

Supplementary Information

Molecular Basis for Cold and Menthol Sensing by mammalian TRPM8

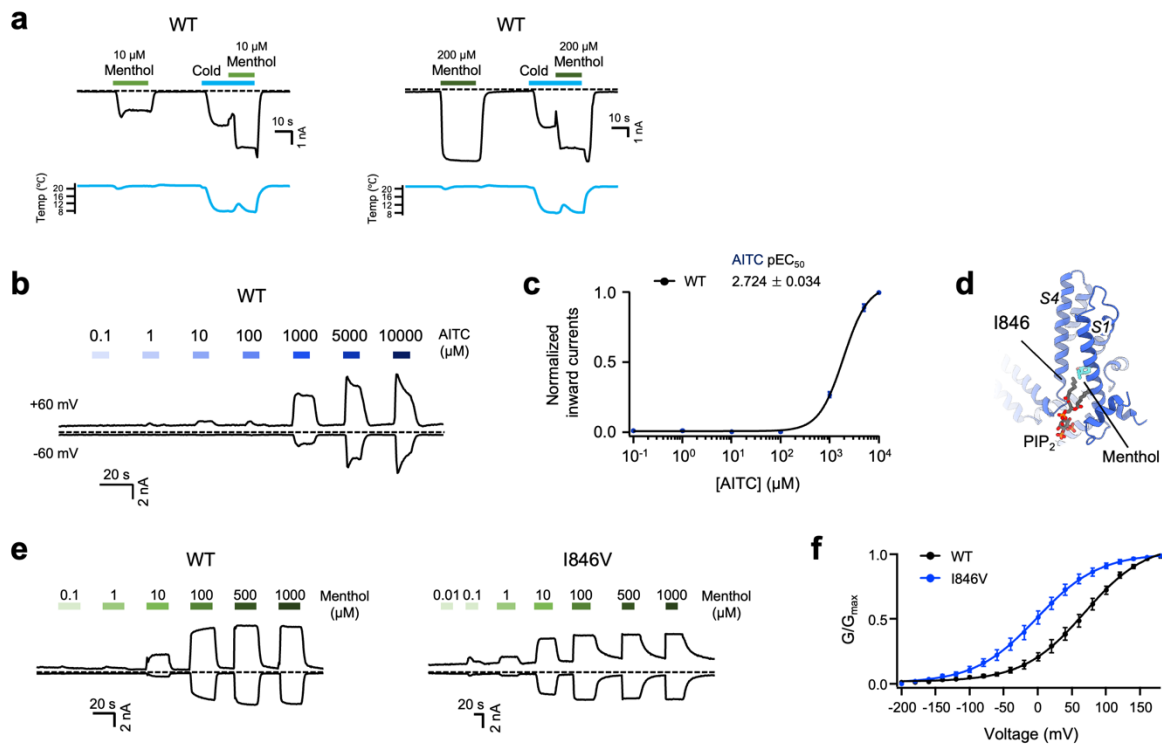
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Seok-Yong Lee

