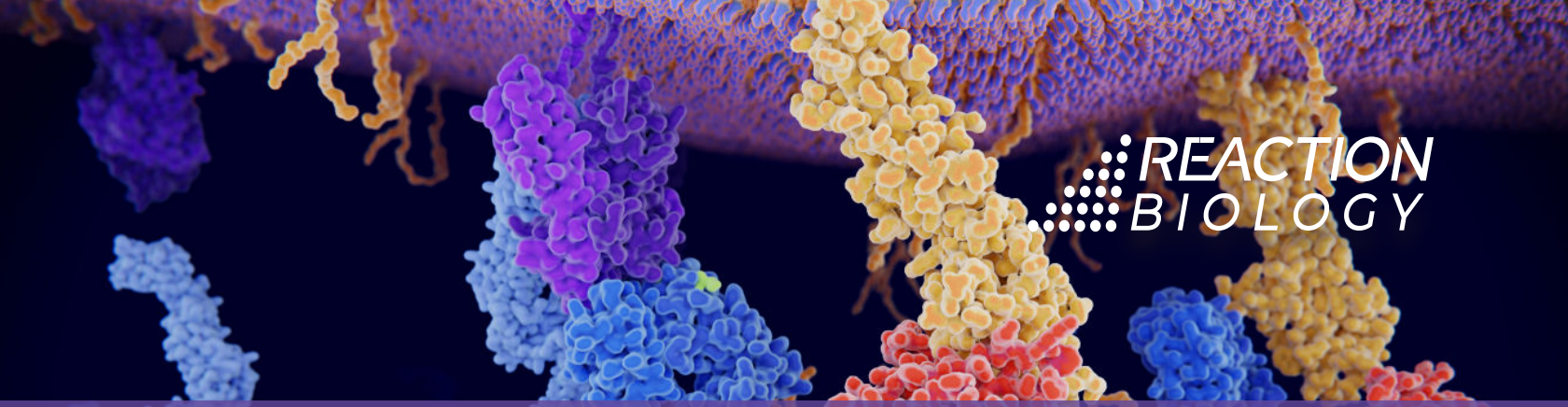


REACTION BIOLOGY

Complete Your GPCR Characterization

LinkLight™

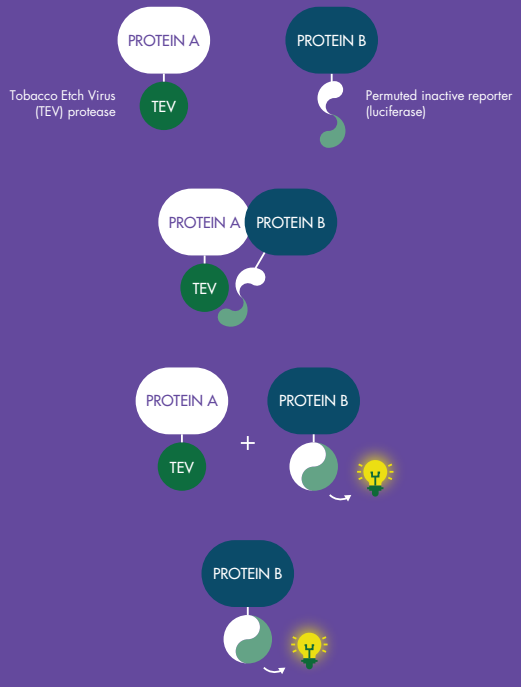
Functional, Cell-based Assay Platform Designed To Detect Fleeting Protein-Protein Interactions

What is LinkLight?

LinkLight is a protein-protein interaction (PPI) detection technology that complements secondary messenger assays for profiling of compounds activity against G-protein coupled receptors (GPCRs).

LinkLight detects β-arrestin (β-arr) and 14-3-3 protein recruitment which, combined with G-protein activation, provides complete pharmacological profiling of GPCR activity across many therapeutic areas, including oncology, CNS, immunology, skeletomuscular, and metabolic disease.

