

## NEUROSCIENCE FOCUS: NEUROTROPHIC FACTORS

# GDNF Family Ligands & Receptors

## FEATURED DATA:

FAK · GDNF · GFR $\alpha$ -like · GRF $\alpha$ -1 · NCAM/CD56 · Neurturin · Phospho-FAK · Phospho-Ret · PLC- $\beta$ 1 · Ret

## GDNF Family Ligands

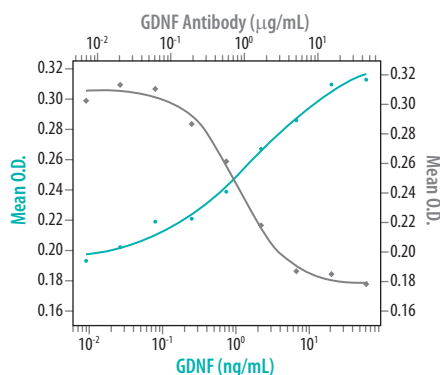
The GDNF family of ligands (GFLs) includes glial cell line-derived neurotrophic factor (GDNF), Neurturin, Artemin, and Persephin. Following its purification from a rat glioma cell line supernatant, GDNF was originally identified as a survival factor for dopaminergic neurons in the midbrain. Subsequent studies have shown that GFLs are critical for the proliferation, migration, and differentiation of several neuronal populations. In addition, GDNF exerts important biological effects outside the central nervous system, including promoting urinary collecting duct formation in the kidneys and spermatogonial differentiation in the testes. All GFLs are produced as prepro-GFL precursors and are activated following proteolytic cleavage.

### R&D Systems Products for GDNF Family Ligands

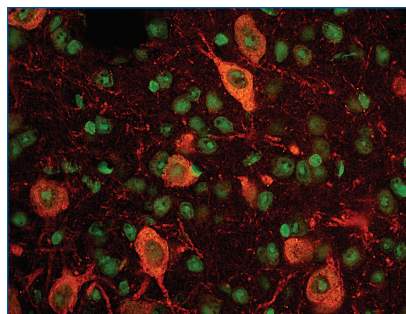
In addition to high performance antibodies, R&D Systems offers the most referenced premium quality proteins and ELISA kits in the industry.

MOLECULE	RECOMBINANT PROTEINS	ANTIBODIES	ELISAs
Artemin	H M	H (WB,IHC), M (WB,IHC,B/N)	
GDNF	H R	H (WB,IHC,B/N,EC,ED), R (WB,IHC,B/N)	H
Neurturin	H M	H (WB,IHC,B/N), M (WB,IHC,B/N)	
Persephin	H M	H (WB,IHC), M (WB)	

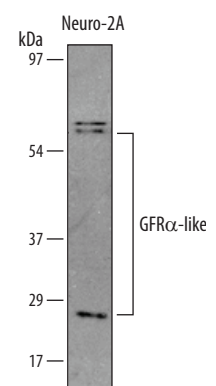
Species Key: H Human M Mouse R Rat Application Key: WB Western blot IHC Immunohistochemistry B/N Blocking/Neutralization EC ELISA Capture ED ELISA Detection



**Neuron Survival in Response to GDNF and Neutralization by a GDNF Antibody.** Recombinant Human GDNF (Catalog # 212-GD) supports the survival of dorsal root ganglion neurons from E10 chick embryos in a dose-dependent manner (green line), as measured by MTT. Neuronal survival elicited by Recombinant Human GDNF (10 ng/mL) is neutralized (gray line) by increasing concentrations of Mouse Anti-Human GDNF Monoclonal Antibody (Catalog # MAB212).



**Detection of GFR $\alpha$ -like in Mouse Brain.** GFR $\alpha$ -like was detected in immersion-fixed frozen sections of mouse brain using Sheep Anti-Mouse GFR $\alpha$ -like Antigen Affinity-purified Polyclonal Antibody (Catalog # AF5728). Tissue was stained using the NorthernLights™ 557-conjugated Anti-Sheep IgG Secondary Antibody (red; Catalog # NL010) and counterstained (green). Specific staining was localized to medullary gigantocellular neurons in the brainstem.