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Supplementary Figs 1–15

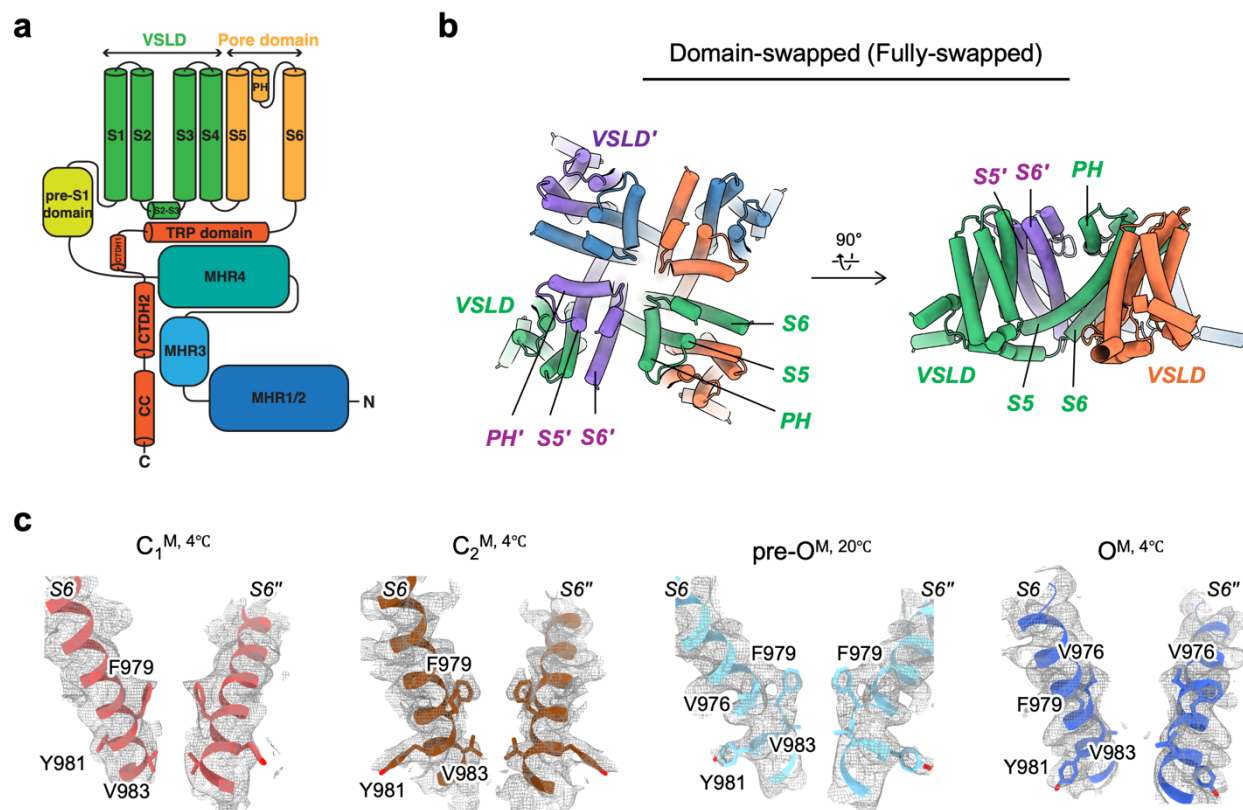
Supplementary Table 1

Supplementary Figures

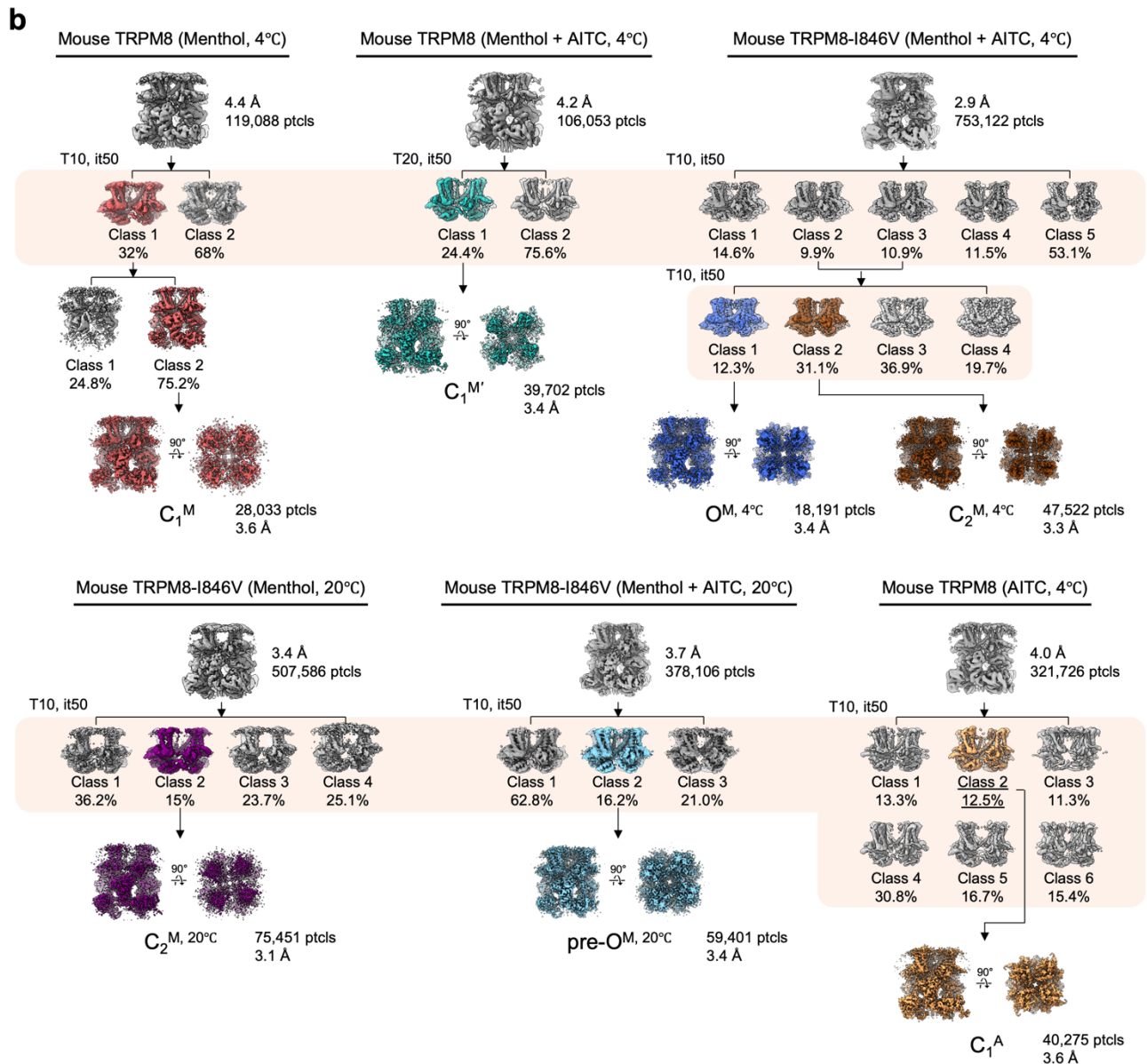
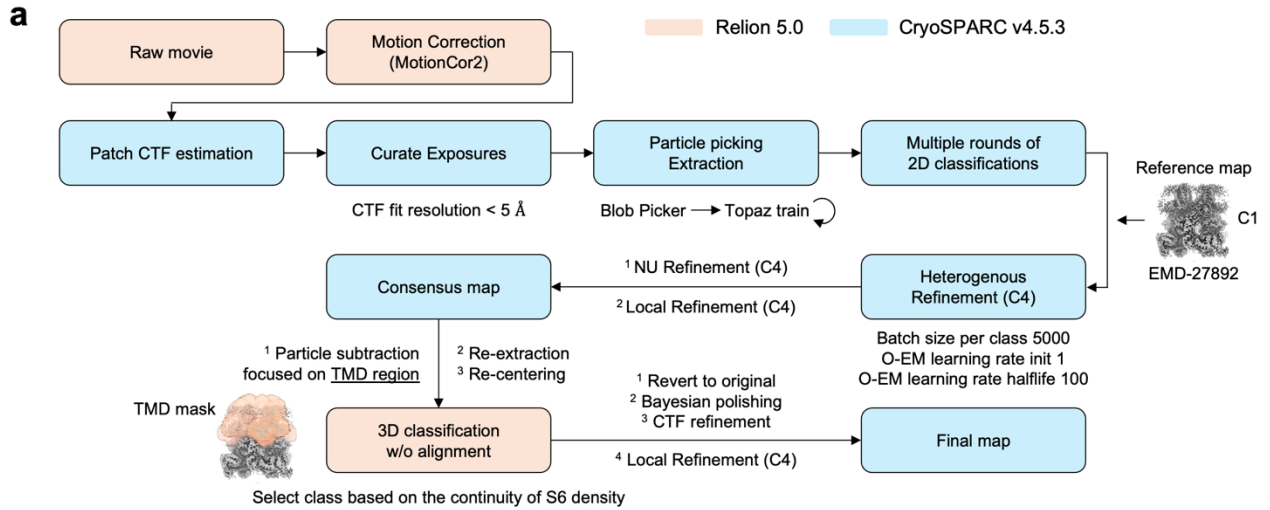