How LinkLight Works



LinkLight assay components

The LinkLigh assay consists of two components, each fused to a protein of interest:

- Protein A: Tobacco Etch Virus (TEV) protease
- Protein B: Rearranged reporter protein fragment connected by a TEV protease cleavage site (permuted inactive reporter)

Protein-protein interaction

When the proteins of interest are in close proximity, the TEV protease cleaves the permuted inactive reporter, which refolds and reconstitutes an active reporter protein

Signal activation

In the presence of luciferin, the now active luciferase generates a luminescent signal, persistent even after interaction ends

Signal detection

Signal is detected instantly, providing immediate and transcription-free readouts

Key Benefits

Persistent Signal

Non-reversible signal enables detection of transient and stable PPIs for insights into fleeting biological events

Immediate, Transcription-Free

Captures a biological "snapshot" without the lag, variability, or off-target effects of reporter gene systems

Broad Applications

β-arr and 14-3-3 pathways allow orphan receptor characterization and biased ligand discovery

Why Complementary GPCR Analysis Matters

cAMP and calcium assays reveal G-protein mediated signaling pathways, but miss the regulatory mechanisms that control therapeutic durability and side effects. LinkLight detects β-arrestin recruitment and 14-3-3 stabilization, regulatory events that determine tolerance, desensitization, and sustained therapeutic effects.

Features	Primary Applications
Complementary GPCR characterization: Comprehensively evaluate G-protein (cAMP/calcium), β-arrestin, and 14-3-3 pathways	**Ligand bias profiling:** Compare activity ratios across compounds that may activate regulatory pathways without classical G-protein effects
Universal platform for pathway discovery: Works across most GPCR families, even when coupling is unknown or complex	**Orphan receptor characterization:** Most activated GPCRs recruit β-arrestin regardless of G-protein coupling, providing universal readout when exact pathways are unknown
GPCR regulatory mechanism: Understand tolerance, desensitization, and therapeutic durability mechanisms	**β-arrestin-specific drug development:** Avoid G-protein triggered side effects or exploit β-arrestin expression patterns for organ-selective or sustained therapeutic response

Comprehensive GPCR Portfolio

β-arrestin Translocation

- Measures receptor desensitization and internalization dynamics
- Reveals biased signaling and functional selectivity profiles
- Essential for understanding trafficking mechanisms

cAMP Generation

- Monitors Gs-stimulated adenylyl cyclase activity
- Detects Gi/o-mediated cAMP inhibition
- Direct second messenger quantification

IP1 Generation

- Quantifies Gq/11-mediated phospholipase C activation
- Captures downstream signal amplification effects
- Orthogonal validation for calcium-independent pathways

FLIPR Calcium Mobilization

- Real-time intracellular calcium flux detection
- High-throughput compound screening capability
- Sensitive detection with broad dynamic range

