

BACKGROUND

Src Homology 2 Domain-Containing Inositol 5-Phosphatase 1 (SHIP-1) is an inositol polyphosphate 5-phosphatase that has been identified by its association with the adapter protein Shc after stimulation of hematopoietic cells by a variety of hematopoietic growth factors. Expression of this protein is restricted to hematopoietic cells where its movement from the cytosol to the plasma membrane is mediated by tyrosine phosphorylation.¹ It has SH2 domain at the amino terminus, an inositol polyphosphate 5-phosphatase domain in the central region, two consensus sequences for interacting with phosphotyrosine binding domains (ie NPXY) and proline-rich regions at the carboxy terminus. Alternate transcriptional splice variants, encoding different isoforms of SHIP, have been characterized.²

SHIP-1 is a negative regulator in a variety of cytokine, immunoreceptor, and growth factor signaling pathways. SHIP-1 has important functions in T cells, B cells, mast cells, basophils, and neutrophils. The phosphoinositide 3-kinase (PI3K) pathway is critical in many biologic processes, including cell proliferation, apoptosis, and migration. Activated PI3K catalyzes the formation of the lipid product phosphatidylinositol-3,4,5-trisphosphate (PIP3), which mediates downstream responses. As one of the negative regulators in this pathway, SHIP-1 selectively hydrolyzes 5'-phosphates from inositolphosphates and phosphoinositides phosphorylated at the D3-position of the inositol ring, ie Ins(1,3,4,5)P₄ and PtdIns(3,4,5)P₃, respectively, thereby SHIP-1 controls the intracellular level of PIP3. The major mechanism of SHIP-1 has been elucidated in the interaction between SHIP-1 and the inhibitory receptor Fc-gamma-RIIB of B lymphocytes. On B-cell antigen receptor-Fc-gamma-RIIB coligation, SHIP-1 is recruited to the immunoreceptor tyrosine-based inhibitory motif domain of the receptor. After localizing to the cell membrane, SHIP-1 dephosphorylates PIP3 to PI-3,4-bisphosphate, effectively reducing or terminating the downstream signaling of the PI3K pathway.³

Evidence for implicating SHIP-1 in the down-regulation of cytokine receptor signal transduction comes from the intriguing phenotype of the SHIP-1 *knockout* mouse which showed increased numbers of granulocyte-macrophage (GM) progenitors in bone marrow and spleen, an extensive infiltration of lungs with macrophages and a hyperresponsiveness to IL-3, SCF and colony-stimulating factors, ie GM-CSF and CSF-1.⁴ It was demonstrated that SHIP-1 acts as a negative regulator of B-cell antigen receptor signaling. It mediates signaling from the FC-gamma-RIIB receptor (FCGR2B), playing a central role in terminating signal transduction from activating immune/hematopoietic cell receptor systems. It also acts as a negative regulator of myeloid cell

proliferation/survival and chemotaxis, mast cell degranulation, immune cells homeostasis, integrin alpha-IIb/beta-3 signaling in platelets and JNK signaling in B-cells. It regulates proliferation of osteoclast precursors, macrophage programming, phagocytosis and activation and is required for endotoxin tolerance. Moreover, SHIP-1 is involved in the control of cell-cell junctions, CD32a signaling in neutrophils and modulation of EGF-induced phospholipase C activity. It was shown that SHIP-1 is a key regulator of neutrophil migration, by governing the formation of the leading edge and polarization required for chemotaxis. Additionally, it modulates FCGR3/CD16-mediated cytotoxicity in NK cells. And it participated in regulation of the activin/TGF-beta-induced apoptosis through its Smad-dependent expression.⁵

References:

1. Liu, Q. et al: J. Exp. Med. 188:1333-42, 1998
2. Liu, L. et al: Leukemia 11:181-4, 1997
3. Tridandapani, S. et al: J. Immunol. 162:1408-14, 1999
4. Huber, M. et al: Prog Biophys Mol Biol. 71:423-34, 1999
5. Kalesnikoff, J. et al: Rev Physiol Biochem Pharmacol. 149:87-103, 2003

TECHNICAL INFORMATION

Source:

SHIP-1 Antibody is a rabbit antibody raised against a short peptide from C-terminal sequence of human SHIP-1.

Specificity and Sensitivity:

This antibody detects endogenous SHIP-1 proteins without cross-reactivity with other family members.

Storage Buffer: Rabbit IgG in phosphate buffered saline (without Mg²⁺ and Ca²⁺), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.

Storage:

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

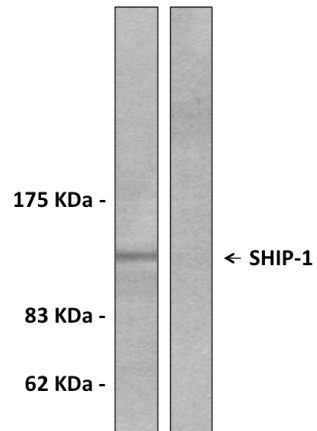
APPLICATIONS

Application:	*Dilution:
WB	1:500-1:1000
IP	n/d
IHC	n/d
ICC	n/d
FACS	n/d
ELISA	1:40000

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



QUALITY CONTROL DATA



Immunoblotting analysis of extracts from HuvEc cells, using Anti-SHIP1, C-Terminal antibody. The lane on the left was treated with the Anti-SHIP1, C-Terminal antibody. The lane on the right (negative control) was treated with both Anti-SHIP1, C-Terminal antibody and the synthesized immunogen peptide.

