# Cardiovascular functions of renal tubule- and vascular smooth muscle-specific transgenic mice expressing dominant negative TRPM7 mutant

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Magnesium ion ($Mg^{2+}$) is an essential divalent cation and cellular $Mg^{2+}$ concentration is tightly regulated by various $Mg^{2+}$ channels/transporters. Therefore, dysfunction of $Mg^{2+}$ channels/transporters may lead to a variety of cardiovascular or neuromuscular disorders. TRPM7 is a non-selective cation channel, which predominantly permeates $Mg^{2+}$ under physiological conditions. We generated tissue-specific transgenic mouse models expressing the dominant negative TRPM7 mutant (TRPM7DN-Tg) to study the physiological and pathophysiological mechanisms of $Mg^{2+}$ regulation. Whole-cell patch-clamp recordings revealed that TRPM6/7 currents in HEK293 cells were almost completely attenuated by co-expression of TRPM7DN mutant. Renal tubule-specific TRPM7DN-Tg exhibited dysregulation of serum $Mg^{2+}$ level and urinary $Mg^{2+}$ excretion. Interestingly, in these mice, phenylephrine (PE)-induced vascular contractile responses was significantly attenuated. On the other hand, vascular smooth muscle-specific TRPM7DN-Tg showed attenuation of PE-induced contractile responses without changing serum $Mg^{2+}$ level and urinary $Mg^{2+}$ excretion. These results suggest that TRPM6/7 channels are tissue-dependently involved in the regulation of $Mg^{2+}$ homeostasis and vascular contraction. Our tissue-specific TRPM7DN-Tg will be useful animal models for studying magnesium disorders.