

*“Think of a disease and there is probably a medicine there that affects the G-protein-coupled receptor.”* - Sven Lidin, chairman of the Nobel prize committee, on the 2012 chemistry award to Messrs. Lefkowitz and Kobilka.

GPCRs are the largest family of cell surface receptors being integral to the number of cellular and physiological functions, including light sensing, smell, appetite control, insulin secretion, and blood pressure modulation. TimTec GPCR Ligands library, ActiTarg-G, currently counts 2,300 molecules available in various formatting options.

The ActiTarg-G Collection is a plated screening set of molecules that contain chemical lattices present in compounds reported in the technical or patent literature to possess GPCR-ligand properties. From our collection of over 7000 compounds in more than 15 different chemical series we have assembled a pre-filtered diversity collection of 2300 compounds that should provide a high value screening library of drug-like molecules for identifying synthesis direction for the development of new GPCR ligands. Structural constraints and novel pendants within these lattices provide the structural variability to identify new chemical directions for hit optimization.

Compounds are available for cherry-picking and/or as a collection in 96, 384-well plates and in vials. [Contact us](#) for structural info, formatting options and pricing.

### **About GPCR Ligands**

G-protein coupled receptors are a ubiquitous super family of proteins with hundreds of members having been identified and cloned. These receptors generally have a seven-membrane spanning alpha-helical topography, and while these receptors are similar in overall structure and function, they differ in key amino acid residues. The potential for this super family of receptors to reveal small molecule modulators of a significant biological function has been responsible the focus of intense drug discovery efforts.

Compounds with structural features and molecular lattices that are present in a large number molecules described in both the patent and technical literature that possess GPCR activity have been identified, and assembled as indicated below.

GPCR

Lattice type

selection of structures from the different GPCR libraries assembled as 5, 10 and 20 plate sets

CRF / NPY

Ar-X-Ar

CRF

4-Ar-2-aminothiazole

5HT

5HT

Indolines

gamma-Carbolines

5HT

5-Substituted indoles

5HT

4-ArylpiperazinesNH

5HT

Aminoethylbenzamides

5HT

Aminopropylbenzamides

BDZ-like

Fused 6,7 ring systems

Various

Spiro systems

Various

Aryl/Heteroaryl piperazines

Various

Benzyl piperazines

Various

4-Aryl/heteroaryl piperidines

Various

4-OH-4Phe-piperidines

Various

Tetrahydroisoquinolines

Chemokine

Diarylureas

G-Protein-Coupled Receptors are the largest gene families in the human genome and, rightfully so, have become the leading molecular target in 2008. In 2009 SBS April meeting in Lille, France, followed-up with screening trends report stating that “GPCRs are expected to replace protein kinases as the most common molecular target used by HTS laboratories.”

Anti-inflammatory therapeutics development is closely linked to exploring G protein-coupled receptor (GPCR) family. For example, one of the successful finds zeros down on an adenosine receptor from GPCR family called A2A that counteracts inflammation and responds to organs in distress.

**Xu F, Wu H, et.al. Structure of an agonist-bound human A2A adenosine receptor. *Science*. 2011 Apr 15;332(6027):322-7**

**Amy Swinderman. NIH researchers show how adenosine receptor is ‘switched on,’ shed light on drug interaction. *Drug Discovery News*. Code: E04111101. 04-11-2011**

**Lefkowitz RJ: Seven transmembrane receptors: something old, something new. *Acta Physiol (oxf)* 2007;190:9-19**

**Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, et al: Initial Sequencing and analysis of the human genome. *Nature* 2001;409:860-921**

**Venter JC, Adams MD, Myers EQ, Li PW, Mural RJ, Sutton GG, et al: The sequence of the human genome. *Science* 2001;291:1304-1354**

**Overington JP, Al-Lazikani B, Hopkins AL: How many drug targets are there? *Nat Rev Drug Discov* 2006;5:993-996**

**Xiao SH, Reagan JD, Lee PH, Fu A, Schwandner R, Zhao X, et al: High throughput screening for orphan and liganded GPCRs. *Comb Chem High Throughput Screen* 2008;11:195-215**

### **Related Products**

ActiTarg-G is one of TimTec targeted libraries. Other targeted screening collections of interest are:

[ActiTarg-K](#) , kinase modulators

[ActiTarg-P](#) , protease modulators

[ActiTarg-S](#) , serine proteinase inhibitors

[ActiTarg-I](#) , ion channel (potassium channel) modulators

[ActiTarg-N](#) , nuclear receptor ligands

[Actitarg-H](#) , HDAC inhibitors     [ActiTarg-CNS](#) , Central Nervous System Receptors Modulators Library