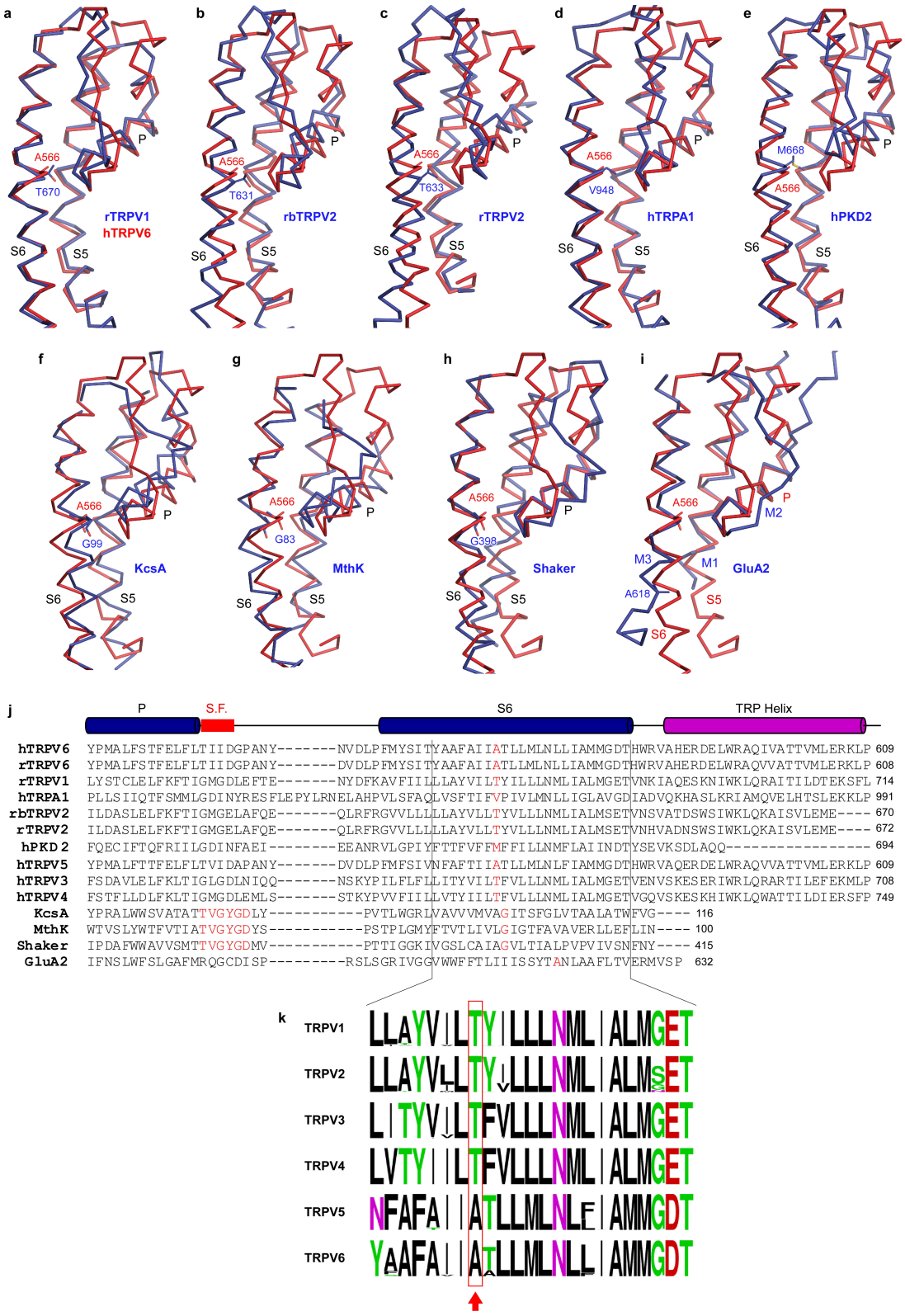

Extended Data Figure 9 | Structural superposition and sequence alignment of the pore domain in tetrameric ion channels. a–i, Pairwise superposition of the pore domain in hTRPV6 with rat TRPV1[18] (**a**, PDB ID: 5IRX; r.m.s.d. = 2.065 Å); rabbit TRPV2[21] (**b**, PDB ID: 5AN8; r.m.s.d. = 3.757 Å); rat TRPV2[24] (**c**, PDB ID: 5HI9; r.m.s.d. = 4.399 Å); human TRPA1[23] (**d**, PDB ID: 3J9P; r.m.s.d. = 1.429 Å); human PKD2[25] (**e**, PDB ID: 5T4D; r.m.s.d. = 2.676 Å); KcsA from *Streptomyces lividans*[47] (**f**, PDB ID: 1BL8; r.m.s.d. = 2.708 Å); MthK from *Methanothermobacter thermautotrophicum*[48] (**g**, PDB ID: 1LNQ; r.m.s.d. = 2.947 Å); rat Shaker[49] (**h**, PDB ID: 2A79; r.m.s.d. = 2.487 Å); and rat GluA2 AMPA-subtype iGluR[28] (**i**, PDB ID: 5WEO; r.m.s.d. = 2.044 Å). **j**, Sequence alignment for the pore region of human TRPV3–TRPV6, TRPA1 and PKD2, rat TRPV1, 2, and 6, Shaker and GluA2, rabbit TRPV2 and bacterial K^+ channels KcsA and MthK. The selectivity filter residues in K^+ channels and gating hinge residues in S6 (M3 in GluA2) are coloured red. **k**, Aligned sequence logos for TRPV channels in S6, generated by WebLogo[50] from 1,200 TRPV1–TRPV6 sequences. The red rectangle and arrow indicate the position of the alanine gating hinge in TRPV6. The relatively small side chain residues threonine or alanine next to the gating hinge alanine position in TRPV5 and TRPV6, instead of the bulky hydrophobic phenylalanine or tyrosine in TRPV1–TRPV4, might be critical for the α-to-π-helical transition in S6 during channel opening.