Cell Line Receptor Information				LinkLight PPI Assays		Secondary Messenger Assays	
Target Name	Gene Name	Additional Synonyms	G-Protein Partner	β-arrestin	14-3-3	cAMP	Calcium Flux
5-hydroxytryptamine receptor 2A	HTR2A	5HT2A, HTR2, 5-HT2A	Gq	✓	✓		✓
5-hydroxytryptamine receptor 2B	HTR2B	5-HT2B, 5HT2B	Gq				✓
adenosine A1 receptor	ADORA1	RDC7, A1AR	Gi	✓		✓	
adenosine A2a receptor	ADORA2A	A2A, A2AR, ADORA2, RDC8	Gs	✓	✓	✓	
adenosine A2b receptor	ADORA2B	A2b	Gs	✓	✓	✓	
adenosine A3 receptor	ADORA3	A3, AD026, A3AR	Gi		✓	✓	
adrenoceptor alpha 1A	ADRA1A	α1A, ADRA1L1, ADRA1C	Gq	✓	✓		✓
adrenoceptor alpha 2A	ADRA2A	α2A, ADRA2A, ADRAR, ADRA2, ADRA2R	Gi	✓	✓	✓	
adrenoceptor beta 2	ADRB2	ADRB2R, ADRBR, BAR, B2AR, ARB2	Gs	✓	✓	✓	
adrenoceptor beta 3	ADRB3	–	Gs		✓	✓	
apelin receptor	APLNR	AGTRL1, FLJ90771, APJ, APJR	Gi	✓		✓	
arginine vasopressin receptor 2	AVPR2	V2R, DIR3, DIR	Gs	✓		✓	
atypical chemokine receptor 3	ACKR3	CMKOR1, CXCR7, GPR159, RDC1	Gi	✓		✓	
bradykinin receptor B1	BDKRB1	BRK1, B1BKR, bradyb1	Gq	✓			✓
bradykinin receptor B2	BDKRB2	BK-2	Gq	✓			✓
C-C motif chemokine receptor 6	CCR6	STRL22, CKR-L3, GPR-CY4, GPR29, CMKBR6, DRY-6, DCR2, BN-1, CD196	Gi	✓		✓	
C-X3-C motif chemokine receptor 1	CX3CR1	V28; CCRL1; GPR13; CMKDR1; CMKBRL1	Gi	✓		✓	
cannabinoid receptor 1	CNR1	CNR, CB1K5, CB-R, CB1, CANN6, CB1A	Gi	✓	✓	✓	
cannabinoid receptor 2	CNR2	CB2	Gi	✓	✓	✓	
chemerin chemokine-like receptor 1	CMKLR1	RVER1, ERV1, ChemR23	Gi	✓		✓	
chemerin chemokine-like receptor 2	CMKLR2	GPR1	Gi	✓		✓	
cholecystokinin A receptor	CCKAR	CCK1R, CCK-AR, CCK-1R	Gq	✓	✓		✓
cholecystokinin B receptor	CCKBR	CCK2R, GASR, CCK-BR, CCK-2R	Gq	✓			✓
cholinergic receptor muscarinic 1	CHRM1	M1	Gq	✓	✓		✓
cholinergic receptor muscarinic 2	CHRM2	M2	Gi	✓		✓	
cholinergic receptor muscarinic 3	CHRM3	M3, m3AChR	Gq	✓	✓		✓
cholinergic receptor muscarinic 5	CHRM5	M5	Gq	✓	✓		✓
complement C5a receptor 1	C5AR1	C5R1, C5A, C5AR, CD88	Gi	✓	✓	✓	
dopamine receptor D1	DRD1	D1, D1R	Gs	✓	✓	✓	
dopamine receptor D2	DRD2	D2, D2R	Gi	✓	✓	✓	
dopamine receptor D3	DRD3	D3	Gi	✓		✓	
dopamine receptor D4	DRD4	D4	Gi	✓	✓	✓	
dopamine receptor D5	DRD5	D5, DRD1B, DRD1L2	Gs	✓	✓	✓	
endothelin receptor type A	EDNRA	ETA, ETAR, ET-A, ETRA	Gq				✓
endothelin receptor type B	EDNRB	ETB, HSCR2, HSCR	Gq	✓			✓
free fatty acid receptor 1	FFAR1	GPR40, FFA1R	Gq	✓			✓
free fatty acid receptor 2	FFAR2	FFA2R, GPR43	Gi	✓		✓	
free fatty acid receptor 3	FFAR3	GPR41, FFA3R	Gi	✓		✓	
free fatty acid receptor 4	FFAR4	O3FAR1, GPR120, GPR129, PGR4	Gi/Gq	✓		✓	
galanin receptor 1	GALR1	GALNR1, GALNR	Gi	✓	✓	✓	
glucagon-like peptide 1 receptor	GLP1R	GLP-1R	Gs	✓	✓	✓	
G protein-coupled bile acid receptor 1	GPBAR1	TGR5, BG37, M-BAR, GPCR19, GPR131, MGC40597	Gs	✓		✓	
G protein-coupled receptor 3	GPR3	ACCA	Gs	✓		✓	
G protein-coupled receptor 6	GPR6	–	Gs	✓		✓	
G protein-coupled receptor 12	GPR12	GPCR21, PPP1R84	Gs	✓		✓	
G protein-coupled receptor 34	GPR34	LPS1	Gi	✓		✓	
G protein-coupled receptor 55	GPR55	–	Gq	✓			✓
G protein-coupled receptor 84	GPR84	EX33	Gi	✓		✓	

