Effect of Bcl-2 associated athanogene (BAG) 3 on cardiac disease in alpha-B crystallin R120G transgenic mouse

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It is known that Bcl-2 associated athanogene (BAG) 3 is strongly expressed in cardiac muscle as well as skeletal muscle. BAG3 can directly bind to Bcl-2 as well as heat shock protein (HSP) as a co-chaperone. Recent study showed that myofibrillar degeneration, disruption of Z-disk architecture and apoptotic cell death were observed in BAG3 knockout mouse. Thus, BAG3 may play a protective role in the muscles. We examined BAG3 protein levels in alpha-B crystallin (CryAB) R120G transgenic (TG) mouse, myofibrillar myopathy (MFM) model. A marked increase in BAG3 was observed in MFM hearts. Little is known, however, detail roles of the increased BAG3 in cardiac muscle. In order to understand functional role of increased cardiac BAG3 in MFM hearts, CryAB R120G TG mice were crossbred with TG mice overexpressing BAG3 to generate CryAB R120G/BAG3 double TG mice. Decrease in fractional shortening and induction of cardiac ANP as well as increase in heart weight/body weight ratio were seen in CryAB R120G TG mice. Moreover, deterioration in cardiac function as well as enhanced cardiac hypertrophy were observed in the CryAB R120G/BAG3 double TG mice. Thus, cardiac BAG3 overexpression may be insufficient for prevention of cardiac disease in CryAB R120G TG mice.