Revision 1

Store at -20C

#42344

Receptor Tyrosine Kinase Antibody Sampler Kit

1 Kit (8 x 20 microliters)

Cell Signaling TECHNOLOGY®

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Product Includes	Product #	Quantity	Mol. Wt	Isotype/Source
Phospho-Tyrosine (P-Tyr-1000) MultiMab® Rabbit mAb mix	8954	20 µl	N/A kDa	Rabbit IgG
Met (D1C2) XP® Rabbit mAb	8198	20 µl	140, 170 kDa	Rabbit IgG
EGF Receptor (D38B1) XP® Rabbit mAb	4267	20 µl	175 kDa	Rabbit IgG
PDGF Receptor α (D1E1E) XP® Rabbit mAb	3174	20 µl	190 kDa	Rabbit IgG
PDGF Receptor β (28E1) Rabbit mAb	3169	20 µl	190 kDa	Rabbit IgG
FGF Receptor 1 (D8E4) XP® Rabbit mAb	9740	20 µl	92 , 120, 145 kDa	Rabbit IgG
FLT3 (8F2) Rabbit mAb	3462	20 µl	130 nonglycosylated form;160 glycosylated mature form kDa	Rabbit IgG
HER2/ErbB2 (D8F12) XP® Rabbit mAb	4290	20 µl	185 kDa	Rabbit IgG
Anti-rabbit IgG, HRP-linked Antibody	7074	100 µl		Goat

Please visit cellsignal.com for individual component applications, species cross-reactivity, dilutions, protocols, and additional product information.

Description

The Receptor Tyrosine Kinase Antibody Sampler Kit provides the means to detect a broad range of common receptor tyrosine kinases, as well as total phospho-tyrosine activity. The kit provides enough antibody to perform two western blot experiments with each primary antibody.

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA, 50% glycerol and less than 0.02% sodium azide. Store at –20°C. Do not aliquot the antibodies.

Background

Tyrosine phosphorylation plays a key role in cellular signaling (1). In cancer studies, unregulated tyrosine kinase activity can drive malignancy and tumor formation by generating inappropriate proliferation and survival signals (2). Antibodies specific for phospho-tyrosine have been invaluable reagents in these studies (3,4).

Met, a tyrosine kinase receptor for hepatocyte growth factor (HGF), is a heterodimer made of α- and β-subunits (5,6). The cytoplasmic region of the β-chain is essential for tyrosine kinase activity. Interaction of Met with HGF results in autophosphorylation at multiple tyrosines (Tyr1003, 1234/1235, 1349) which recruit downstream signaling components, including Gab1, c-Cbl, and PI3 kinase (7-9). Altered Met levels and/or tyrosine kinase activities are found in several types of tumors, including renal, colon, and breast (10,11).

The epidermal growth factor (EGF) receptor is a transmembrane tyrosine kinase that belongs to the HER/ErbB protein family. Ligand binding results in receptor dimerization, autophosphorylation, activation of downstream signaling, internalization, and lysosomal degradation (12,13). c-Src mediated phosphorylation of EGF receptor (EGFR) at Tyr845 provides a binding surface for substrate proteins (14-16). The SH2 domain of PLCγ binds at phospho-Tyr992, activating PLCγ-mediated downstream signaling (17). Adaptor protein c-Cbl binds at phospho-Tyr1045, leading to receptor ubiquitination and degradation (18,19). The GRB2 adaptor protein binds activated EGFR at phospho-Tyr1068 (20), while phospho-Tyr1148 and -Tyr1173 provide a docking site for the Shc scaffold protein, playing a role in MAP kinase signaling (13).

Platelet derived growth factor (PDGF) family proteins bind to two closely related receptor tyrosine kinases, PDGF receptor α (PDGFRα) and PDGF receptor β (PDGFRβ) (21). PDGFRα and PDGFRβ can each form heterodimers with EGFR, which is also activated by PDGF (22). Ligand binding induces receptor dimerization and autophosphorylation, followed by binding and activation of signal transduction molecules such as GRB2, Src, GAP, PI3 kinase, PLCγ, and NCK. Signaling pathways initiated by activated PDGF receptors lead to control of cell growth, actin reorganization, migration, and differentiation (23).

Tyr751 and Tyr740 of PDGFRβ regulate binding and activation of PI3 kinase (24,25).

Fibroblast growth factors (FGFs) produce mitogenic and angiogenic effects in target cells by signaling through cell surface receptor tyrosine kinases, after ligand binding and dimerization (26,27). Tyr653 and Tyr654 are important for catalytic activity of activated FGFR and are essential for signaling (28). The other phosphorylated tyrosine residues (Tyr463, 583, 585, 730, and 766) may provide docking sites for downstream signaling components such as Crk and PLCγ (29,30).

FMS-related tyrosine kinase 3 (FLT3), a member of the type III receptor tyrosine kinase family, is expressed on early hematopoietic progenitor cells and supports growth and differentiation within the hematopoietic system (31,32). FLT3 is activated after binding with its ligand FL, which results in a cascade of tyrosine autophosphorylation and tyrosine phosphorylation of downstream targets (33). The p85 subunit of PI3 kinase, SHP2, GRB2 and Shc are associated with FLT3 after FL stimulation (34-36). Tyr589/591 may play an important role in regulation of FLT3 tyrosine kinase activity (37).

The ErbB2 (HER2) proto-oncogene encodes a transmembrane, receptor-like glycoprotein with tyrosine kinase activity (38). ErbB2 kinase activity can be activated in the absence of a ligand when overexpressed and through associations with other ErbB family members (39). Phosphorylation at Tyr877 may be involved in regulating ErbB2 activity. Autophosphorylation of ErbB2 at Tyr1248 and Tyr1221/1222 couples ErbB2 to the Ras-Raf-MAP kinase signal transduction pathway (38,40).

Background References

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