

## BACKGROUND

Extracellular signal-regulated protein kinases (ERKs) are members of the mitogen-activated protein kinase (MAPK) family and play an important role in intracellular signaling pathways that lead to the division or differentiation of a number of cell types. This is probably attributable to their ability to phosphorylate a variety of transcription factors and other signaling and structural proteins. Three closely related mammalian ERKs have been identified with ERK1 and ERK2 being the most widely distributed. ERKs are in turn activated by highly specific MAPK (or ERK) kinases (MEK1 or MEK2). Both MEK1 and MEK2 are closely related, dual-specificity tyrosine/threonine protein kinases. They activate ERKs by phosphorylation of a Tyr and a Thr residue in a conserved TEY motif. MEKs and ERKs are activated through protein-tyrosine kinase- and G protein-coupled receptors. The tyrosine kinase-mediated activation involves Ras and the MEK kinase c-Raf, which phosphorylates Ser217 and Ser221 in MEK1 (or corresponding Ser residues in other MEKs). Approximately 30% of all human cancers have a constitutively activated MAPK pathway, and constitutive activation of MEK1 results in cellular transformation. In addition, MEK can be activated by Mos and Tpl2 in some specific cells.<sup>1</sup>

MEK1 and MEK2 display 85% amino acid identity overall and are expressed ubiquitously in cell lines and tissues. Although it is commonly assumed that the two isoforms are functionally equivalent, several lines of evidence, however, indicate that they are regulated differentially and may exert non-redundant functions.<sup>2</sup> Studies using RNA interference have suggested that both MEK1 and MEK2 are required for *in vitro* cell proliferation, and that they contribute to distinct cell cycle regulatory events.<sup>3</sup> It has shown that activated MEK1 but not MEK2 can promote epidermal hyperplasia in transgenic mice, even though both MEK proteins trigger ERK1/ERK2 phosphorylation.<sup>4</sup> Moreover, it was found recently that MEK1 has a role in downregulating MEK2-dependent ERK signaling. MEK1 mediates the regulation of MEK2 in the context of a previously undiscovered MEK1-MEK2 complex. The MEK heterodimer is negatively regulated by ERK-mediated phosphorylation of MEK1 on Thr292, a residue missing in MEK2. Disabling this ERK-proximal negative-feedback step stabilizes the phosphorylation of both MEK2 and ERK in cultured cells and *in vivo* in MEK1 knockout embryos and mice. Thus, in disagreement with the current perception of the pathway, the role of MEK1 and MEK2 in growth factor-induced ERK phosphorylation is not interchangeable. It is suggested that MEK1 is the crucial modulator of MEK and ERK signaling and have potential implications for the role of MEK1 and MEK2 in tumorigenesis.<sup>5</sup>

## References:

1. Zheng, C.F. & Guan, K.F.: EMBO J. 13:1123-31, 1994
2. Eblen, S.T. et al: Mol. Cell. Biol. 22:6023-33, 2002
3. Liu, X. et al: Oncogene 23:763-76, 2004
4. Scholl, S.A. et al: Cancer Res. 64:6035-40, 2004
5. Catalanotti, F. et al: Nature Struct. Mol. Biol. 16:294-303, 2009

## TECHNICAL INFORMATION

### Source:

MEK2 Antibody is a mouse monoclonal antibody raised against recombinant human MEK2 fragments expressed in *E. coli*.

### Specificity and Sensitivity:

This antibody detects endogenous MEK2 proteins without cross-reactivity with other family members.

**Storage Buffer:** PBS and 30% glycerol

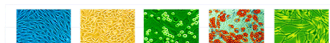
### Storage:

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

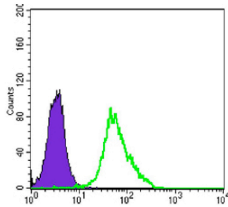
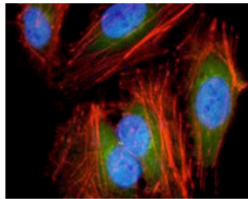
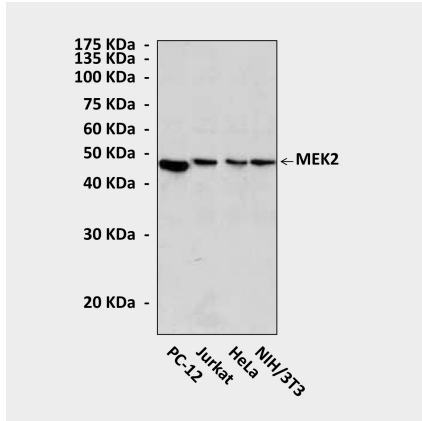
## APPLICATIONS

Application:	*Dilution:
WB	1:1000
IP	n/d
IHC	n/d
ICC	1:50-200
FACS	1:50-200

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



**QUALITY CONTROL DATA**



**Top:** Western Blot detection of MEK2 proteins in various cell lysates using MEK2 Antibody. **Middle:** This antibody stains HeLa cells in confocal immunofluorescent analysis (MEK2 Antibody: Green; Actin filaments: Red; DRAQ5 DNA Dye: Blue). **Bottom:** It also specifically reacts with MEK2 proteins in HeLa cells by FACS testing (MEK2 Antibody: Green; control; Purple).

