

## BACKGROUND

TBX5 is a T-box transcription factor belonging to the T-box gene family, the members of which share a highly conserved 180-aminoacid domain required for DNA binding. TBX5 has been characterized in most vertebrate lineages and is widely expressed during the development of various embryonic structures, including the heart, the eyes and the anterior set of paired appendages (tetrapod forelimbs and fish pectoral fins). Mutations in TBX5 cause Holt–Oram syndrome, an autosomal dominant human “heart-hand” condition characterized by upper limb and heart malformations. During embryogenesis TBX5 localizes to cellular nuclei. The protein transport is mediated by two distinct, evolutionary conserved nuclear localization signals (NLS) acting cooperatively. Missense mutations within these conserved sequences impair nuclear localization and cause “functional” haploinsufficiency due to decreased protein concentration at the location of its biological function. Heart formation requires a highly balanced network of transcriptional activation of genes. TBX5 is known to interact with the homeodomain protein NKX2.5 and the zinc finger protein GATA4 to coactivate the *ANF* gene and promote cardiomyocyte differentiation. Moreover, Stat3 is required for the differentiation of cardiomyocytes through direct transcriptional regulation of TBX5, NKX2.5, and GATA4.<sup>1</sup> The homeodomain transcription factor, *Shox2*, is essential for the formation of the sinoatrial valves and for the development of the pacemaking system. It was shown that TBX5 is a regulator of *Shox2* expression in the inflow tract and that *Bmp4* is regulated by *Shox2* in this compartment of the embryonic heart. In addition, it was also shown that *Tbx5* acts cooperatively with NKX2.5 to regulate the expression of *Shox2* and *Bmp4*. Thus, there is a link between TBX5, *Shox2* and *Bmp4* in the pacemaker region of the developing heart, which mediated the intricate interplay between the heart-specific transcriptional machinery and developmental signaling pathways.<sup>2</sup> TBX5 also associates with TBX20, TAZ, SALL4, and LMP4. Recent studies have shown that the functional cooperation of TBX5 and NKX2.5 on the *Id2* promoter is important for the development of the cardiac conduction system. It was shown that a physical interaction between TBX5 and MEF2C leads to a synergistic activation of the alpha-cardiac myosin heavy chain (*MYH6*). Studies suggest that the genetic interaction of these proteins is not only required for *MYH6* expression but also essential for the early stages of heart development and survival.<sup>3</sup> In addition, it was demonstrated that TBX5 regulates ventricular myocyte relaxation in a cell-autonomous manner by direct modulation of the expression of SERCA2a. Patients with HOS also have diastolic defects that resemble restrictive cardiomyopathy. This defines a TBX5-dependent pathway for the transcriptional control of diastolic function, with potential implications for the pathogenesis of heart

failure and the management of altered heart function in patients with congenital heart defects (CHDs).<sup>4</sup> Interestingly, it was reported that TBX5 can form a complex with splicing factor SC35 and plays an important role in constitutive pre-mRNA splicing, alternative splicing, and transcriptional activation. We further show that TBX5-associated splicing is relevant to the pathogenesis of Holt-Oram syndrome.<sup>5</sup>

## References

1. Snyder, M. et al: J. Biol. Chem. 285:23639-46, 2010
2. Puskaric, S. et al: Hum. Mol. Genet. 19:4625-3, 2010
3. Ghosh, T.K. et al: Mol. Cell. Biol. 29:2205-18, 2009
4. Zhu, Y. et al: proc. Natl. Acad. Sci. USA 105:5519-24, 2008
5. Fan, C. et al: J. Biol. Chem. 284:25653-63, 2009

## TECHNICAL INFORMATION

### Source:

TBX5 Antibody is a mouse monoclonal antibody raised against purified recombinant human TBX5 fragments expressed in *E. coli*.

### Specificity and Sensitivity:

This antibody detects TBX5 proteins without cross-reactivity with other related proteins.

**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.

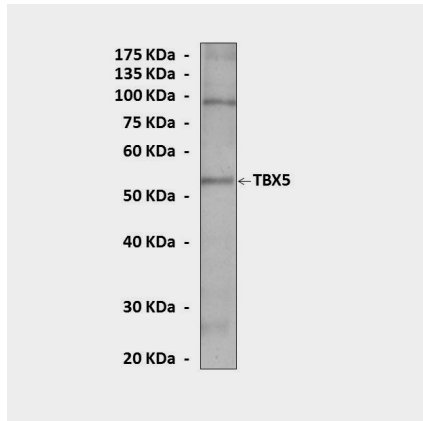
## APPLICATIONS

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

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



### QUALITY CONTROL DATA



Western Blot detection of TBX5 proteins in HepG2 cell lysate using TBX5 Antibody.