Supplementary Fig. 1 | Synergistic activation of TRPM8 by cold and menthol, and channel sensitizing mutant I846V. **a**, Representative current traces, as in Fig. 1a, demonstrating the effect of 10 μ M and 200 μ M menthol alone and when co-applied with cold. Horizontal colored lines represent the application of cold (sky blue), 1 μ M menthol (light green), and 200 μ M menthol (green), as indicated. Dotted lines indicate the zero-current level. **b**, Representative currents of the WT mTRPM8 at -60 mV (lower traces) and +60 mV (upper traces) in HEK293T cells at $\sim$ 20 $^{\circ}$ C in response to increasing concentrations of AITC. Dotted lines indicate the zero-current level. **c**, Concentration-response curve of AITC activation derived from whole-cell recordings at -60 mV. Data points were normalized to the maximal response and represent the mean $\pm$ SEM ($n = 6$ biological replicates). The continuous curves were fit to the Hill equation, and the corresponding pEC₅₀ value (pEC₅₀ = -log₁₀[EC₅₀ in M]) indicated in the figure. **d**, mTRPM8 VSLD (S1-S4 in cartoon) showing the relative position of I846 to the menthol and PIP₂ sites. **e**, Representative currents of the WT and I846V of mTRPM8 at -60 mV (lower traces) and +60 mV (upper traces) in HEK293T cells at $\sim$ 20 $^{\circ}$ C in response to increasing concentrations of menthol. Dotted lines indicate the zero-current level. **f**, G-V relationships of the WT ($n = 8$ biological replicates) and

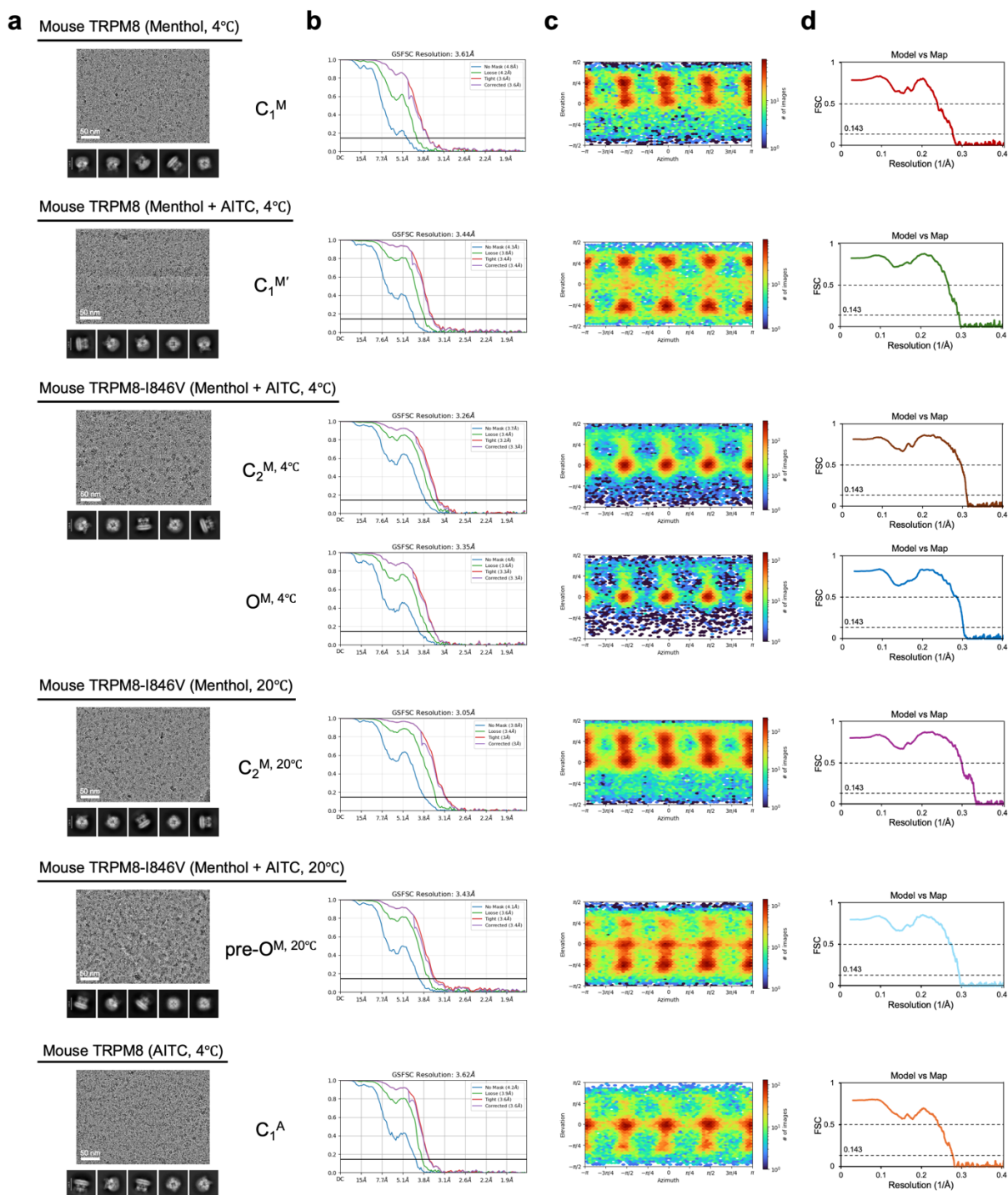
I846V ($n = 11$ biological replicates) of mTRPM8 obtained from peak tail currents and fitted with Boltzmann functions. Data are mean $\pm$ SEM. Source data are provided as a Source Data file.



