



Extended Data Figure 8 | Comparison of cryo-EM and crystal structures of rTRPV6, cryo-EM structures of hTRPV6(R470E) and rTRPV6 and regions in hTRPV6 and hTRPV6(R470E) encompassing D489 and T581. **a–c**, Superimposed are the transmembrane domain of a single subunit (**a**), and the pore-forming region viewed parallel to the membrane (**b**) or intracellularly (**c**) from the cryo-EM (green) and crystal (orange) structures of rTRPV6. Only two of four rTRPV6 subunits are shown in **b**, with the front and back subunits omitted for clarity. Residues lining the selectivity filter and gate are shown as sticks. **d**, **e**, Superposition of the P loop and S6 in cryo-EM structures of hTRPV6(R470E) (blue) and

rTRPV6 (green), viewed parallel to the membrane (**d**) and intracellularly (**e**). In **d**, only two of four subunits are shown, with the front and back subunits removed for clarity. The residues lining the pore are shown as sticks. **f**, **g**, Regions in hTRPV6 (**f**) and hTRPV6(R470E) (**g**) encompassing D489 and T581. The closest distance between D489 and T581 is indicated by dashed lines. Note, M485 and M577 either surround the potentially interacting D489 and T581 (**f**, hTRPV6) or reside between these residues (**g**, hTRPV6(R470E)), apparently preventing their interaction. Blue mesh shows cryo-EM density at 4σ .