Cell Line Receptor Information				LinkLight PPI Assays		Secondary Messenger Assays	
Target Name	Gene Name	Additional Synonyms	G-Protein Partner	β-arrestin	14-3-3	cAMP	Calcium Flux
G protein-coupled receptor 101	GPR101	–	Gs	✓		✓	
G protein-coupled receptor 119	GPR119	GPCR2, hGPCR2	Gs	✓		✓	
G protein-coupled receptor 141	GPR141	PGR13	Gi	✓		✓	
G protein-coupled receptor 183	GPR183	EBI2	Gi	✓		✓	
growth hormone secretagogue receptor	GHSR	GHS-R1a,GHS-R,GHSR-1a	Gq	✓			✓
histamine receptor H1	HRH1	H1R, H1, HH1R	Gq				✓
histamine receptor H2	HRH2	H2R, H2, HH2R	Gs				✓
hydroxycarboxylic acid receptor 2	HCAR2	GPR109A,HCA2, HM74A, PUMAG, Puma-g, NIACR1	Gi	✓		✓	
KISS1 receptor	KISS1R	GPR54, HOT7T175, AXOR12	Gq	✓	✓		✓
lysophosphatidic acid receptor 2	LPAR2	EDG4, EDG-4, LPA2	Gi/Gq	✓		✓	
lysophosphatidic acid receptor 3	LPAR3	EDG7, LP-A3, Edg-7, RP4-67813, HOFNH30, LPA3	Gi/Gq	✓	✓	✓	
lysophosphatidic acid receptor 4	LPAR4	P2Y9, GPR23, LPA4, P2RY9, P2Y5-LIKE	Gi/Gq	✓		✓	
melanocortin 3 receptor	MC3R	MC3	Gs	✓	✓	✓	
melanocortin 4 receptor	MC4R	–	Gs	✓		✓	
motilin receptor	MLNR	GPR38	Gq	✓	✓		✓
neuromedin U receptor 1	NMUR1	FM-3, GPR66, NMU1R, GPC-R	Gq	✓			✓
neuropeptide S receptor 1	NPSR1	GPR154, PGR14, GPRA	Gs	✓	✓	✓	
neurotensin receptor 1	NTSR1	NTR	Gq	✓	✓		✓
opioid receptor delta 1	OPRD1	–	Gi	✓	✓	✓	
opioid receptor kappa 1	OPRK1	KOR, OPRK	Gi	✓	✓	✓	
opioid receptor mu 1	OPRM1	MOR1, MOP	Gi	✓	✓	✓	
P2Y4 receptor	P2RY4	P2Y4, P2P, NRU, UNR	Gq	✓			✓
P2Y10 receptor	P2RY10	P2Y10, LPS2	Gs	✓		✓	
P2Y12 receptor	P2RY12	P2Y12, SP1999, HORK3	Gi	✓		✓	
parathyroid hormone 1 receptor	PTH1R	PTHR1, PTHR	Gs	✓	✓	✓	
prostaglandin D2 receptor	PTGDR	DP1, PTGDR1, DP	Gs	✓		✓	
prostaglandin D2 receptor 2	PTGDR2	DP2, CRTH2, CD294, GPR44	Gi	✓		✓	
prostaglandin E receptor 1	PTGER1	EP1	Gq	✓			✓
prostaglandin E receptor 2	PTGER2	EP2, COX-2	Gs	✓		✓	
prostaglandin E receptor 3	PTGER3	EP3, Inc003875	Gi	✓		✓	
prostaglandin E receptor 4	PTGER4	EP4	Gs	✓		✓	
relaxin family peptide/INSL5 receptor 4	RXFP4	GPR100, RLN3R2, GPCR142, RXFPR4	Gi	✓		✓	
sphingosine-1-phosphate receptor 1	S1PR1	EDG1, edg-1, d1S3362, CD363	Gi	✓	✓	✓	
sphingosine-1-phosphate receptor 2	S1PR2	EDG5, DFNB68, GPCR13, H218, AGR16	Gi/Gq	✓		✓	
sphingosine-1-phosphate receptor 3	S1PR3	EDG3, C9orf47, C9orf108, EDG-3, FLJ37523, bA791021.3	Gi/Gq	✓		✓	
sphingosine-1-phosphate receptor 4	S1PR4	EDG6	Gi	✓	✓	✓	
sphingosine-1-phosphate receptor 5	S1PR5	EDG8, edg-8	Gi	✓		✓	

Illuminate elusive biology with LinkLight

REACTION BIOLOGY

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www.reactionbiology.com
1 Great Valley Parkway, Suite 2 Malvern, 19355, PA, USA
+1.610.722.0247 | sales@reactionbiology.com
Reaction Biology Corporation

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