Novel Human Peptide Agonists for GPCRs

Catalog No.	Peptide Name	Protein Name	Species
036-27	P33	HWKM1940	human
036-28	P58	B9	human
036-29	P58-5	B9	human
036-30	P58-4	B9	human
036-31	P59	C1qT8	human
036-32	P60	C5orf29	human
036-33	P61	TIMMP-9	human
036-34	P63	BMP3b	human
036-35	P94	BMP3b	human

G-protein coupled receptors (GPCRs) represent an important group of targets for pharmaceutical therapeutics. The completion of the human genome revealed a large number of putative GPCRs. However, the identification of their natural ligands, and especially peptides, suffers from low discovery rates, thus impeding development of therapeutics based on these potential drug targets. We describe the discovery of novel GPCR ligands encrypted in the human proteome. Hundreds of potential peptide ligands were predicted by machine learning algorithms. In vitro screening of selected 33 peptides on a set of 152 GPCRs, including a group of designated orphan receptors, was conducted by intracellular calcium measurements and cAMP assays. The screening revealed eight novel peptides as potential agonists that specifically activated six different receptors in a dose dependent manner. Most of the peptides showed distinct stimulatory patterns targeted at designated and orphan GPCRs. Further analysis demonstrated a significant in-vivo effect for one of the peptides in a mouse inflammation model.

Shemesh R, et al. J Biol Chem. 2008 Oct 9. [Epub ahead of print]

PHOENIX PHARMACEUTICALS, INC.
330 Beach Rd, Burlingame, CA, 94010, USA
PHONE (650) 558 8898 EMAIL info@phoenixpeptide.com
WWW.PHOENIXPEPTIDE.COM

PHOENIX EUROPE GmbH
VISTORIASTR, 3 S. D 76133 KARLSRUHE, GERMANY
PHONE +49 721 1611950 EMAIL germany@phoenixpeptide.com
WWW.PHOENIXPEPTIDE.COM

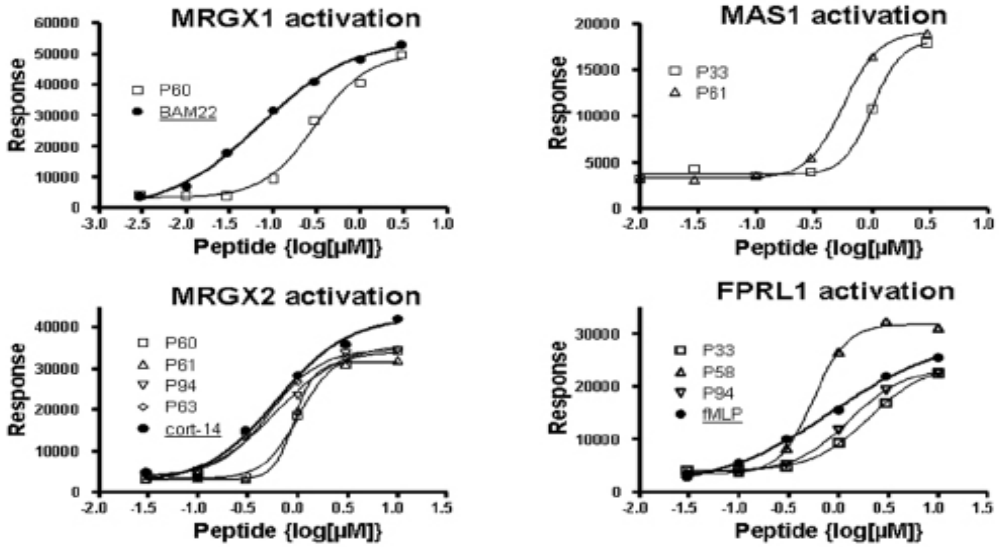
Table2: GPCRs activation and specificity by screened peptides:

Positive hits and calculated EC50 for Compugen's peptides and receptor specific positive controls. Each hit is indicated by a "+" mark as well as a calculated EC50 value (μM). The observed affinity (EC50) value is also indicated for the positive control peptides (with the exception of Ang 1-7, where no activation of the MAS1 receptor was observed - NA). ND = No data

Receptor	Positive controls (EC50 μM)	P60	P61	P94	P63	P58	P33	P59	P74	Other GPCRs** activated by same positive control
MRGX1	BAM22 (0.08)	+ (0.3)	-	-	-	-	-	-	-	OPRM, OPRK, OPRL & OPRD
MRGX2	Cort14 (0.61)	+ (1.0)	+ (0.9)	+ (0.6)	+ (0.5)	-	-	-	-	SSTR (1-5)
MAS1	(Ang1-7) (NA)	-	+ (0.57)	-	-	-	+ (1.0)	-	-	AGTR1, AGTR 2
FPRL1	fMLP (0.85)	-	-	+ (1.3)	-	+ (0.55)	+ (2.0)	-	-	FPR1
LGR7 (RXFP1)*	Relaxin (ND)	-	-	-	-	-	-	+ (ND)	+ (ND)	GPR135 (RXFP3)
LGR8 (RXFP2)*	Relaxin (ND)	-	-	-	-	-	-	+ (ND)	+ (ND)	GPR135 (RXFP3)

* Examined by cAMP inhibition assay. No dose response was performed (ND).

** Receptors were included in the screening. No activation by Compugen peptides was observed. Activation by positive control is indicated from the literature.



Catalog Number	Description	Std. Size
036-27	P-33 (Human)	100ug
036-28	P-58 (Human)	100ug
036-29	P-58-5 (Human)	100ug
036-30	P-58-4 (Human)	100ug
036-31	P-59 (Human)	100ug
036-32	P-60 (Human)	100ug
036-33	P-61 (Human)	100ug
036-34	P-63 (Human)	100ug
036-35	P-94 (Human)	100ug