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Involvement of heat shock protein 90 in cardiac fibrosis

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Raf/Mek/Erk pathway plays a crucial role in the development of cardiac fibrosis. It is assumed that heat shock protein 90 (Hsp90) may regulate the Raf/Mek/Erk signal pathway. However, the role of Hsp90 in cardiac fibrosis under pathophysiological conditions remains unclear. In this study, effects of Hsp90 inhibitor on signal transducers in cultured cardiac fibroblasts were examined. Cardiac fibroblasts prepared from neonatal rats were treated with combination of Hsp90 inhibitor 17-(allylamino)-17-dimethoxy-geldanamycin (17-AAG) and proteasome inhibitor MG132. Proliferation of cardiac fibroblasts was attenuated by 17-AAG treatment for 48 h. 17-AAG treatment also reduced an expression of collagen I and III. c-Raf content of cardiac fibroblasts was decreased in the presence of 17-AAG. An increase in phosphorylation levels of Erk1/2 in cardiac fibroblasts attenuated by 17-AAG treatment. MG132 reversed the loss of c-Raf in cardiac fibroblasts treated with 17-AAG. These findings suggest that Hsp90 involves an activation of Raf/Mek/Erk pathway via c-Raf stability in cardiac fibroblasts, leading to the development of cardiac fibrosis.