Anti-Phospho-Tyr$^{749/753/754}$ MerTK Antibody

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Catalog #: p186-749 **Size:** 100 µl

Cite this Antibody: PhosphoSolutions Cat# p186-749: RRID:AB_2744537

Host	Applications	Species Tested	Species Reactivity*	Molecular Weight
Rabbit	WB 1:1000	H, M, R	A, B, C, GP, Ha, NHP	160 kDa

Product Description: Affinity purified rabbit polyclonal antibody.

Biological Significance: Along with **T**yro-3 and **A**xl, **M**erTK is a member of the **TAM** family of receptor tyrosine kinases (RTKs). The TAM family of RTKs regulates cell proliferation/survival, cell adhesion and migration, and blood clot stabilization processes, along with the regulation of inflammatory cytokine release (Linger et al, 2008). Additionally, the TAM family has been linked to coagulopathy and cancer when altered experimentally or genetically (Linger et al, 2008). Tri-phosphorylation of MerTK at tyr749, tyr753 and tyr754 has been identified as a key target in platelet aggregation for developing a new anti-platelet drug that decreases bleeding complications, which are current side effects of similar drugs on the market today (Zhang et al, 2013). MerTK is also seen as a therapeutic target for treating lymphoblastic leukemias, melanoma, breast, lung, colon, liver, gastric, kidney, ovarian, uterine and brain cancers (Graham et al, 1994). There has recently been increased interest in synthesizing novel ATP-competitive small molecule tyrosine kinase inhibitors to decrease tri-phosphorylation of MerTK at tyr749, tyr753, and tyr754 as a therapeutic target to treat AML (Lee-Sherick et al, 2013).

Antigen: Phosphopeptide corresponding to amino acid residues surrounding the phospho-Tyr$^{749/753/754}$ of human MerTK.

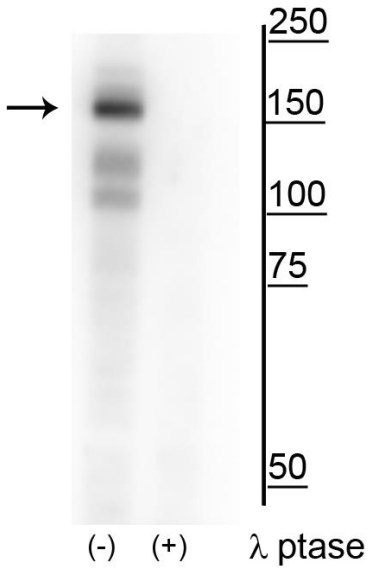
Antibody Specificity: Specific for the ~160 kDa MerTK protein phosphorylated at Tyr$^{749/753/754}$. Due to post-translational modifications of the Mer protein, a significant shift in molecular weight is seen from the predicted molecular weight of 110 kDa. For optimal results immunoprecipitation is recommended due to the 91% homology of the related receptor tyrosine kinase, Axl, that runs at ~140 kDa.

Purification Method: Prepared from pooled rabbit serum by affinity purification via sequential chromatography on phospho and non-phosphopeptide affinity columns.

Quality Control Tests: Western blots performed on each lot.

Packaging: 100 µl in 10 mM HEPES (pH 7.5), 150 mM NaCl, 100 µg BSA per ml and 50% glycerol.

Storage and Stability: Shipped on blue ice. Storage at -20°C is recommended, as aliquots may be taken without freeze/thawing due to presence of 50% glycerol. Stable for at least 1 year at -20°C.



Western blot of HEK293 lysate showing specific immunolabeling of the ~160 kDa MerTK phosphorylated at Tyr$^{749/753/754}$ in the first lane (-). Phosphospecificity is shown in the second lane (+) where the immunolabeling is completely eliminated by blot treatment with *lambda* phosphatase (λ-Ptase, 1200 units for 60 minutes).

Application Key: **WB** = Western Blot **IF** = Immunofluorescence **IHC** = Immunohistochemistry **IP** = Immunoprecipitation
Species Reactivity Key: **All**-All Species **A**-Avian **Amp**-Amphibian **Ar**-*Arabidopsis* **B**-Bovine **C**-Canine **Ch**-Chicken **D**-*Drosophila* **GP**-Guinea Pig **H**-Human **Ha**-Hamster **M**-Mouse **NHP**- Non-human primate **P**-Pig **R**-Rat **S**-Sheep **X**-*Xenopus* **Z**-Zebrafish
*Species assumed based on 100% homology with sequence used as antigen **For Research Use Only**

Product Specific References:

Da, C., Zhang, D., Stashko, M., Vasileiadi, E., Parker, R., Minson, K.A., Huey, M.G., Huelse, J.M., Hunter, D., Gilbert, T.S. and Norris-Drouin, J., 2019. Data-driven construction of anti-tumor agents with controlled polypharmacology. *Journal of the American Chemical Society*, 141(39):15700-15709.

