JSAP1 Suppresses the ERK MAPK Signaling Pathways

Y. Kuboki, M. Ito, K. Yamamoto, K. Yoshioka

We previously reported that JSAP1 functions as a putative scaffold factor in the JNK MAPK cascades. In that study we also found MEK1 and Raf-1, which are involved in the ERK MAPK cascades, bind to JSAP1. Here we have defined the regions of JSAP1 responsible for the interactions with MEK1 and Raf-1. Both of the binding regions were mapped to the carboxy-terminal region (residues 1054-1305) of JSAP1. We next examined the effect of overexpressing JSAP1 on the activation of ERK by phorbol 12-myristate 13-acetate in transfected COS-7 cells, and found that JSAP1 inhibits ERK's activation and that the carboxy-terminal region of JSAP1 was required for the inhibition. Finally, we investigated the molecular mechanism of JSAP1's inhibitory function, and showed that JSAP1 prevents MEK1 phosphorylation and activation by Raf-1, resulting in the suppression of the activation of ERK. Taken together, these results suggest that JSAP1 is involved both in the JNK MAPK cascades, as a scaffolding factor, and the ERK MAPK cascades, as a suppressor.