

BACKGROUND

The TIMPs are well-studied inhibitors of MMPs and consist of a family of four structurally related proteins (TIMP-1-4), with core proteins of ~21 kDa. TIMPs inhibit MMP activity by a common mechanism involving interaction of the amino-terminal cysteine residue with the zinc atom at the MMP active site. The TIMPs inhibit MMP activity associated with tumor invasion and angiogenesis. In addition to their MMP-inhibitory activity, it is now widely appreciated that TIMPs have direct effects on cellular behaviors such as cell growth, apoptosis, migration, and differentiation.¹

TIMP-4 is a 195 amino acid polypeptide with molecular mass of 22 kDa. The TIMP-4 polypeptide is 37% identical to TIMP-1 and 51% identical to TIMP-2 and -3. TIMP-4 is the most neutral TIMP protein under physiological conditions (pH 7.4), having an isoelectric point of 7.34, compared with values of 8.00, 6.45 and 9.04 for human TIMP-1, TIMP-2 and TIMP-3, respectively. The TIMP-4 gene is transcribed into 1.4 kb mRNA species. Of the calcified tissues, TIMP-4 has been detected in human cartilage. TIMP-4 differs from the other three TIMPs by its restricted expression pattern. TIMP4 is characterized by being primarily restricted to cardiovascular structures and ovary. It was suggested that that TIMP-4 plays a role in the normal physiology of the heart and the ovary, most likely related to maintenance of the delicate balance between MMPs and TIMPs. Moreover, it can inhibit smooth muscle cell migration and induce apoptosis *in vitro* and *in vivo*.² Animal studies have suggested a role for TIMP4 in several inflammatory diseases and cardiovascular pathologies. TIMP4 was most clearly visible in cardiovascular tissue areas populated by abundant inflammatory cells, mainly macrophages and CD3+ T cells. Human blood derived lymphocytes, monocytes/macrophages and mast cells were shown to produce TIMP4. In advanced atherosclerotic lesions, TIMP4 was detected around necrotic lipid cores, whereas TIMP3 and caspase 3 resided within and around the core regions, indicating different roles for TIMP3 and TIMP4 in inflammation-induced apoptosis and in matrix turnover. TIMP-4 may be a novel systemic marker for vascular inflammation.³

References:

1. Gomez, D.E.: Eur J Cell Biol. 74:111-22, 1997
2. Guo, Y.H. et al: Life Sci. 75:2483-93, 2004
3. Koskivirta, I. et al: Histochem. Cell Biol. 126:335-42, 2006

TECHNICAL INFORMATION

Source: Anti-TIMP-4 is a rabbit polyclonal antibody raised against a peptide mapping at the C-terminal end of human TIMP-4, different from the related mouse sequence by three amino acids.

Specificity and Sensitivity: It reacts specifically with TIMP-4 of human, mouse, and rat origin in immunohistochemical staining and western blotting, no cross-reactivity with other members of the family.

Storage Buffer: PBS and 30% glycerol.

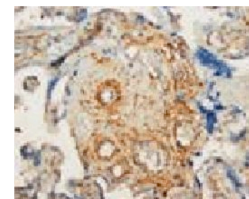
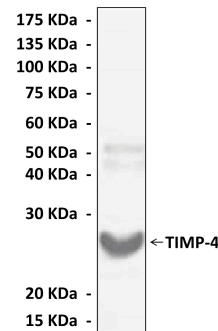
Storage: Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

APPLICATIONS

Application:	*Dilution:
WB	1:100 – 400
IP	n/d
IHC	1:50 - 200
ICC	n/d
FACS	n/d

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

QUALITY CONTROL DATA



Top: Detection of TIMP-4 from rat kidney tissue lysate in Western blot assay, using Anti-TIMP-4. **Bottom:** Immunohistochemical staining of paraffin-embedded human placental tissue, using Anti-TIMP-4.

