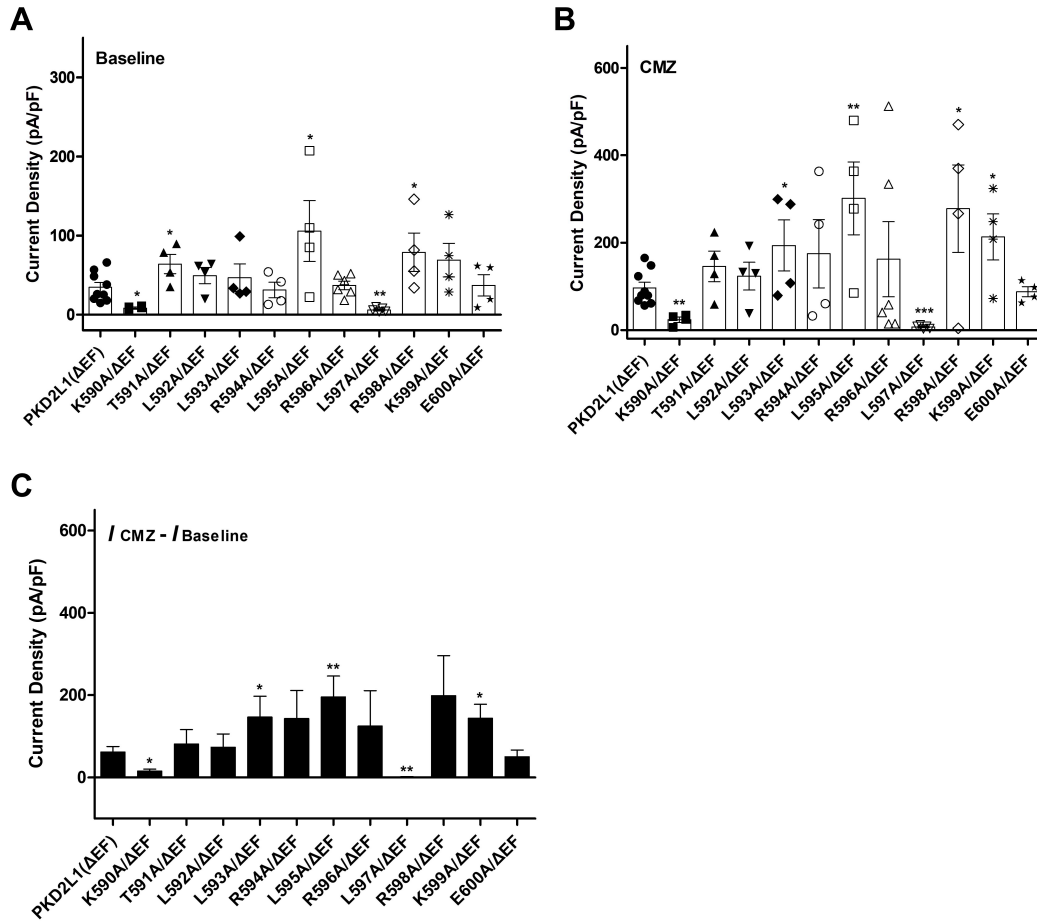


**Supplementary Fig. 1. The effects of calmidazolium (CMZ) on putative calmodulin-binding domain (CaMBD) (K590-E600) single mutants under 100 nM intracellular free calcium concentration.** (A) A summarized basal current amplitude of PKD2L1 and single mutants under 100 nM free  $Ca^{2+}$  (n = 4–17). (B) A summarized CMZ-induced current amplitude of PKD2L1 and single mutants under 100 nM free  $Ca^{2+}$  (n = 4–17). (C) A summarized current changes of PKD2L1 and single mutants by CMZ under 100 nM free  $Ca^{2+}$ . \*p < 0.05.



**Supplementary Fig. 2. The effects of calmidazolium (CMZ) on putative calmodulin-binding domain (CaMBD) (K590-E600)/ΔEF mutants under 100 nM intracellular free calcium concentration.** (A) A summarized basal current amplitude of PKD2L1 (ΔEF) and mutants under 100 nM free  $\text{Ca}^{2+}$  ( $n = 4-6$ ). (B) A summarized CMZ-induced current amplitude of PKD2L1 (ΔEF) and mutants under 100 nM free  $\text{Ca}^{2+}$  ( $n = 4-6$ ). (C) A summarized current changes of PKD2L1 (ΔEF) and mutants by CMZ under 100 nM free  $\text{Ca}^{2+}$ . \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

		1-----10
		^          ^
<b><i>hTRPV1</i></b> (768-802)*	EGVKRTLSFSLRSSRVSGRHW-KNFALVPLLRREASA	
<b><i>mTRPV1</i></b> (768-802)*	EGVKRTLSFSLRSGRVSGRNW-KNFALVPLLRDAST	
<b><i>rTRPV1</i></b> (767-801)	EGVKRTLSFSLRSGRVSGRNW-KNFALVPLLRDAST	
<b><i>hPKD2L1</i></b> (584-610)		<u>L-KQGYNKTLRLRLR</u> LRKEFVSDVQKVLQ
<b><i>mPKD2L1</i></b> (584-610)		L-KQSYNKTLRLRLRLRKEFVSDVQKVLK

**Supplementary Fig. 3. Protein sequence alignment of polycystic kidney disease 2-like-1 (PKD2L1) with transient receptor potential vanilloid 1 (TRPV1).** An alignment of putative calmodulin-binding domain (CaMBD) of PKD2L1 and CaMBD of TRPV1 with identical residues shaded in gray. The putative CaMBD of PKD2L1 is underlined and the anchor residue is marked in red. Asterisks are unpublished and similar sequences with the CaMBD of rTRPV1.