

SIGNIFICANCE STATEMENT

Although the genetics of CKD are beginning to be deciphered, interpretation of how variants result in disease remains a challenge that is increasing as more and more genomes are being sequenced. In this paper, we use our workflow designed to assess variants to develop mechanistic insights into CKD variants, highlighting new knowledge of both common noncoding and rare coding variants within *SHROOM3*. The detailed knowledge gleaned for function of SHROOM3 in podocytes advances novel pathways and mechanisms for CKD.