## BACKGROUND

Trk (neurotrophin) receptors are single transmembrane catalytic receptors with intracellular tyrosine kinase activity. Trk receptors are coupled to the Ras, Cdc42/Rac/RhoG, MAPK, PI 3-K and PLCgamma signaling pathways. There are four members of the Trk family; TrkA, TrkB and TrkC and a related p75NTR receptor. p75NTR lacks tyrosine kinase activity and signals via NF-kappaB activation. Each family member binds different neurotrophins with varying affinities. TrkA potently binds nerve growth factor (NGF) and is involved in differentiation and survival of neurons and in control of gene expression of enzymes involved in neurotransmitter synthesis. TrkB has highest affinity for brain-derived neurotrophic factor (BDNF) and is involved in neuronal plasticity, longterm potentiation and apoptosis of CNS neurons. TrkC is activated by neurotrophin-3 (NT-3) and is found on proprioceptive sensory neurons. p75NTR binds neurotrophin precursors with high affinity and retains low affinity to the mature cleaved forms. TrkA was originally identified as an oncogene as it is commonly mutated in cancers, particularly colon and thyroid carcinomas.

The transmembrane protein-tyrosine kinase TrkC is the high affinity receptor for neurotrophin-3 (NT-3). The interaction between TrkC and NT-3 elicits a more efficient biological response than when NT-3 binds to its other Trk receptors. Thus, TrkC may play an important role in mediating the neurotrophic effects of NT-3.[1] Upon neurotrophin binding, TrkC become dimerized and activated. It phosphorylates itself. The putative regulatory tyrosines 674, 678, and 679 in the tyrosine kinase homology region are major ligand-stimulated autophosphorylation sites, which are required for full-activation of TrkC tyrosine kinase activity. Moreover, it was shown that the putative phospholipase Cgamma and Shc binding sites on TrkC (tyrosines 485 and 789, respectively) are indeed autophosphorylated. Kinase inserts occur between subdomains VII and VIII of the tyrosine kinase homology region and immediately C-terminal to tyrosines 674, 678, and 679, and specifically block the autophosphorylation of tyrosine 785 and this prevents phospholipase Cgamma association with TrkC and its tyrosine phosphorylation.[2] TrkC signaling is mediated by downstream MAPK and PI-3 kinase pathway. Signaling through this kinase leads to cell differentiation and may play a role in the development of proprioceptive neurons that sense body position. Moreover, it was shown that neurotrophin 3 activation of TrkC induces Schwann cell migration through the Rho GTPases (Rac1 and Cdc42) and JNK signaling pathway.[3] In addition, TrkC may atc outside of neural system. It was demonstrated that TrkC directly binds to the BMP type II receptor (BMPRII) in colon cancer cells, thereby preventing it from interacting with the BMPRI. This activity requires a functional TrkC protein tyrosine kinase, and the BMPRII seems to be a direct target of TrkC. TrkC can block BMP tumor-suppressor activity.[4] Mutations in TrkC have been associated with medulloblastomas, secretory breast carcinomas and other cancers. However, TrkC has several distinct characteristics: (a) its expression is a good-prognosis factor in different types of cancer and more specifically in melanomas, medulloblastomas and neuroblastomas (NBs); (b) its expression and activation have been shown to trigger apoptosis in medulloblastoma cells; and (c) as opposed to TrkA and TrkB, it was recently proposed to act as a dependence receptor. Such receptors are able to initiate 2 completely opposite signaling pathways, depending on ligand availability. In the presence of ligand, a positive differentiation, guidance, or survival signal is transduced. In the absence of ligand, however, they induce an active process of apoptotic cell death. These dependence receptors also include p75$^{ntr}$, deleted in colorectal cancer (DCC), UNC5H, Patched, and neogenin and the RET, EPHA4, and Alk tyrosine kinase receptors. The proapoptotic activity of dependence receptors is believed to be important for adequate neuron migration or localization during the development of the nervous system but also for inhibiting tumor growth.

**References**:

1. Lamballe, F. et al: Cell 66:967-979, 1991
2. Guiton, M. et al: J. Biol. Chem. 270:20384-90, 1995
3. Yamauchi, J. et al: Proc. Natl. Acad. Sci. USA 100:14421-6, 2003
4. Jin, W. et al: Cancer Res. 67:9869-77, 2007

## TECHNICAL INFORMATION

**Source:**
TrkC antibody is a mouse monoclonal antibody raised against purified recombinant human TrkC ECD expressed in 293 cells.

**Specificity and Sensitivity:**
This antibody detects TrkC proteins without cross-reactivity with other family members.

**Storage Buffer**: PBS and 30% glycerol

**Storage**:
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

# TrkC Antibody
Cat. No. CP10188

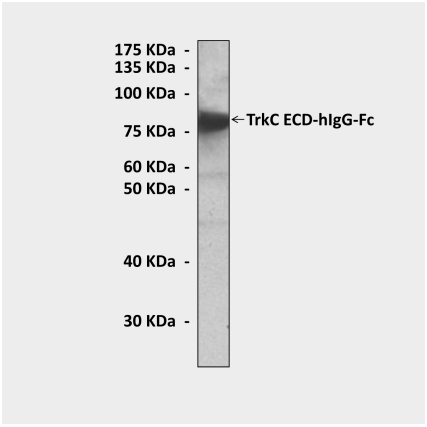
| | |
|---|---|
| **Applications:** | **WB, IP, IHC** |
| **Detected MW:** | **145 kDa** |
| **Species & Reactivity:** | **Human** |
| **Isotype:** | **Mouse IgG1** |

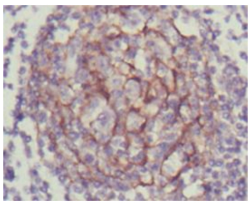
## APPLICATIONS

| Application: | *Dilution: |
|---|---|
| **WB** | 1:1000 |
| **IP** | 1:50 |
| **IHC** | 1:100 |
| **ICC** | n/d |
| **FACS** | n/d |

*****Optimal dilutions must be determined by end user.*

## QUALITY CONTROL DATA



**Top:** Western Blot detection of human TrkC ECD-hIgG-Fc fusion proteins expressed in 293 cell lysate using TrkC Antibody. **Bottom:** This antibody stains paraffin-embedded human lymph node tissue in immunohistochemical analysis.