

## **SIGNIFICANCE STATEMENT**

Intronic variants of *MYH9* gene are associated with diabetic nephropathy and sickle cell disease-associated nephropathy. The *MYH9* E1841K mutation is a common *MYH9* missense mutation characterized by macrothrombocytopenia and associated with the development of kidney disease. This paper reports the effect of the E1841K mutation in two mouse models of kidney injury. Mice with two copies of the *MYH9 E1841K* alleles had accelerated podocyte foot effacement and albuminuria in angiotensin II-induced hypertension, and severe glomerulosclerosis in the reduced nephron mass model of CKD. Furthermore, the mutation induces a migratory phenotype in podocytes in culture. Delineating the role of *MYH9* in podocytes may improve the understanding of nephropathy in diabetes and sickle cell, and identify novel therapeutic targets