**Detection of GFR $\alpha$ -like by Western Blot.** Western blot shows lysates of Neuro-2A mouse neuroblastoma cell line. PVDF membrane was probed with Sheep Anti-Mouse GFR $\alpha$ -like Antigen Affinity-purified Polyclonal Antibody (Catalog # AF5728) followed by HRP-conjugated Anti-Sheep IgG Secondary Antibody (Catalog # HAF016). GFR $\alpha$ -like was detected at approximately 26 and 60 kDa (as indicated). The doublet of bands at approximately 60 kDa may represent differences in glycosylation state.

# GDNF Family Receptors

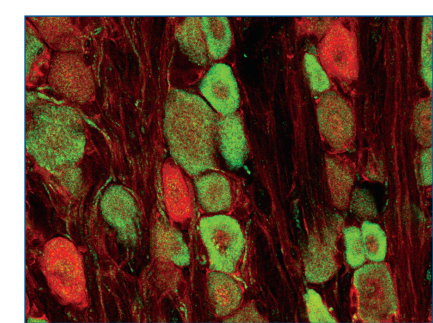
Although some cross-talk exists, GFLs preferentially signal as homodimers through their cognate GDNF-family receptor  $\alpha$  subtype (GFR $\alpha$ ). Following ligand binding, GLF-GFR $\alpha$  complexes associate with the extracellular domain of the receptor tyrosine kinase Ret. GDNF can also signal independently of Ret through interactions between GFR $\alpha$ -1 and neuronal cell adhesion molecule (NCAM). Predominantly linked to the plasma membrane at lipid rafts by a glycosyl phosphatidylinositol (GPI) anchor, cleavage by proteases or phospholipases generates a soluble form of GFR $\alpha$  that can exert distant actions through distinct signaling pathways.

## R&D Systems Products for GDNF Family Receptors

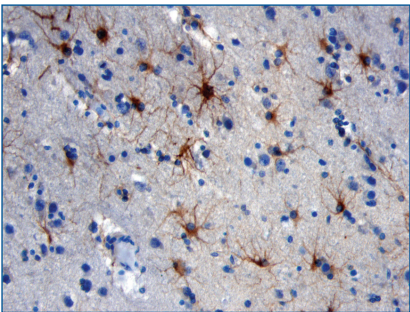
MOLECULE	RECOMBINANT PROTEINS	ANTIBODIES	ELISAs
Gas1	H M	H (WB, EC, ED), M (WB, IHC, EC, ED)	H, M
GFR $\alpha$ -1/GDNF R $\alpha$ -1	H M	H (WB, EC, ED), M (WB, IHC, EC, ED)	
GFR $\alpha$ -2/GDNF R $\alpha$ -2	H M	H (WB, IHC, B/N), M (WB, IHC, B/N)	
GFR $\alpha$ -3/GDNF R $\alpha$ -3	H M	H (WB, IHC), M (WB, IHC)	
GFR $\alpha$ -4/GDNF R $\alpha$ -4		H (WB), M (WB, IHC)	
GFR $\alpha$ -like		M (WB, IHC)	
NCAM-1/CD56	H	H (WB, IHC, FC, EC, ED), M (WB), R (WB)	H
Ret	H M	H (WB, IHC, FC), M (WB, IHC)	H
Syndecan-3	H M	H (WB, IHC, FC), M (WB, IHC)	

Species Key: H Human M Mouse R Rat Application Key: WB Western blot IHC Immunohistochemistry FC Flow Cytometry B/N Blocking/Neutralization EC ELISA Capture ED ELISA Detection

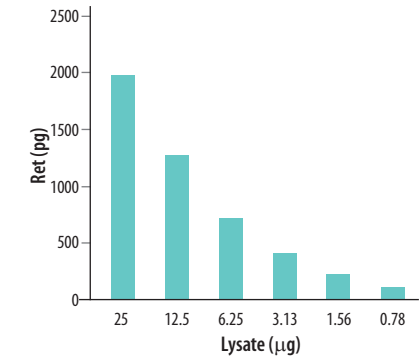
For more information visit our website at [www.RnDSystems.com/go/GDNF](http://www.RnDSystems.com/go/GDNF)