Supplementary Fig. 2 | Overall and pore architecture of TRPM8. **a**, Protomer topology illustrated schematically. **b**, Structure of TMD region is depicted as cartoons, with neighboring protomers distinctly colored to highlight that the pore domain from one protomer is intercalated between the VSLD and pore domain of its neighbor (fully-swapped). **c**, For structural comparison, opposing S6 helices from $C_1^M, 4^\circ\text{C}$ (red), $C_2^M, 4^\circ\text{C}$ (brown), $\text{pre-O}^M, 20^\circ\text{C}$ (sky blue), and $\text{O}^M, 4^\circ\text{C}$ (blue) states are shown as cartoons. Grey meshes represent the corresponding EM densities of the S6 helices. Residues surrounding the S6 gate are shown as sticks and labeled.



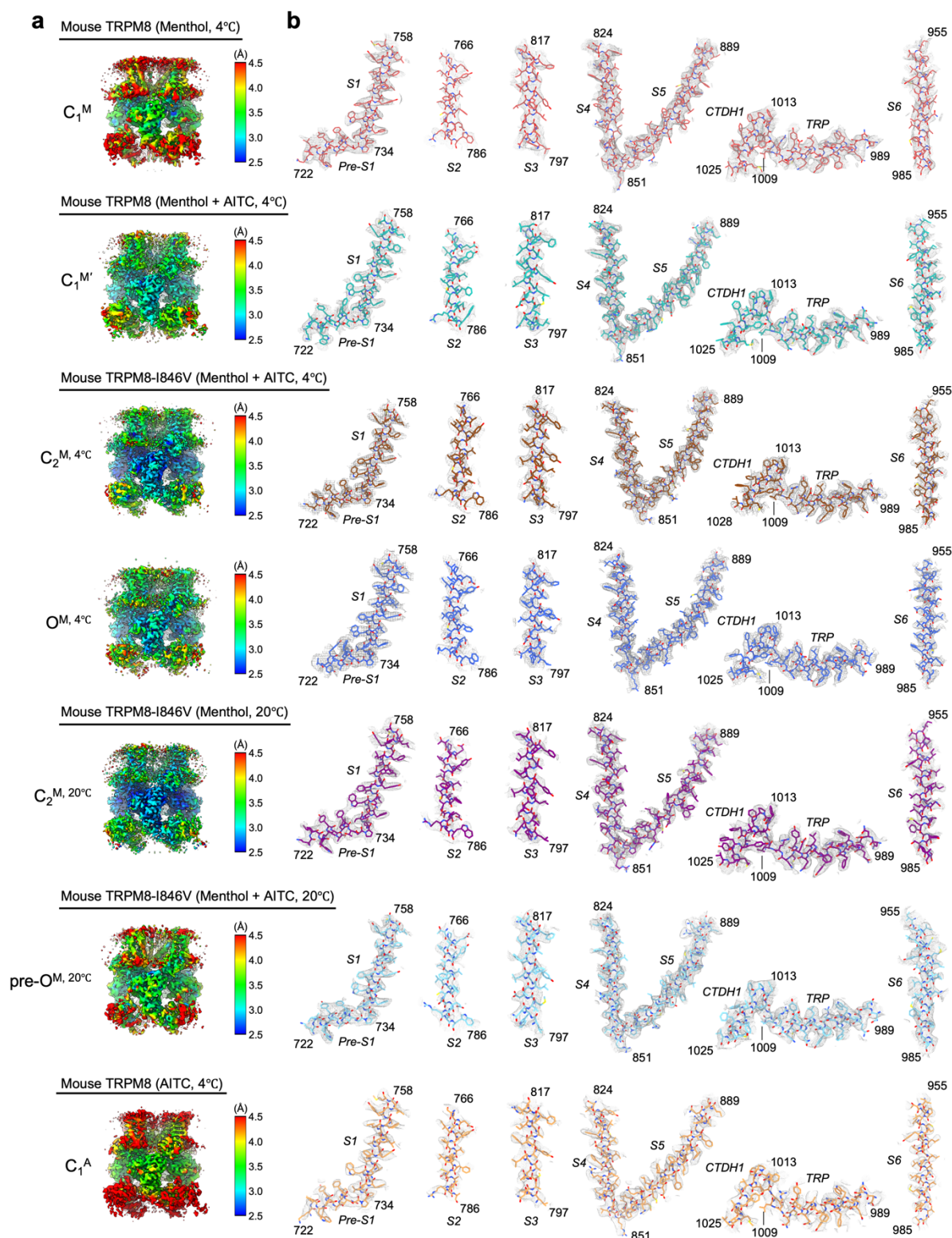
Supplementary Fig. 3 | Cryo-EM data processing workflow. **a**, Overview of the cryo-EM image processing pipeline employed to determine TRPM8 structures presented in this study. Due to the intrinsic flexibility of the pore domain, the workflow specifically targets heterogeneity within the transmembrane domain (TMD) through focused 3D classification without alignment. Classes for subsequent processing were selected based on the clear continuity of the S6 helix density. **b**, For all datasets, TMD-focused classification was performed using varying parameters in RELION, followed by final map reconstruction in CryoSPARC. Detailed procedures are described in the Methods.



