sub>i</sub> coupled receptors. GTP $\gamma$ S assays can be performed to identify antagonist activity (Top panel: CXCR2 receptor) and inverse agonist activity (Bottom panel: CB<sub>2</sub> receptor).

### Secondary Assays



To broaden the understanding of compound activity beyond traditional G protein-dependent assays, GPCR FlexLab Service can investigate more complex activities of receptor function such as downstream activation of the MAP kinase pathway or whole cell responses such as cellular migration. **Top panel:** 5-HT<sub>2B</sub> receptor activation was measured by the change in Erk-1/2 phosphorylation (Erk-P) relative to total Erk-1/2 (Erk-T) following treatment of cells with (1  $\mu\text{M}$  serotonin). **Bottom panel:** Migration of ChemiScreen Chem-1 cells stably expressing FPLR1 receptor towards agonist containing media detected by Millipore's QCM™ Cell Migration Assay kit.

### Primary Functional Agonist Assays



For in-depth analysis of hits, Millipore's GPCR FlexLab Service can perform a spectrum of cell based functional assays to look at G protein-dependent signaling, including phosphatidylinositol (PI) hydrolysis and cAMP assays. **Left panel:** Determining the agonist activity of carbachol at M<sub>1</sub> receptors expressed in Chem-1 cells by PI hydrolysis. **Middle and Right Panels:** cAMP is a common readout to determine functional activities of molecules at G<sub>s</sub> and G<sub>v</sub> coupled receptors. Using Millipore's cAMP HTS kit, we can detect agonist response such as D<sub>1</sub> (G<sub>s</sub> coupled receptor) treated with its native ligand, dopamine, (Middle panel) or antagonist responses as demonstrated in cells expressing CXCR2 (G<sub>v</sub> coupled receptor) following treatment with the indicated ligands in the presence of forskolin and IL-8 (Right panel).

## TO PLACE AN ORDER OR FOR MORE INFORMATION

Visit [www.millipore.com/GPCR](http://www.millipore.com/GPCR) or contact your sales representative by calling 1-800-MILLIPORE or emailing [drugdiscovery@millipore.com](mailto:drugdiscovery@millipore.com).



[www.millipore.com/offices](http://www.millipore.com/offices)

Millipore is a registered trademark of Millipore Corporation.  
M Logo, Advancing Life Science Together, FlexLab, QCM, Ready-to-Assay, ChemiScreen, and GPCRProfiler are trademarks of Millipore Corporation.  
Lit. No. PF1108EN00 08DD019 03/08 Printed in U.S.A. 08-157  
© 2008 Millipore Corporation, Billerica, MA 01821 U.S.A. All rights reserved.