S18-1 Role of TRPC channels in the development of cardiac hypertrophy

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Cardiac hypertrophy is induced by various stresses such as hypertension and myocardial infarction. It is believed that hypertrophy is adaptive in the early phase but becomes maladaptive in the late phase. Cardiac hypertrophy develops heart failure when the heart is exposed persistently to the stresses. The sustained increase in intracellular Ca^{2+} ($[Ca^{2+}]_i$) plays an important role in the development of hypertrophy. It is generally thought that the sustained increase in $[Ca^{2+}]_i$ for hypertrophy occurs via G_q-stimulated production of inositol-1,4,5-trisphosphate (IP_3) and IP_3-meditaed release of Ca^{2+} from intracellular store. However, we demonstrated that diacylglycerol-sensitive transient receptor potential canonical channels (TRPC3/TRPC6) are responsible for the agonist-induced increase in $[Ca^{2+}]_i$, activation of nuclear factor of activated T cells (NFAT), and hypertrophic responses. As TRPC channels participate in pathological hypertrophy but not physiological contraction and the relaxation cycle, these results suggest that TPRC channels are a new target for the treatment of hypertrophy.