

## BACKGROUND

The small Ras-related GTPase, TC10, has been classified on the basis of sequence homology to be a member of the Rho family. This family, which includes the Rho, Rac and CDC42 subfamilies, has been shown to regulate a variety of apparently diverse cellular processes such as actin cytoskeletal organization, mitogen-activated protein kinase (MAPK) cascades, cell cycle progression and transformation. TC10 is highly expressed in muscle and adipose tissues and localizes to caveolin-enriched lipid microdomains at the plasma membrane. *In vitro* binding assays have indicated that active GTP-bound TC10 can bind a number of potential effectors, including mixed lineage kinase 2, myotonic dystrophy-related Cdc42 kinase, p21-activated protein kinases, the Borg family of interacting proteins, the mammalian partition-defective homolog Par6, and the N-WASP isoform of the Wiskott-Aldrich Syndrome Protein.<sup>1</sup>

TC10 has been shown to play a role in insulin-stimulated glucose uptake and translocation of the glucose transporter GLUT4 in adipocytes. GLUT4 translocation requires activation of two distinct pathways involving phosphatidylinositol 3-kinase (PI 3-K) and TC10, respectively.<sup>2</sup> In this signaling cascade, the insulin receptor and TC10 reside constitutively in lipid raft microdomains of the plasma membrane. Upon binding to insulin, the insulin receptor catalyzes the tyrosine phosphorylation of the c-Cbl and Cbl-b protooncogenes after their recruitment via the adapter proteins APS and CAP (adapter protein containing PH and Src homology 2 domains and c-Cbl-associated protein, respectively). Once phosphorylated, Cbl interacts with the adapter protein CT10-related kinase (Crk)II through the Src homology 2 domain of the latter protein. Crk is constitutively associated with the nucleotide exchange factor C3G. Thus, binding of Crk to Cbl brings C3G into proximity with TC10 in lipid rafts, where it converts the inactive GDP-bound TC10 protein to the GTP-bound activated state. Once activated, TC10 can interact with multiple downstream effectors including Exo70, CIP4/2, Par6B, and TCGAP. Some of these effectors, such as CIP4, Par6, and TCGAP, interact with both Cdc42 as well as TC10, whereas Exo70 specifically interacts with TC10. Several studies have also suggested a role for actin in insulin-stimulated GLUT4 translocation. It was shown that TC10 exerts two distinct effects in adipocytes, depolymerizing cortical F-actin beneath the plasma membrane and greatly increasing F-actin polymerization in the perinuclear region. This latter function is dependent upon N-WASP and mediates secretory membrane trafficking through the engagement of actin with COPI vesicle coat proteins.<sup>3</sup> Furthermore, insulin-induced phosphorylation of GSK-3beta appears to be mediated not only by the PI 3-kinase-PKB pathway, but also by the TC10-Par6-atypical PKC

signaling pathway. Thus, PKC zeta/lambda appears to function as a convergent downstream target that can differentiate these two pathways through restricted spatial compartmentalization. (Kanzaki, M. et al: J.Cell Biol. 164:279-90, 2004). Additionally, TC10 function can be regulated by phosphorylation. Insulin stimulation results in the activation of cyclin-dependent kinase-5 (CDK5) in lipid raft domains via a Fyn-dependent phosphorylation on tyrosine residue 15. In turn, activated CDK5 phosphorylates the Rho family GTP-binding protein TC10alpha on threonine 197. CDK5-dependent phosphorylation maintains TC10alpha in lipid raft compartments thereby disrupting cortical actin, whereas subsequent dephosphorylation of TC10alpha through inactivation of CDK5 allows for the re-assembly of F-actin.<sup>4</sup>

### References:

1. Murphy, G.A. et al: Oncogene 18:3831-45, 1999
2. Maffucci, T. et al: EMBO J. 22:4178-89, 2003
3. Chang, L. et al: Endocrinol. 148:27-33, 2007
4. Okada, S. et al: J. Biol. Chem. 283:35455-63, 2008

## TECHNICAL INFORMATION

### Source:

TC10 Antibody is a rabbit antibody raised against a short peptide from human TC10 sequence.

### Specificity and Sensitivity:

This antibody detects endogenous TC10 proteins without cross-reactivity with other family members.

**Storage Buffer:** Supplied in PBS with 0.09% (W/V) sodium azide

### Storage:

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

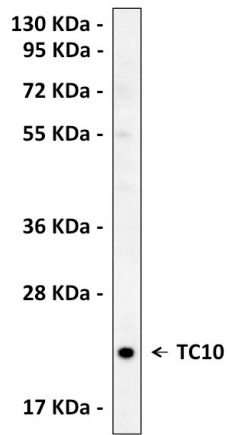
## APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	1:10-1:50
ICC	n/d
FACS	n/d

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



### QUALITY CONTROL DATA



TC10 Antibody (Center) western blot analysis in T47D cell line lysates (35 µg/lane).

