

## BACKGROUND

Mitogen-activated protein kinases, including ERK1/ERK2, JNK/SAPK, and p38/RK, are important signal transducing molecules for control of gene expression, cell proliferation, and apoptosis. In response to cellular stresses, such as heat or osmotic shock, bacterial lipopolysaccharide, proinflammatory cytokines, and tumor necrosis factor-alpha, p38 MAP kinase is activated by its upstream kinases MKK3 and MKK6. Activated p38 phosphorylates MAPKAPK-2, MAPKAPK-3, PRAK, MNK1/2, MSK1, and transcription factors ATF2, CHOP/GADD153, Elk-1, and MEF2C. MAPKAPK-2 is activated *in vivo* only by p38/p40/RK. Multiple residues of MAPKAPK-2 are phosphorylated by p38 MAPK. Phosphorylation at Thr222, Ser272 and Thr334 appears to be essential for the activity of MAPKAPK-2.<sup>1</sup> The p38 C-terminal regulatory domain contains a bipartite nuclear localization signal and a nuclear export signal. Following phosphorylation of MAPKAPK-2, nuclear p38 was exported to the cytoplasm in a complex with MAPKAPK-2. The p38 activators MKK3 and MKK6 were present in both the nucleus and the cytoplasm, consistent with a role in activating p38 in the nucleus. Thus, MAPKAPK-2 serves both as an effector of p38 by phosphorylating substrates and as a determinant of cellular localization of p38. Nuclear export of p38 and MAPKAP kinase-2 may permit them to phosphorylate substrates in the cytoplasm.<sup>2</sup>

Mice that lack MAPKAPK-2 show increased stress resistance and survive bacterial lipopolysaccharide-induced endotoxic shock due to a 90% reduction in the production of tumor necrosis factor-alpha.<sup>3</sup> MAPKAPK-2 is in the nucleus of unstimulated cells and moves rapidly to the cytoplasm after stimulation. In the nucleus, MAPKAPK-2 contributes to the phosphorylation of CREB at Ser133 and may regulate its ability to activate transcription in response to cAMP, Ca<sup>2+</sup>, and nerve growth factor. MAPKAPK-2 phosphorylates serum response factor at Ser103 both *in vivo* and *in vitro* in response to tumor-promoting and stress inducing stimuli. Both MAPKAPK-2 and MAPKAPK-3 interact with basic helix-loop-helix transcription factor E47 *in vivo* and phosphorylate E47 *in vitro*, suggesting that they are regulators of E47 activity and E47-dependent gene expression. In the cytoplasm, MAPKAPK-2 phosphorylates small heat shock protein HSP25/HSP27 and lymphocyte-specific protein LSP-1, both F-actin-binding proteins. Other substrates of MAPKAPK-2 include glycogen synthase, tyrosine hydroxylase, and 5-lipoxygenase. MAPKAPK-2 is directly responsible for phosphorylating Cdc25B and C and maintaining the G<sub>1</sub>, S, and G<sub>2</sub>/M checkpoints in response to UV-induced DNA damage.<sup>4</sup> In addition, MAPKAPK-2 can also phosphorylate HDM2 on serine 157 and 166. Phosphorylation of these sites appears to contribute to the activation of HDM2 and therefore a reduction in p53 stability, and may play a role in

moderating the extent and duration of a stress-induced induction of the p53 response.<sup>5</sup>

### References:

1. Ben-Levy, R. et al: EMBO J. 14:5920-30, 1995
2. Ben-Levy, R. et al: Curr. Biol. 8:1049-57, 1998
3. Hegen, M. et al: J. Immunol. 177:913-17, 2006
4. Manke, I.A. et al: Mol. Cell 17:37-48, 2005
5. Weber, H.O. et al: Oncogene 24:1964-75, 2005

## TECHNICAL INFORMATION

### Source:

MAPKAPK-2/MK-2 antibody is a rabbit antibody raised against a short peptide from C-terminal sequence of human MAPKAPK-2.

### Specificity and Sensitivity:

This antibody detects endogenous MAPKAPK-2 proteins without cross-reactivity with other family members.

**Storage Buffer:** Solution in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide.

### Storage:

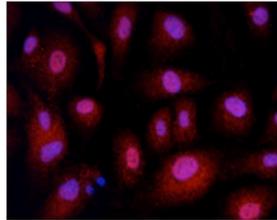
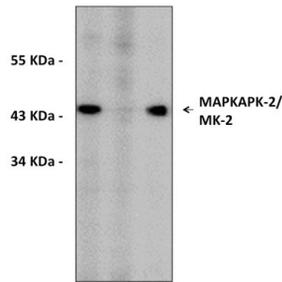
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

## APPLICATIONS

Application:	*Dilution:
WB	1:500-2,000
IP	n/d
IHC	n/d
ICC	n/d
FACS	n/d
*Optimal dilutions must be determined by end user.	



## QUALITY CONTROL DATA



**Top:** Lysate of HEK-293T cells overexpressing human MAPKAPK2 was separated on SDS-PAGE, blotted with Anti-MAPKAPK2 (1-14) and developed using Goat Anti-Rabbit IgG-Peroxidase and a chemiluminescent substrate. Lanes (left to right): 1.) Antibody dilution 1:500 2.) Antibody dilution 1:500 + MAPKAPK2 immunizing peptide (human, 1-14) 3.) Antibody dilution 1:1,000

**Bottom:** Immunofluorescence of HUVEC cells using MAPKAPK2 (1-14) (RB), (red) at a 1:200 dilution, taken at 40× magnification and nuclear staining with Hoescht 33342 (blue). Yale HTCB IF procedure used.

