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Abstract

Heat shock protein 27 (HSP27/HSPB1), one of small heat shock proteins, is constitutively expressed in various tissues. HSP27 and its phosphorylation state participate in regulation of multiple physiological and pathophysiological cell functions. However, the exact roles of HSP27 in osteoblasts remain unclear. In the present study, we investigated the role of HSP27 in the platelet-derived growth factor-BB (PDGF-BB)-stimulated migration of osteoblast-like MC3T3-E1 cells. PDGF-BB by itself hardly up-regulated the expression of HSP27 protein, but stimulated the phosphorylation of HSP27 in these cells. The PDGF-BB-induced cell migration was significantly down-regulated by the HSP27 overexpression. The PDGF-BB-induced migrated cell numbers of the wild type (WT) HSP27-overexpressing cells and the phospho-mimic HSP27-overexpressing (3D) cells were less than those of the unphosphorylatable HSP27-overexpressing (3A) cells. PD98059, an inhibitor of MEK1/2, SB203580, an inhibitor of p38 mitogen-activated protein (MAP) kinase, or SP600125, an inhibitor of stress-activated protein kinase/c-*Jun* N-terminal kinase (SAPK/JNK) reduced the PDGF-BB-induced migration of these cells, whereas Akt inhibitor or rapamycin, an inhibitor of upstream kinase of p70 S6 kinase (mTOR), hardly affected the migration. However, the PDGF-BB-induced phosphorylation of p44/p42 MAP kinase, p38 MAP kinase or SAPK/JNK was not affected by HSP27 overexpression. There were no significant differences in the phosphorylation of p44/p42 MAP kinase, p38 MAP kinase or SAPK/JNK between the 3D cells and the 3A cells. These results strongly suggest that HSP27 functions as a negative regulator in the PDGF-BB-stimulated migration of osteoblasts, and the suppressive effect is amplified by phosphorylation state of HSP27.