TRPM4 IN VENTRICULAR MYOCARDIUM, CAN IT BE A NOVEL TARGET IN CARDIOVASCULAR DISEASE?

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TRPM4 is a unique member of melastatin subfamily of the transient receptor potential channels as it is permeable to only monovalent cations. TRPM4 is activated by the increase of intracellular Ca2+, PIP2, and membrane potential. The presence and role of TRPM4 in human cardiac conducting tissue is well established, but much less is known about TRPM4 in working myocardium. The controversial role of TRPM4 in ventricular hypertrophy, heart failure and ischemia-reperfusion injury will be discussed. A major difficulty of TRPM4 research is the need of a specific and selective inhibitor. Although TRPM4 knock-out animal models provide valuable information, they cannot be used in large animals like the dog, which is a good electrophysiological model of human heart. TRPM4 expression was low but detectable in ventricular myocardium in rats and mice, and we show TRPM4 protein expression in canine isolated left ventricular cells. We recorded APs in isolated left ventricular canine cells using sharp microelectrode and applied whole-cell patch clamp technique in both conventional and AP voltage clamp modes. We described poor selectivity of both the recently discovered CBA and the previously widely used 9-phenanthrol. CBA proved to be slightly better as it blocked Ito and late sodium currents, while 9-phenanthrol reduced many major potassium currents including Ito, IK1, and IKr. The contribution of TRPM4 to canine cardiac AP still needs to be further studied. Clearly more experiments are needed to establish TRPM4 as a novel ventricular target of cardiovascular diseases.

Keywords: TRPM4, CBA, 9-phanenthrol, action-potential, canine left ventricular cell

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