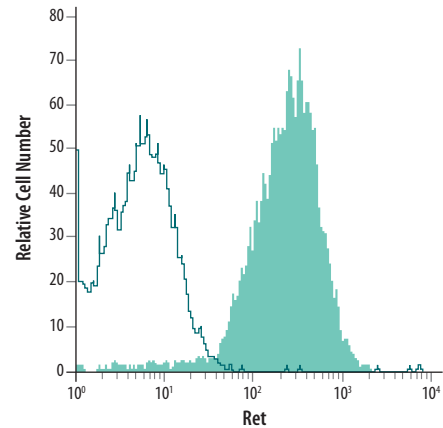
**GDNF and GFR $\alpha$ -1 in Rat Dorsal Root Ganglion.** GDNF and GFR $\alpha$ -1 were detected in perfusion-fixed frozen sections of rat dorsal root ganglion using Goat Anti-Human/Rat GDNF Antigen Affinity-purified Polyclonal Antibody (green; Catalog # AF-212-NA) and a Biotinylated Goat Anti-Rat GFR $\alpha$ -1 Antigen Affinity-purified Polyclonal Antibody (red; Catalog # BAF560).



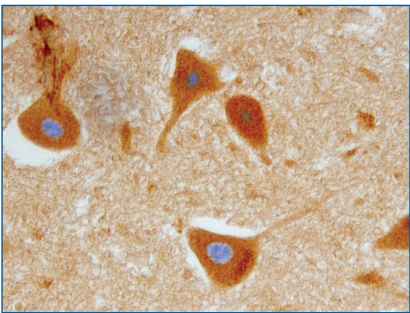
**NCAM-1/CD56 in Human Brain.** NCAM-1/CD56 was detected in immersion-fixed paraffin-embedded sections of human brain using Mouse Anti-Human NCAM-1/CD56 Monoclonal Antibody (Catalog # MAB24081). Tissue was stained using the Anti-Mouse HRP-DAB Cell & Tissue Staining Kit (brown; Catalog # CTS002) and counterstained with hematoxylin (blue). Specific staining was localized to astrocytes in the cerebral cortex.



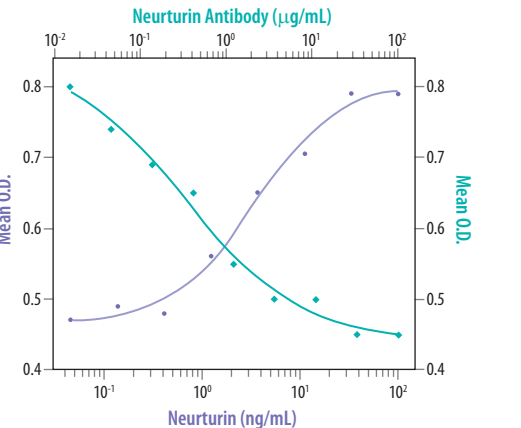
**Detection of Ret in the TT Human Cell Line by ELISA.** Lysates prepared from the TT human medullary thyroid cancer cell line were serially diluted and analyzed using the Human Total Ret DuoSet IC ELISA Development System (Catalog # DYC1168).



**Detection of Ret in the SH-SY5Y Human Cell Line by Flow Cytometry.** The SH-SY5Y human neuroblastoma cell line was stained with Mouse Anti-Human Ret Monoclonal Antibody (Catalog # MAB718, filled histogram) or isotype control antibody (Catalog # MAB002, open histogram), followed by Allophycocyanin-conjugated Anti-Mouse IgG Secondary Antibody (Catalog # F0101B). To facilitate intracellular staining, cells were fixed with paraformaldehyde and permeabilized with saponin.



**GFR $\alpha$ -1 in Human Spinal Cord.** GFR $\alpha$ -1 was detected in immersion-fixed paraffin-embedded sections of human spinal cord using Goat Anti-Human GFR $\alpha$ -1 Antigen Affinity-purified Polyclonal Antibody (Catalog # AF714). Tissue was stained using the Anti-Goat HRP-DAB Cell & Tissue Staining Kit (brown; Catalog # CTS008) and counterstained with hematoxylin (blue). Specific staining was localized to ventral horn motor neurons.



