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Role of Vascular Smooth Muscle Cell Transferrin Receptor 1 in Salt Sensitive Hypertension

Yoshiro Naito, Masaharu Ishihara

Department of Cardiovascular and Renal Medicine, School of Medicine, Hyogo Medical University

Summary

Background: We have shown that a cellular iron transport protein, transferrin receptor 1 (TfR1) is linked to hypertensive vascular remodeling in salt sensitive hypertensive rats. However, the role of TfR1 in the pathophysiology of hypertensive vascular remodeling remains obscure. In this study, we assessed the role of TfR1 in hypertensive vascular remodeling using vascular smooth muscle cells (VSMC) specific TfR1 knockout mice.

Methods and Results: To assess the role of TfR1 in VSMC in the pathophysiology of hypertensive vascular remodeling, we generated inducible VSMC specific TfR1 deleted mice. Inducible VSMC specific TfR1 deleted mice are generated by crossing mice expressing a fusion protein of Cre recombinase with the modified estrogen receptor ligand binding domain ($CreER^{T2}$) under the control of the smooth muscle myosin heavy chain (Myh11-$CreER^{T2}$) with TfR1Flox/Flox mice. The VSMC TfR1 deletion is induced by treating Myh11-$CreER^{T2}$/$TfR1^{Flox/Flox}$ mice with the estrogen receptor antagonist tamoxifen. Systolic blood pressure and aortic morphology were not different between inducible VSMC specific TfR1 deleted mice and control mice. Then, deoxycorticosterone acetate (DOCA)-salt hypertension was induced in inducible VSMC specific TfR1 deleted mice and control mice by uninephrectomy and administration of DOCA and 0.9% NaCl in the drinking water. Systolic blood pressure was elevated similarly in both control and inducible VSMC specific TfR1 deleted mice after DOCA-salt administration; however, hypertensive vascular remodeling was increased to a lesser extent in inducible VSMC specific TfR1 deleted mice compared to control mice.

Conclusions: These results suggest that TfR1 in VSMC plays a role in the pathophysiology of hypertensive vascular remodeling in salt sensitive hypertension.