Supplementary Fig. 4 | Representative micrographs, 2D class averages, and FSC curves.

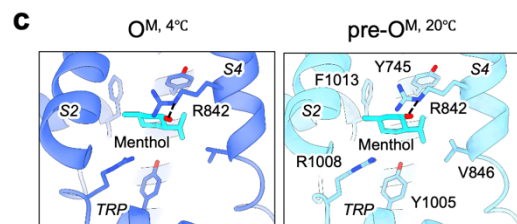
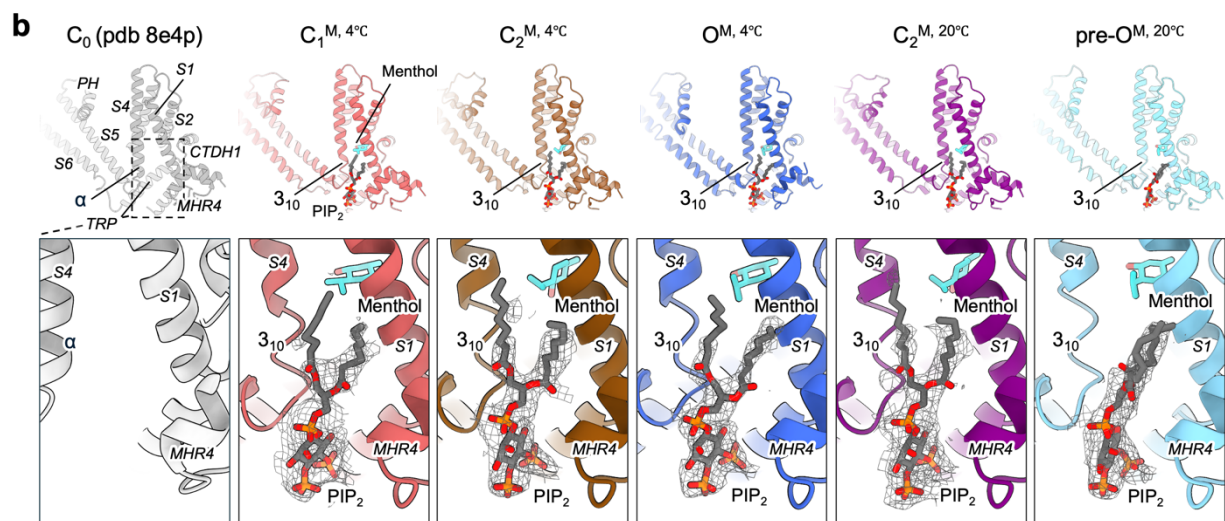
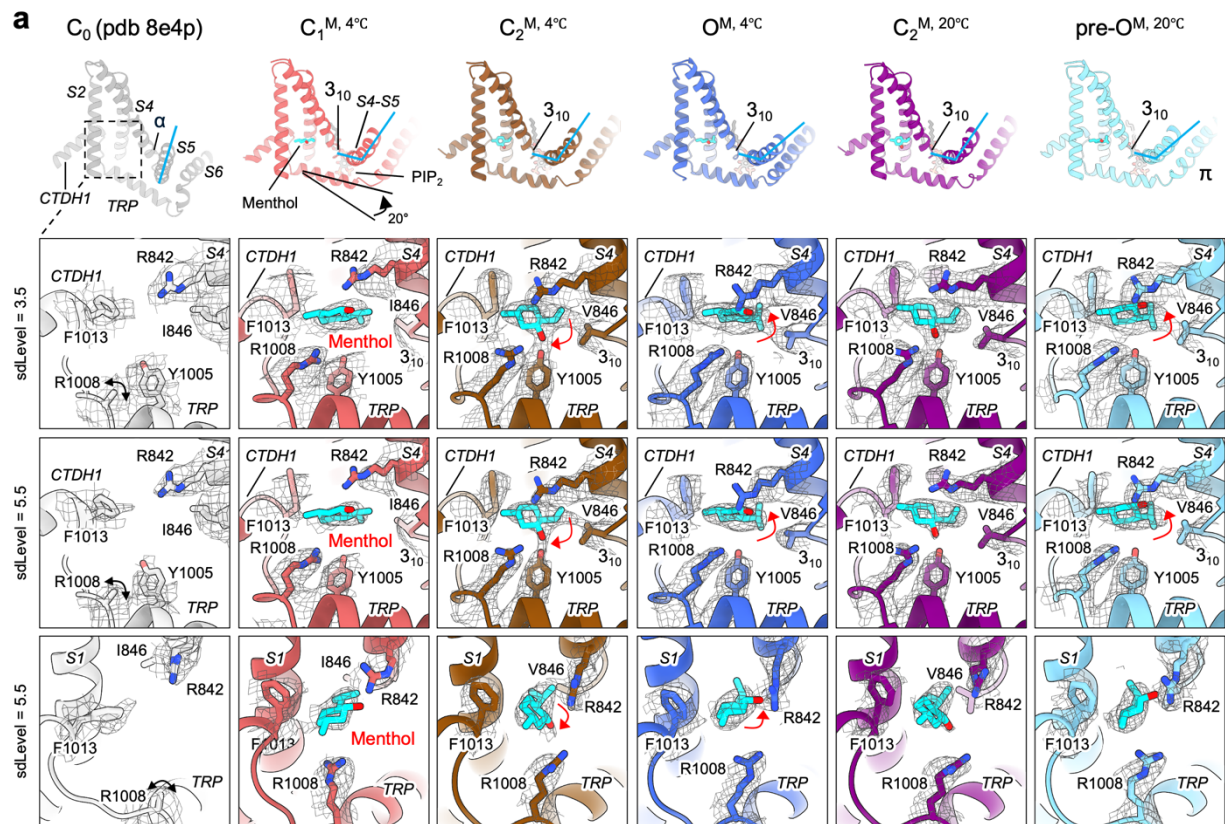
a, For each dataset, a representative micrograph, five 2D class averages, a plot showing the distribution of particle orientations, and a Fourier shell correlation (FSC) plot of the final map are presented from left to right, respectively. FSC curves between two half-maps were calculated using