**Neuron Survival in Response to Neurturin and Neutralization by a Neurturin Antibody.** Recombinant Human Neurturin (Catalog # 1297-NE-025) supports the survival of dorsal root ganglion neurons from E11 chick embryos in a dose-dependent manner (purple line), as measured by MTT. Neuronal survival elicited by Recombinant Human Neurturin (6 ng/mL) is neutralized (green line) by increasing concentrations of a Goat Anti-Human Neurturin Affinity-purified Polyclonal Antibody (Catalog # AF387).

# GDNF Family Signaling Molecules

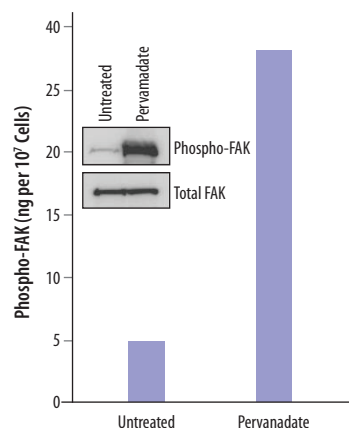
Interaction between GLF-GFR $\alpha$  complexes and Ret cause Ret to dimerize, autophosphorylate, and stimulate the Ras/MAPK, PI3-K/Akt, and PLC/Ca<sup>2+</sup> signaling pathways. GDNF also induces activation of the Fyn/FAK pathway through interactions with GFR $\alpha$ -1 and NCAM. Following cleavage by membrane-associated phospholipases, soluble GFR $\alpha$ -1 (sGFR $\alpha$ -1) is shed from the cell surface and can induce non-cell-autonomous actions.

## R&D Systems Products for GDNF Family Signaling Molecules

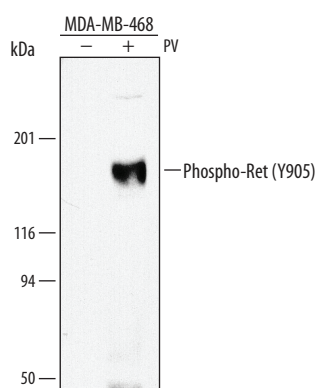
MOLECULE	RECOMBINANT PROTEINS	ANTIBODIES	ELISAs
Akt		H (WB, IHC, FC), M (WB, IHC, FC), R (WB, IHC, FC)	H M R
Akt1	H	H (WB, IHC, FC), M (WB), R (WB)	H M R
Akt2		H (WB, IHC, FC), M (WB, IHC), R (WB, IHC)	
Akt3		H (WB, IHC, FC)	
CREB		H (WB, IHC), M (WB), R (WB)	H M R
DOK4		H (WB, IHC)	
ERK1/ERK2		H (WB, IHC, FC), M (WB, IHC, FC), R (WB, IHC, FC)	H M R
ERK1	H	H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
ERK2	H	H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
ERK3		H (WB, IHC)	
FAK	H	H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
FRS2		H (WB, IHC, FC), M (WB), R (WB)	H M R
Gab2		H (WB)	
GRB7		H (WB), M (WB), R (WB)	
IRS1		H (WB, IHC), M (WB), R (WB)	
IRS2		H (WB)	
Jak1		H (WB, IHC, FC), M (WB, IHC, FC), R (WB, IHC, FC)	
Jak2		M (WB), R (WB)	
Jak3		H (WB, FC)	
JNK1/JNK2		H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
JNK1	M	H (WB, IHC), M (WB, IHC), R (WB, IHC)	
JNK2		H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
p38 MAP Kinase		H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M

