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Block of HERG Channels Expressed in *Xenopus* oocytes by External Ca^{2+}

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Rapidly activating delayed K current (IKr) in cardiac muscles plays an important role in repolarization. Expression of HERG cloned by the study on inherited LQT revealed that it encodes a potassium channel with biophysical properties similar to those of IKr in cardiac myocytes: outward currents activating on depolarization with large tail currents on repolarization, implying the inward rectifying property. We investigated the current of HERG expressed in *Xenopus* oocytes by using two microelectrode voltage clamp. Outward currents were activated by applying depolarizing step pulses from the holding potential of -60 mV. The amplitude of the outward current decreased and its activation started at more positive potential when external Ca^{2+} was increased. The activation of the tail current started at more positive potential and reached its maximum at more positive potential on increasing external Ca^{2+} . The time course of deactivation represented by the decay of tail current became faster, whereas that of activation became slower, as Ca^{2+} was increased. However, the inward rectifying property of HERG was independent on the Ca^{2+} concentration. To test whether the effect of external Ca^{2+} on HERG resulted from the surface charge effect, the activation curve of HERG in 2 mM K^+ Ringer was compared with that in 20 mM K^+ Ringer. Although there was no noticeable difference between them in high Ca^{2+} (5 mM), the shift of activation in low Ca^{2+} was larger in 20 mM K^+ than in 2 mM K^+ , implying that Ca^{2+} competes with K^+ . This result contradicts to the effect predicted by surface charge screening, but conforms to the competition of blocking ions with permeating ions to the same binding site. In summary, the external Ca^{2+} blocks the current of HERG, molecular equivalent of IKr.