the 0.143 criterion. **b**, For each dataset, FSC curves comparing the final model to the corresponding map are shown.



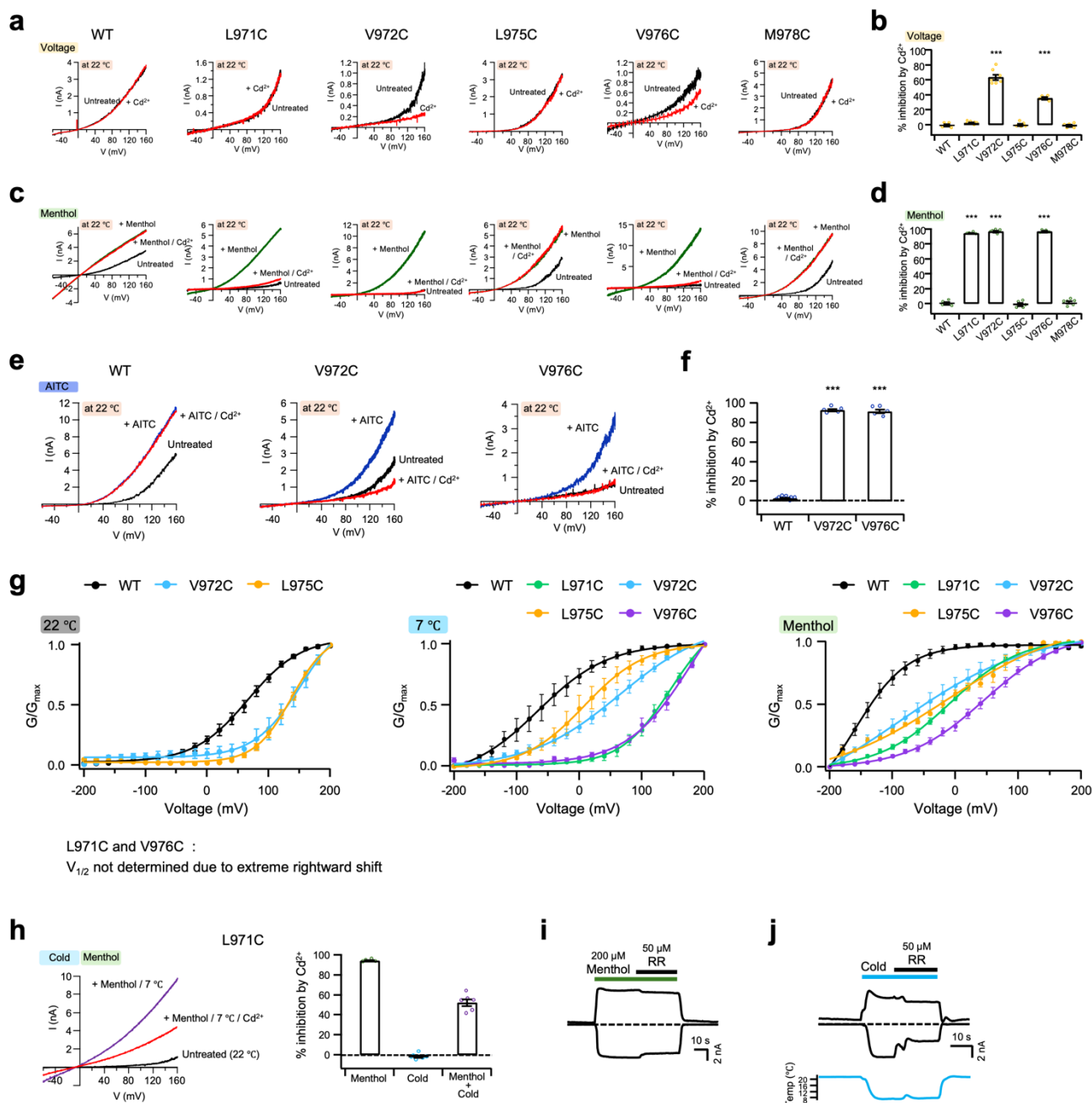
Supplementary Fig. 5 | Quality of cryo-EM maps. a, Final cryo-EM maps colored according to local resolution estimates. The color scale indicates local resolution in Å, as shown in the

accompanying bar. **b**, Densities corresponding to the transmembrane domain (TMD) regions of each structure are displayed as grey meshes overlaid with the corresponding atomic models.