Sinik, L., Minson, K.A., Tentler, J.J., Carrico, J., Bagby, S.M., Robinson, W.A., Kami, R., Burstyn-Cohen, T., Eckhardt, S.G., Wang, X. and Frye, S.V., 2019. Inhibition of MERTK promotes suppression of tumor growth in BRAF mutant and BRAF wild-type melanoma. *Molecular cancer therapeutics*, 18(2), pp.278-288.

Zhao, J., Zhang, D., Zhang, W., Stashko, M.A., DeRyckere, D., Vasileiadi, E., Parker, R.E., Hunter, D., Liu, Q., Zhang, Y. and Norris-Drouin, J., 2018. Highly selective MERTK inhibitors achieved by a single methyl group. *Journal of medicinal chemistry*, 61(22), pp.10242-10254.

Yan, D., Parker, R.E., Wang, X., Frye, S.V., Earp, H.S., DeRyckere, D. and Graham, D.K., 2018. MERTK Promotes Resistance to Irreversible EGFR Tyrosine Kinase Inhibitors in Non–small Cell Lung Cancers Expressing Wild-type EGFR Family Members. *Clinical Cancer Research*, 24(24), pp.6523-6535.

McDaniel, N.K., Cummings, C.T., Iida, M., Hülse, J., Pearson, H.E., Vasileiadi, E., Parker, R.E., Orbuch, R.A., Ondracek, O.J., Welke, N.B. and Kang, G.H., 2018. MERTK mediates intrinsic and adaptive resistance to AXL-targeting agents. *Molecular cancer therapeutics*, 17(11), pp.2297-2308.

Branchford, B.R., Stalker, T.J., Law, L., Acevedo, G., Sather, S., Brzezinski, C., Wilson, K.M., Minson, K., Lee-Sherick, A.B., Davizon-Castillo, P. and Ng, C., 2018. The small-molecule MERTK inhibitor UNC 2025 decreases platelet activation and prevents thrombosis. *Journal of Thrombosis and Haemostasis*, 16(2), pp.352-363.

Sufit A, Lee-Sherick AB, DeRyckere D, Rupji M, Dwivedi B, Varella-Garcia M, Pierce AM, Kowalski J, Wang X, Frye SV, Earp HS, Keating AK, Graham DK. MERTK Inhibition Induces Polyploidy and Promotes Cell Death and Cellular Senescence in Glioblastoma Multiforme. *PLoS One.* 2016 Oct 26;11(10):e0165107.

DeRyckere D, Lee-Sherick AB, Huey MG, Hill AA, Tyner JW, Jacobsen KM, Page LS, Kirkpatrick GG, Eryildiz F, Montgomery SA, Zhang W, Wang X, Frye SV, Earp HS, Graham DK. UNC2025, a MERTK Small-Molecule Inhibitor, Is Therapeutically Effective Alone and in Combination with Methotrexate in Leukemia Models. *Clin Cancer Res*. 2017 Mar 15;23(6):1481-1492.

Minson KA, Smith CC, DeRyckere D, Libbrecht C, Lee-Sherick AB, Huey MG, Lasater EA, Kirkpatrick GD, Stashko MA, Zhang W, Jordan CT, Kireev D, Wang X, Frye SV, Earp HS, Shah NP, Graham DK. The MERTK/FLT3 inhibitor MRX-2843 overcomes resistance-conferring FLT3 mutations in acute myeloid leukemia. *JCI Insight*. 2016 Mar;1(3):e85630.

Cummings CT, Zhang W, Davies K, Kirkpatrick GD, Zhang D, DeRyckere D, Wang X, Frye SV, Shelton Earp H, Graham DK. Small molecule inhibition of MERTK is efficacious in non-smal cell lung cancer models independent of driver oncogene status. *Mol Cancer Ther.* 2015 Sept;14(9):2014-2022.

Lee-Sherick AB, Zhang W, Menachof KK, Hill AA, Rinella S, Kirkpatrick G, Page LS, Stashko MA, Jordan CT, Wei Q, Liu J, Zhang D, DeRyckere D, Wang X, Frye S, Earp HS, Graham DK. Efficacy of a Mer and lt3 tyrosine kinase small molecule inhibitor, UNC1666, in acute myeloid leukemia. *Oncotarget*. 2015 Mar 30;6(9):6722-36.

Cummings CT, Linger RM, Cohen RA, Sather S, Kirkpatrick GD, Davies KD, DeRyckere D, Earp HS, Graham DK. Mer590, a novel monoclonal antibody targeting MER receptor tyrosine kinase, decreases colony formation and increases chemosensitivity in non-small cell lung cancer. *Oncotarget.* 2014 Nov 15;5(21):10434-45.

