

BACKGROUND

Tcf proteins (Tcf1, Tcf3, Tcf4, and Lef1 in mammals) are the DNA-binding transcriptional regulators of the canonical Wnt signaling pathway, which play important role in cell fate decisions and differentiation. Although some contexts allow certain Tcfs to share a degree of functional redundancy, different Tcf family members do not always behave similarly when expressed in the same cell type. Through a highly conserved HMG domain and an amino-terminal beta-catenin interaction domain, each Tcf protein can promote transcription of downstream targets (for example, siamois and Xnr3) when Wnt-stabilized beta-catenin accumulates intracellularly. In the absence of stabilized beta-catenin, Tcf proteins have been shown to function as transcriptional repressors by interacting with corepressor proteins, such as Groucho, CtBP, and HIC-5. Interaction between Tcf3 and beta-catenin occurs at the NH₂ terminus of Tcf3 and is separate from the Groucho and CtBP binding regions. Models of the wnt pathway suggest a role for Tcf3 as an unregulated scavenger of free beta-catenin. However, CBP binds and acetylates a lysine in the beta-catenin interaction domain of Tcf3, thereby lowering its affinity for beta-catenin. Some members of the Sox family of HMG box proteins also bind beta-catenin and block its binding to Tcf. In *Caenorhabditis elegans*, components of the mitogen-activated kinase pathway phosphorylate Tcf-bound beta-catenin so as to block nuclear localization. These studies indicate that the interaction between beta-catenin and Tcf3 is dynamic and that regulating it may play an important role in modulating wnt signaling. It was demonstrated that GSK3 and casein kinase (CK) 1epsilon both have direct but opposite effects in regulating the beta-catenin-Tcf3 interaction. Phosphorylation of Tcf3 by CK1epsilon stimulates its binding to beta-catenin, an effect reversed by GSK3. Tcf3 synergizes with CK1epsilon to inhibit beta-catenin degradation.¹

Direct relationships between the biochemical properties of Tcf proteins and their physiological effects have been demonstrated by several studies expressing mutated forms of the proteins in model organisms. Three transcription factors, Nanog, Oct4, and Sox2, have been reported to form a feedforward circuit promoting pluripotent cell self-renewal in embryonic stem cells (ESC). It was shown that Tcf3 acts broadly on a genome-wide scale to reduce the levels of several promoters of self-renewal (Nanog, Tcf1, Tbx3, Esrrb) while not affecting other ESC genes (Oct4, Sox2, Fgf4) and Tcf3 counteracted effects of both Nanog and Oct4. Thus, Tcf3 is a cell-intrinsic inhibitor of pluripotent cell self-renewal that functions by limiting steady-state levels of self-renewal factors.² In addition, Tcf3 plays important role in regulation of skin stem cells. In the absence of Wnt signals, Tcf3 may function in skin stem cells to maintain an undifferentiated state and, through Wnt signaling,

directs these cells along the hair lineage.³ Moreover, studies reveal an essential and unique role for mouse Tcf3 in early development. It was demonstrated that Tcf3 is involved directly in restricting anteroposterior (AP) axis induction during the onset of gastrulation. Similar to its *Xenopus* and zebrafish homologs, mouse Tcf3 appears to function by repressing target genes in the early embryo.⁴ Finally, the t(1;19)(q23;p13.3) is one of the most common chromosomal abnormalities in B-cell precursor acute lymphoblastic leukemia (BCP-ALL) and usually gives rise to the *Tcf3-PBX1* fusion gene. In addition to its role as a fusion partner gene, it was found that *Tcf3* can also act as a tumor suppressor gene in BCP-ALL.⁵

References:

1. Lee, E. et al: J. Cell Biol. 154:983-94, 2001
2. Yi, F. et al: Stem Cells 26:1951-60, 2008
3. Nguyen, H. et al: Cell 127:171-83, 2006
4. Merrill, B.J. et al: Development 131:263-74, 2004
5. Barber, K.E. et al: Gene Chromosome Cancer 46:478-86, 2007

TECHNICAL INFORMATION

Source:

TCF3 mAb Monoclonal Antibody is a Mouse monoclonal antibody raised against a short peptide from purified recombinant human TCF3 fragments expressed in *E. coli*.

Specificity and Sensitivity:

This antibody detects endogenous TCF3 proteins without cross-reactivity with other family members.

Storage Buffer: PBS and 30% glycerol

Storage:

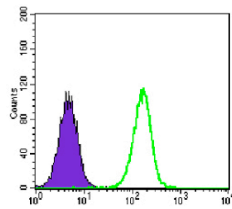
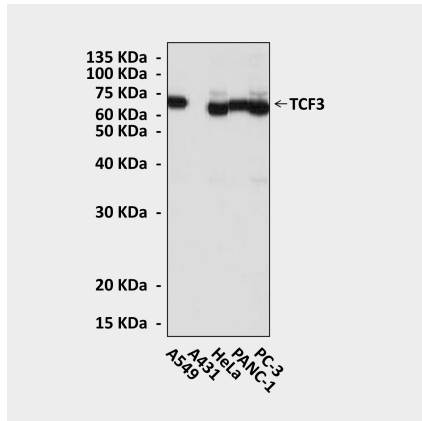
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

APPLICATIONS

Application:	*Dilution:
WB	1:500 – 2000
IP	n/d
IHC	n/d
ICC	n/d
FACS	1:200 – 400
*Optimal dilutions must be determined by end user.	



QUALITY CONTROL DATA



Top: Western Blot detection of TCF3 proteins in various cell lysates using TCF3 Antibody. **Bottom:** This antibody detect TCF3 protein in A549 cells by FACS analysis (TCF3 Antibody: Green; Control mouse IgG: purple).