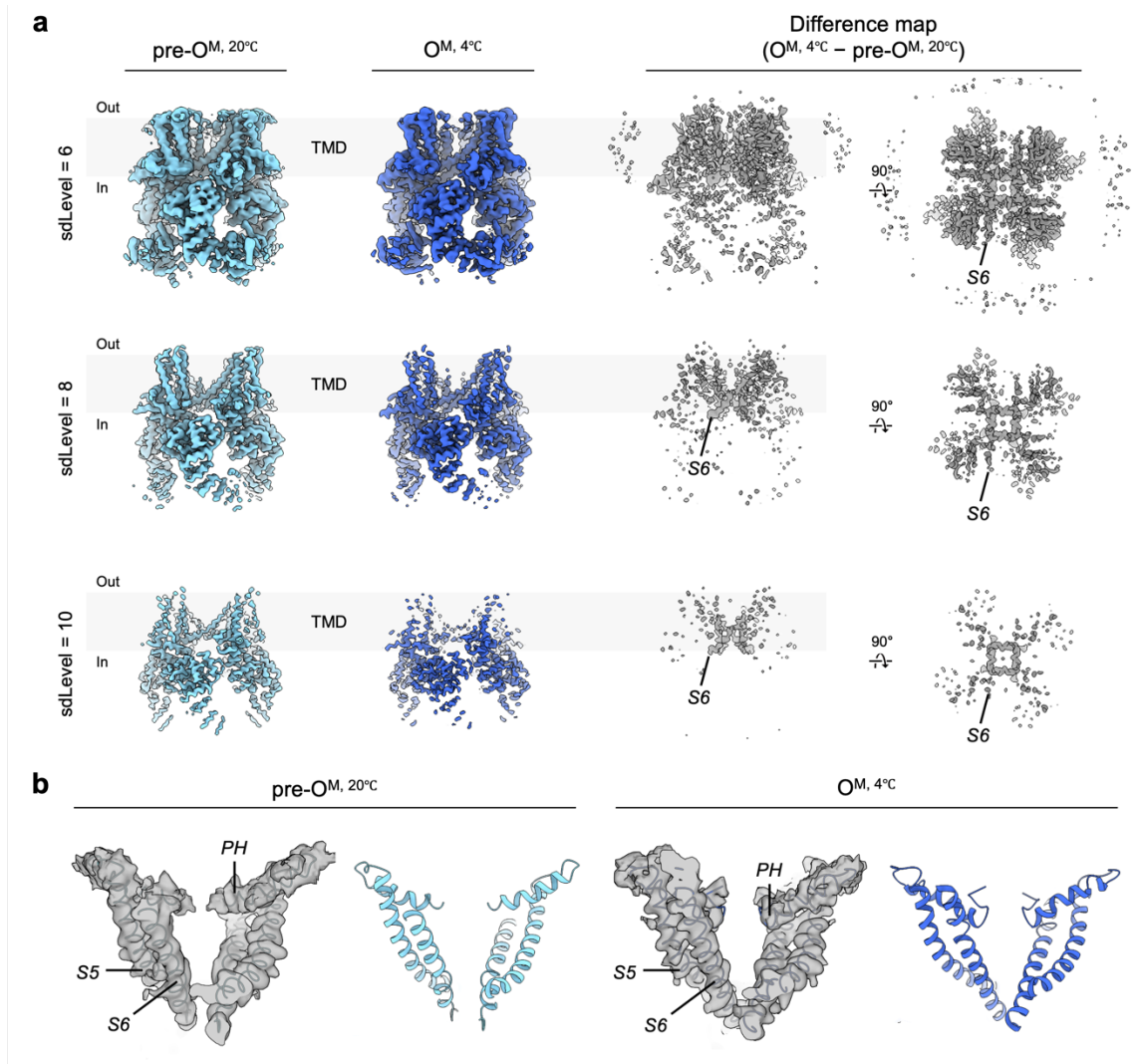
Supplementary Fig. 6 | PIP₂ and menthol binding modes across different states. a,b, Structural comparison between C₀ (PDB 8E4P; grey), C₁^{M,4°C} (red), C₂^{M,4°C} (brown), O^{M,4°C} (blue), C₂^{M,20°C} (purple) and pre-O^{M,20°C} (sky blue) states, shown as cartoons. Hallmark conformational changes are highlighted in the upper section: binding of PIP₂ and menthol, movement of the TRP helix, S4-S5/S5 movement, and helical transition in the cytoplasmic half of S4 (S4b). S4b is shown as an α -helix in C₀, and as a 3₁₀-helix in other states. Menthol and interacting residues are depicted as sticks and labeled. EM densities corresponding to menthol (**a**) and PIP₂ (**b**) from each structure are depicted as grey mesh. Menthol and PIP₂ are shown as cyan and grey sticks, respectively. One-sided arrows indicate rotation of menthol. **c,** No significant differences in menthol binding pose or interactions between O^{M,4°C} and pre-O^{M,20°C}.

at distinct positions in S6 among the pre-O^{M,20°C}, O^{M,4°C}, and D (PDB: 9B6F) states. In view 1, L841 in S4, L864 in S4–S5, and L970 in the neighboring S6 (S6') are depicted as sticks. Black dashed lines indicate hydrophobic interaction networks, while black arrows highlight rotations of S6 helix and rotation of residues. In view 2, R862 in S4–S5 and N990 in the TRP domain are shown as sticks, with putative hydrogen bonds indicated by black dashed lines. This interaction is lost as the channel transitions towards opening and desensitization.

