

Roles of Hsp90 on cardiac remodeling in the development of chronic heart failure.

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Hsp90 is a highly conserved molecular chaperone involved stabilization of client proteins. Hsp90 clients are various signal transducers including protein kinases. It is well known that the cardiac remodeling such as cardiac hypertrophy and fibrosis is involved in the development of chronic heart failure. The cardiac remodeling is regulated by many signaling pathways. c-Raf and JNK are signal transducers involved in cardiac remodeling, and are also Hsp90 client proteins. Therefore, to clarify the roles of Hsp90 and its clients in progression to the chronic heart failure, we examined effects of Hsp90 inhibitor on the signal transducers in the development of chronic heart failure in animal models. Treatment of the animals with Hsp90 inhibitor resulted in a suppression of cardiac remodeling and a preservation of cardiac pump function. Furthermore, c-Raf/Erk signaling was attenuated by an administration of Hsp90 inhibitor. These results suggest that Hsp90 contributes to stabilization of several cardiac remodeling-associated protein kinases during the development of chronic heart failure.