MOLECULE	RECOMBINANT PROTEINS	ANTIBODIES	ELISAs
p38 $\alpha$	H	H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
p38 $\beta$		H (WB, IHC), M (WB), R (WB, IHC)	
p38 $\gamma$		H (WB, IHC), M (WB, IHC), R (WB, IHC)	H M R
p38 $\delta$		H (WB, IHC)	H
PKC-1	H	H (WB), M (WB), R (WB)	
PI 3-Kinase p55 $\gamma$		H (WB), M (WB), R (WB)	
PI 3-Kinase p85 $\alpha$		H (WB), M (WB), R (WB)	
PI 3-Kinase p110 $\beta$		H (WB)	
PI 3-Kinase p110 $\gamma$		H (WB)	
PI 3-Kinase p110 $\delta$		H (WB)	
PLC- $\beta$ 1		H (WB), M (WB)	
PLC- $\beta$ 3		H (WB)	
PLC- $\beta$ 4		H (WB), M (WB), R (WB)	
PLC- $\gamma$ 1		H (WB), M (WB), R (WB)	
PLC- $\gamma$ 2		H (WB, IHC), M (WB, IHC)	
PLC- $\delta$ 3		H (WB), M (WB)	
Ras		H (WB), M (WB), R (WB)	
Phospho-Ret		H (WB)	
Src	H V	H (WB, IHC), M (WB, IHC), R (WB, IHC)	H
STAT3		H (WB, IHC, FC, IP), M (WB, IHC, FC, IP), R (WB, IHC, FC, IP)	H M
Tyk2		H (WB)	
Phospho-Tyrosine		MS (WB, IHC, IP)	

Species Key: H Human M Mouse R Rat MS Multi Species V Virus  
Application Key: WB Western blot IHC Immunohistochemistry B/N Blocking/Neutralization FC Flow Cytometry  
IP Immunoprecipitation EC ELISA Capture ED ELISA Detection



**Detection of Phospho-FAK by ELISA and Western Blot.** Focal Adhesion Kinase 1 (FAK) phosphorylated at Y397 was detected in lysates of NRK rat normal kidney cell line using the Human/Mouse/Rat Phospho-FAK (Y397) DuoSet<sup>®</sup> IC ELISA Development System (Catalog # DY4528). Cells were untreated or treated with 100 mM sodium pervanadate for 10 minutes to induce FAK phosphorylation. For comparison the same lysates were also immunoblotted (inset) with either Rabbit Anti-Human/Mouse/Rat Phospho-FAK (Y397) Antigen Affinity-purified Polyclonal Antibody (Catalog # AF4528) or Sheep Anti-Human/Mouse/Rat FAK Antigen Affinity-purified Polyclonal Antibody (Catalog # AF4467).



**Detection of Human Phospho-Ret (Y905) by Western Blot.** Western blot shows lysates of the MDA-MB-468 human breast cancer cell line untreated (-) or treated (+) with 100  $\mu$ M pervanadate (PV) for 10 minutes. PVDF membrane was probed with a Rabbit Anti-Human Phospho-Ret (Y905) Antigen Affinity-purified Polyclonal Antibody (Catalog # AF3269), followed by a HRP-conjugated Goat Anti-Rabbit IgG Secondary Antibody (Catalog # HAF008). Phospho-Ret (Y905) was detected at approximately 175 kDa (as indicated).

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tyrosine kinases (RTKs) using  
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## Recent Citations: R&D Systems GDNF Family-related Products

1. Hadaczek, P. *et al.* (2010) Pharmacokinetics and bioactivity of glial cell line-derived factor (GDNF) and neurturin (NTN) infused into the rat brain. *Neuropharmacology* **58**:1114.

**Human GDNF DuoSet** (Catalog # DY212)

**Sample:** Rat brain homogenate  
**Application:** ELISA Development

**Recombinant Human Neurturin** (Catalog # 1297-NE)

**Recombinant Human GDNF** (Catalog # 212-GD)

**Sample:** Rat  
**Application:** *In vivo*

**Goat Anti-Human/Rat GDNF Affinity-purified Polyclonal Antibody** (Catalog # AF-212-NA)

**Goat Anti-Mouse/Human Neurturin Affinity-purified Polyclonal Antibody** (Catalog # AF477)

**Sample:** Rat brain  
**Application:** Immunohistochemistry

2. Kawaguchi, J. *et al.* (2010) Isolation and propagation of enteric neural crest progenitor cells from mouse embryonic stem cells and embryos. *Development* **137**:693.