Zhang, W., DeRyckere, D., Hunter, D., Liu, J., Stashko, M.A., Minson, K.A., Cummings, C.T., Lee, M., Glaros, T.G., Newton, D.L. and Sather, S., 2014. UNC2025, a potent and orally bioavailable MER/FLT3 dual inhibitor. *Journal of medicinal chemistry*, 57(16), pp.7031-7041.

Zhang, W., McIver, A.L., Stashko, M.A., DeRyckere, D., Branchford, B.R., Hunter, D., Kireev, D., Miley, M.J., Norris-Drouin, J., Stewart, W.M. and Lee, M., 2013. Discovery of Mer specific tyrosine kinase inhibitors for the treatment and prevention of thrombosis. *Journal of medicinal chemistry*, 56(23), pp.9693-9700.

Zhang, W., Zhang, D., Stashko, M.A., DeRyckere, D., Hunter, D., Kireev, D., Miley, M.J., Cummings, C., Lee, M., Norris-Drouin, J. and Stewart, W.M., 2013. Pseudo-cyclization through intramolecular hydrogen bond enables discovery of pyridine substituted pyrimidines as new Mer kinase inhibitors. Journal of Medicinal Chemistry, 56(23), pp.9683-9692.

Christoph S, Deryckere D, Schlegel J, Frazer JK, Batchelor LA, Trakhimets AY, Sather S, Hunter DM, Cummings CT, Liu J, Yang C, Kireev D, Simpson C, Norris-Drouin J, Hull-Ryde EA, Janzen WP, Johnson GL, Wang X, Frye SV,

Earp HS 3rd, Graham DK. UNC569, a novel small-molecule mer inhibitor with efficacy against acute lymphoblastic leukemia in vitro and in vivo. *Mol Cancer Ther.* 2013 Nov;12(11):2367-77.

Liu J, Zhang W, Stashko MA, Deryckere D, Cummings CT, Hunter D, Yang C, Jayakody CN, Cheng N, Simpson C, Norris-Drouin J, Sather S, Kireev D, Janzen WP, Earp HS, Graham DK, Frye SV, Wang X. UNC1062, a new and potent Mer inhibitor. *Eur J Med Chem.* 2013 Jul;65:83-93.

Schlegel J, Sambade MJ, Sather S, Moschos SJ, Tan AC, Winges A, DeRyckere D, Carson CC, Trembath DG, Tentler JJ, Eckhardt SG, Kuan PF, Hamilton RL, Duncan LM, Miller CR, Nikolaishvili-Feinberg N, Midkiff BR, Liu J, Zhang W, Yang C, Wang X, Frye SV, Earp HS, Shields JM, Graham DK. MERTK receptor tyrosine kinase is a therapeutic target in melanoma. *J Clin Invest.* 2013 May;123(5):2257-67.

Lee-Sherick AB, Eisenman KM, Sather S, McGrananhan A, Armistead PM, McGary CS, Hunsucker SA, Schlegel J, Martinson H, Cannon C, Keating AK, Earp HS, Liang X, DeRyckere D, Graham DK(2013). Aberrant Mer receptor tyrosine kinase expression contributes to leukemogenesis in acute myeloid leukemia. Oncogene. 2013 Nov 14;32(46):5359-68.

Brandao LN, Winges A, Christoph S, Sather S, Migdall-Wilson J, Schlegel J, McGranahan A, Gao D, Liang X, Deryckere D, Graham DK. Inhibition of MerTK increases chemosensitivity and decreases oncogenic potential in T-cell acute lymphoblastic leukemia. *Blood Cancer J.* 2013 Jan 25;3:e101.

Linger R, Cohen RA, Cummings CT, Sather S, Migdall-Wilson J, Middleton DH, Lu X, Baron AE, Franklin WA, Merrik DT, Jedlicka P, DeRyckere D, Heasley LE, Graham DK. Mer or Axl Receptor Tyrosine Kinase Inhibition Promotes Apoptosis, Blocks Growth, and Enhances Chemosensitivity of Human Non-Small Cell Lung Cancer. *Oncogene.* 2013 July 18; 32(29):3420-3431.

General References

Linger R, Keating A, Earp HS, Graham D (2008) TAM Receptor Tyrosine Kinases: Biologic Functions, Signaling, and Potential Therapeutic Targeting in Human Cancer. Adv. Cancer Res. July 12 (100): 35-83.

Sather S, Kenyon KD, Lefkowitz JB, Liang X, Varnum BC, Henson PM, Graham DK. A soluble form of the Mer receptor tyrosine kinase inhibits macrophase clearance of apoptotic cells and platelet aggregation *Blood.* 2007;109:1026-1033.

Graham DK, Dawson TL, Mullaney DL, Snodgrass HR, Earp HS. Cloning and mRNA expression analysis of a novel human protooncogene, c-mer. Cell Growth Differ. 1994; 5(6):647–657.

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