Revision 1

Store at -20C

#14745

Phospho-SLP-76 (Ser376) (D9D6E) Rabbit mAb

Cell Signaling TECHNOLOGY®

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Applications:	Reactivity:	Sensitivity:	MW (kDa):	Source/Isotype:	UniProt ID:	Entrez-Gene Id:
W	H M	Endogenous	76	Rabbit IgG	#Q13094	3937

Product Usage Information

Application	Dilution
Western Blotting	1:1000

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/ml BSA, 50% glycerol and less than 0.02% sodium azide. Store at –20°C. Do not aliquot the antibody.

Specificity/Sensitivity

Phospho-SLP-76 (Ser376) (D9D6E) Rabbit mAb recognizes endogenous levels of SLP-76 protein only when phosphorylated at Ser376.

Source / Purification

Monoclonal antibody is produced by immunizing animals with a synthetic phosphopeptide corresponding to residues surrounding Ser376 of human SLP-76 protein.

Background

SH2 domain-containing leukocyte protein of 76 kDa (SLP-76) is a hematopoietic adaptor protein that is important in multiple biochemical signaling pathways and necessary for T cell development and activation (1). ZAP-70 phosphorylates SLP-76 and LAT as a result of TCR ligation. SLP-76 has amino-terminal tyrosine residues followed by a proline-rich domain and a carboxy-terminal SH2 domain. Phosphorylation of Tyr113 and Tyr128 result in recruitment of the GEF Vav and the adaptor protein Nck (2). TCR ligation also leads to phosphorylation of Tyr145, which mediates an association between SLP-76 and Itk, which is accomplished in part via the proline-rich domain of SLP-76 and the SH3 domain of Itk (3). Furthermore, the proline-rich domain of SLP-76 binds to the SH3 domains of Grb2-like adaptor Gads (3,4). In resting cells, SLP-76 is predominantly in the cytosol. Upon TCR ligation, SLP-76 translocates to the plasma membrane and promotes the assembly of a multi-protein signaling complex that includes Vav, Nck, Itk, and PLCγ1 (1). The expression of SLP-76 is tightly regulated; the protein is detected at very early stages of thymocyte development, increases as thymocyte maturation progresses, and is reduced as cells mature to $CD4^+$ $CD8^+$ double-positive thymocytes (5).

Following TCR ligation, SLP-76 is phosphorylated at Ser376 by the hematopoietic progenitor kinase 1 (HPK1) (6,7). This phosphorylation induces interaction with 14-3-3ε, which leads to the disassembly of TCR signaling complexes and down regulation of TCR signaling (6-8).

Background References

1. Clements, J.L. (2003) *Immunol Rev* 191, 211-9.
2. Bubeck Wardenburg, J. et al. (1998) *Immunity* 9, 607-16.
3. Bunnell, S.C. et al. (2000) *J Biol Chem* 275, 2219-30.
4. Liu, S.K. et al. (1999) *Curr Biol* 9, 67-75.
5. Clements, J.L. et al. (1998) *J Immunol* 161, 3880-9.
6. Shui, J.W. et al. (2007) *Nat Immunol* 8, 84-91.
7. Di Bartolo, V. et al. (2007) *J Exp Med* 204, 681-91.
8. Lasserre, R. et al. (2011) *J Cell Biol* 195, 839-53.

Species Reactivity

Species reactivity is determined by testing in at least one approved application (e.g., western blot).

Western Blot Buffer

IMPORTANT: For western blots, incubate membrane with diluted primary antibody in 5% w/v BSA, 1X TBS, 0.1% Tween® 20 at 4°C with gentle shaking, overnight.

Applications Key

W: Western Blotting

Cross-Reactivity Key

H: Human **M:** Mouse

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