

## Effects of thrombospondin-4 on voltage-gated ion channels in rat ventricular myocytes

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Thrombospondin (TSP)-4, a matricellular protein, is highly expressed in heart tissues of various cardiac disease models. Although TSP-4 is known to regulate voltage-dependent calcium channel activity in dorsal root ganglionic neurons, it remains to be clarified whether it affects electrical activity in cardiomyocytes. We examined the effects of TSP-4 on voltage-gated ion channels in rat ventricular myocytes. Ventricular myocytes isolated from male Wistar rats were seeded on a glass plate coated with laminin. Recombinant mouse TSP-4 (5 nM) or its vehicle was treated for 4 hours. L-type calcium channel (LTCC) current, voltage-gated potassium channel (VGKC) current, and action potential duration (APD) were measured by a whole-cell patch-clamp method. TSP-4 inhibited both currents of LTCC and VGKC. TSP-4 tended to prolong APD<sub>50</sub> and APD<sub>90</sub>. This study for the first time demonstrated that TSP-4 inhibits the activity of LTCC and VGKC, which consequently leads to APD prolongation. The APD prolongation might be partly due to the suppression of VGKC activity because the inhibition of LTCC should lead to an APD shortening. It is suggested that TSP-4 might be related to the ventricular arrhythmia via regulating voltage-gated ion channels.