S08-5 Catecholamine receptors in cardiovascular diseases

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Frank-Starling and the autonomic nervous system are the two major mechanisms to regulate cardiac function. Cardiac insults, regardless of their nature when they are prolonged, may lead to the development of congestive heart failure, which is the most prominent, end-stage phenotype of the heart in human. The sympathetic nervous system and the Frank Starling mechanism may try to compensate decreased cardiac function at the early stage, however, these are mostly acute responses to the decreased cardiac function and thus may not improve cardiac function in the chronic stage. Increased end-diastolic volume may enhance cardiac contractility via the Frank Starling mechanism, which may enable the heart to increase its output under the volume overload condition. Similarly, catecholamine released from the sympathetic nerve terminal can binds to beta-adrenergic receptors in the heart, leading to the activation of the stimulatory G protein and thus adenylyl cyclase. Adenylyl cyclase is a membrane bound enzyme that can catalyze the conversion of ATP to cAMP. cAMP is an intracellular second messenger that activates protein kinase A that initiates cascades of phosphorylation reactions within the cardiac myocyte. Cardiac myocytes, thorough the phosphorylation of phospholamban or its contractile proteins, can increase the speed and force of cardiac contraction. This enables the heart to beat quickly and strongly. These acute responses to increased catecholamine signal are known to protect the heart from acute de-compensation. However, it is now obvious that chronic catecholamine stimulation plays an opposite role. Indeed, prolonged activation of beta-adrenergic receptors can induce cardiac myocyte apoptosis, which can be observed in multiple pathological conditions, such as end-stage heart failure. To elucidate this issues at molecular levels, various transgenic mouse models have been produced, demonstrating novel mechanism to regulate cardiac myocyte viability.