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Review

Ca^{2+} currents in cardiac myocytes: Old story, new insights ☆

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Abstract

Calcium is a ubiquitous second messenger which plays key roles in numerous physiological functions. In cardiac myocytes, Ca^{2+} crosses the plasma membrane via specialized voltage-gated Ca^{2+} channels which have two main functions: (i) carrying depolarizing current by allowing positively charged Ca^{2+} ions to move into the cell; (ii) triggering Ca^{2+} release from the sarcoplasmic reticulum. Recently, it has been suggested than Ca^{2+} channels also participate in excitation–transcription coupling. The purpose of this review is to discuss the physiological roles of Ca^{2+} currents in cardiac myocytes. Next, we describe local regulation of Ca^{2+} channels by cyclic nucleotides. We also provide an overview of recent studies investigating the structure–function relationship of Ca^{2+} channels in cardiac myocytes using heterologous system expression and transgenic mice, with descriptions of the recently discovered Ca^{2+} channels α_{1D} and α_{1E}. We finally discuss the potential involvement of Ca^{2+} currents in cardiac pathologies, such as diseases with autoimmune components, and cardiac remodeling.

Keywords: Cardiac; Myocytes; Calcium current; L-type calcium channel; T-type calcium channel; Modulation; Auto immune; Remodeling

☆ Since the acceptance of this manuscript, a study showing a mutation in human $Ca_v1.2$ has appeared in Cell (Splawski et al., 2004). In this paper, the authors demonstrated that Timothy syndrome is linked to a missense mutation in $Ca_v1.2$ (G406R, at the end of S6 in the first domain, see Fig. 6). Interestingly, functional expression reveals that this mutation induces a gain of function by dramatically reducing the voltage dependent inactivation of the channel. Therefore, this mutation might explain the long QT observed in patient with this disorder.

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Contents

1. Introduction

The importance of extracellular Ca^{2+} in cardiac contraction has been known since the classical experiments of Ringer at the end of the XIXth century, which demonstrated that frog cardiac muscle cannot contract in Ca^{2+} free solutions (Ringer, 1883). More than half a century