6. SUMMARY

Expression of the atrial myosin light chain 1 (ALC-1) is not detectable in the ventricle of the normal adult human heart. However, ALC-1 is reexpressed in the hypertrophied ventricle of patients with different cardiac diseases. Several *in vitro* studies as well as transgenic animal models have shown that ALC-1 overexpression leads to an increased cardiac contractility. However, the regulation of ALC-1 expression has not been unravelled so far. Therefore, the cardiomyoblast H9c2 cell line was stably transfected with a reporter gene construct consisting of the luciferase reporter gene under the control of the human ALC-1 (hALC-1) promoter (H9c2T1), which served as a model to investigate factors that regulate hALC-1 promoter activity. Vasopressin induced hypertrophy and activated a panel of signaling pathways in H9c2T1 cardiomyoblasts. Moreover, it led to an upregulation of hALC-1 promoter activity. Intracellular rather than extracellular Ca^{2+} sources were involved in the upregulation of the hALC-1 promoter under vasopressin-induced hypertrophy. Inhibition of the protein kinase C with bisindolylmaleimide had no significant influence on hALC-1 promoter activity. However, vasopressin-induced upregulation of the hALC-1 promoter was associated with nuclear translocation of NFAT. Inhibition of calcineurin with cyclosporin A reduced the vasopressin effect. Moreover, the Ca^{2+}-calmodulin-dependent protein kinases (CaMKs) inhibitor KN93 decreased the hALC-1 promoter activity to almost basal levels. Localization studies showed that CaMKIV, but not CaMKIIδ, accumulated in the nucleus in response to vasopressin. Thus, both the Ca^{2+}-calmodulin-calcineurin-NFAT pathway and the CaMKs play a role in the activation of the human ALC-1 promoter. Therefore, the same pathways that are involved in human heart hypertrophy were shown to be important for the activation of the hALC-1 promoter.