

**The alterations of  $\text{Ca}^{2+}$ -activated  $\text{K}^+$  channels in coronary artery during cardiac hypertrophy**

Nari Kim<sup>1,2</sup>, Sang Kyeong Lee<sup>2</sup>, Joon-Yong Chung<sup>2</sup>, Dae-Hyun Seog<sup>2</sup>, Euiyong Kim<sup>1</sup>, Jin Han<sup>1,2</sup>

<sup>1</sup>Department of Physiology & Biophysics, <sup>2</sup>Molecular and Cell Physiology Research Group, College of Medicine, Inje University, Busan 614-735, Korea

It has been suggested that the impairment of smooth muscle cell (SMC) function by alterations in the  $\text{Ca}^{2+}$ -activated  $\text{K}^+$  ( $\text{K}_{\text{Ca}}$ ) channels accounts for the reduction in coronary reserve during left ventricular hypertrophy (LVH). However, this hypothesis has not been fully investigated. The main goal of this study was to assess whether the properties of  $\text{K}_{\text{Ca}}$  channels in coronary SMCs were altered during LVH. New Zealand white rabbits (0.8-1.0 kg) and Sprague-Dawley rats (300-400 g) were randomly selected to receive either an injection of isoproterenol (300  $\mu\text{g}/\text{kg}$  body weight) or an equal volume of 0.9% saline (1 mL/kg body weight). The animals developed LVH 10 days after injection. In patch-clamp experiments, the unitary current amplitude and open probability for the  $\text{K}_{\text{Ca}}$  channels were significantly reduced in LVH patches compared with control patches. The concentration-response curve of the  $\text{K}_{\text{Ca}}$  channel to  $[\text{Ca}^{2+}]_i$  was shifted to the right. Inhibition of the  $\text{K}_{\text{Ca}}$  channels with TEA was more pronounced in LVH cells than in the control cells. The whole-cell currents of  $\text{K}_{\text{Ca}}$  channels were reduced during LVH. Western blot analysis indicated no differences in  $\text{K}_{\text{Ca}}$  channel expression between the control and LVH coronary SM membranes. In contraction experiments, the effect of a high  $\text{K}^+$  concentration on the resting tension of the LVH coronary artery was greater than on that of the control. The effect of TEA on the resting tension of the LVH coronary artery was reduced as compared with the effect on the control. Our findings imply a novel mechanism for reduced coronary reserve during LVH.

Key words: LVH, reduced coronary reserve, smooth muscle cell,  $\text{K}_{\text{Ca}}$  channel