**Goat Anti-Mouse Ret Affinity-purified Polyclonal Antibody** (Catalog # AF482)

**Sample:** Mouse embryonic stem cell-derived neural crest progenitor cells  
**Application:** Immunocytochemistry

**Recombinant Mouse BMP-4** (Catalog # 5020-BP)

**Recombinant Rat GDNF** (Catalog # 512-GF)

**Recombinant Human TGF- $\beta$ 3** (Catalog # 243-B3)

**Recombinant Mouse Noggin** (Catalog # 1967-NG)

**Recombinant Mouse Wnt-3a** (Catalog # 1324-WN)

**Sample:** Mouse embryonic stem cells  
**Application:** Bioassay

3. Bourane, S. *et al.* (2009) Low-threshold mechanoreceptor subtypes selectively express MafA and are specified by Ret signaling. *Neuron* **64**:857.

**Goat Anti-Mouse GFR $\alpha$ -2 Affinity-purified Polyclonal Antibody** (Catalog # AF429)

**Goat Anti-Mouse Ret Affinity-purified Polyclonal Antibody** (Catalog # AF482)

**Goat Anti-Mouse TrkC Affinity-purified Polyclonal Antibody** (Catalog # AF1404)

**Sample:** Mouse skin and spinal cord  
**Application:** Immunohistochemistry

4. Glavaski-Joksimovic, A. *et al.* (2010) Glial cell line-derived neurotrophic factor-secreting genetically modified human bone marrow-derived mesenchymal stem cells promote recovery in a rat model of Parkinson's disease. *J. Neurosci. Res.* **88**:2669.

**Human GDNF DuoSet** (Catalog # DY212)

**Sample:** Cell culture supernates from human GDNF lentiviral transduced SB623 bone marrow-derived mesenchymal stem cells  
**Application:** ELISA Development

**Human Endoglin/CD105 Affinity-purified Polyclonal Antibody** (Catalog # AF1097)

**Sample:** Human GDNF lentiviral-transduced SB623 bone marrow-derived mesenchymal stem cells  
**Application:** Immunocytochemistry

5. Kang, J. *et al.* (2010) Artemin is estrogen regulated and mediates anti-estrogen resistance in mammary carcinoma. *Oncogene* **29**:3228.

**Goat Anti-Human Artemin Affinity-purified Polyclonal Antibody** (Catalog # AF2589)

**Sample:** MCF-7 human breast cancer cell lysates  
**Application:** Western blot

6. Duveau, V. & Fritschy, J.M. (2010) PSA-NCAM-dependent GDNF signaling limits neurodegeneration and epileptogenesis in temporal lobe epilepsy. *Eur. J. Neurosci.* **32**:89.

**Mouse Anti-Human GDNF Monoclonal Antibody (Clone 27106)** (Catalog # MAB212)

**Sample:** Mouse  
**Application:** *In vivo*

7. Golden, J.P. *et al.* (2010) RET signaling is required for survival and normal function of nonpeptidergic nociceptors. *J. Neurosci.* **30**:3983.

**Goat Anti-Mouse GFR $\alpha$ -2 Affinity-purified Polyclonal Antibody** (Catalog # AF429)

**Goat Anti-Mouse GFR $\alpha$ -3 Affinity-purified Polyclonal Antibody** (Catalog # AF2645)

**Sample:** Mouse lumbar spinal cord and dorsal root ganglia  
**Application:** Immunohistochemistry

8. Perrinjaquet, M. *et al.* (2010) Protein-tyrosine phosphatase SHP2 contributes to GDNF neurotrophic activity through direct binding to phospho-Tyr687 in the RET receptor tyrosine kinase. *J. Biol. Chem.* **285**:31867.

**Recombinant Rat GDNF** (Catalog # 512-GF)

**Recombinant Rat GFR $\alpha$ -1 Fc Chimera** (Catalog # 560-GR)

**Sample:** PC-12 rat adrenal pheochromocytoma cell line  
**Application:** Neurite outgrowth assay

9. Negri, T. *et al.* (2010) Functional mapping of receptor tyrosine kinases in myxoid liposarcoma. *Clin. Cancer Res.* **16**:35814.

**Goat Anti-Human GFR $\alpha$ -3 Affinity-purified Polyclonal Antibody** (Catalog # AF670)

**Sample:** Human tumor  
**Application:** Immunohistochemistry and Western blot

**Proteome Profiler™ Human Phospho-RTK Array Kit** (Catalog # ARY001)

**Sample:** Human tumor homogenate  
**Application:** Profiling the phosphorylation states of 42 receptor tyrosine kinases