

Phosphorylation-dependent Scaffolding Role of JSAP1/JIP3 in the ASK1-JNK Signaling Pathway

H. Matsuura, K. Yoshioka, H. Ichijo

JSAP1 (also termed JIP3) is a scaffold protein that interacts with specific components of the JNK MAPK signaling pathway. Apoptosis signal-regulating kinase (ASK) 1 is a MAPKKK that activates the JNK and p38 MAPK cascades in response to environmental stresses such as reactive oxygen species. Here we show that JSAP1 bound ASK1 and enhanced ASK1- and H₂O₂-induced JNK activity. ASK1 phosphorylated JSAP1 *in vitro* and *in vivo*, and the phosphorylation facilitated interactions of JSAP1 with SEK1/MKK4 MAPKK, MKK7 MAPKK and JNK3 MAPK. Furthermore, ASK1-dependent phosphorylation was required for JSAP1 to recruit and thereby activate JNK in response to H₂O₂. We thus conclude that JSAP1 functions not only as a simple scaffold, but it dynamically participates in signal transduction by forming a phosphorylation-dependent signaling complex in the ASK1-JNK signaling module.