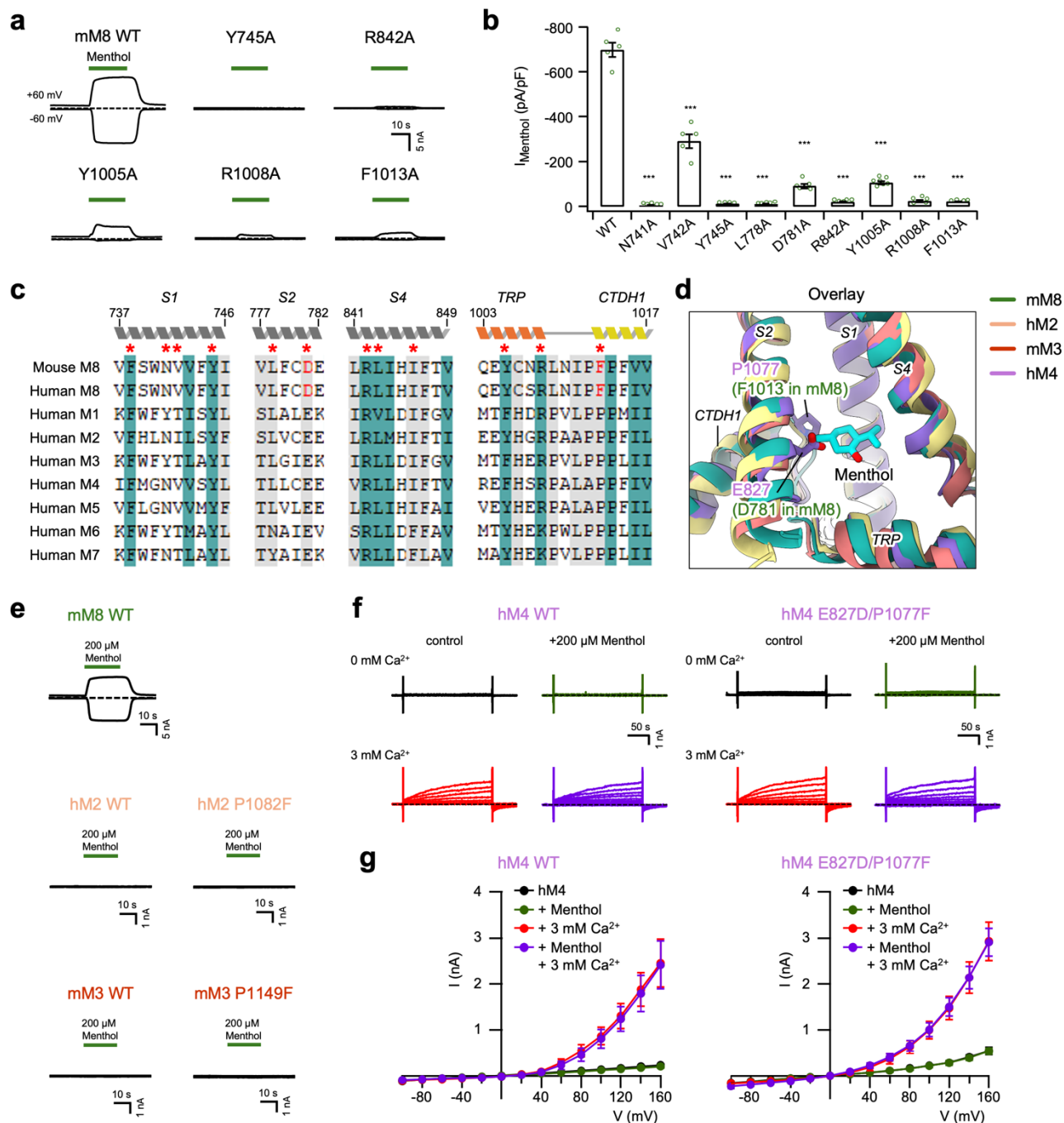


Supplementary Fig. 8 | Cd^{2+} block of cysteine mutant scanning of S6. **a**, Representative I-V plots of mTRPM8 WT and cysteine mutants using a 300-ms voltage ramp from -60mV to +160mV, Traces show basal currents (black), followed by 20 μ M Cd^{2+} (red). **b**, Cd^{2+} inhibition of basal current at +160mV. n = 4 (WT, V976C), n = 5 (L975C, M978C), n = 6 (L971C), n = 7 (V972C). *** P < 0.001, one-way ANOVA with Dunnett's multiple-comparisons test. Adjusted P values (WT vs mutant): L971C, P = 0.8441; V972C, P = $< 1.0 \times 10^{-15}$; L975C, P = 0.9997; V976C, P = 4.3×10^{-9} ;

M978C, $P=0.9997$. **c**, Representative I-V plots of WT and cysteine mutants showing basal currents (black), 200 μ M menthol (green), and 200 μ M menthol with 20 μ M Cd²⁺(red). **d**, Cd²⁺ inhibition of menthol-evoked current at +160mV. $n=4$ (WT, L971C, V976C), $n=5$ (V972C, L975C), $n=6$ (M978C). *** $P<0.001$, one-way ANOVA with Dunnett's multiple-comparisons test. Adjusted P values (WT vs mutant): L971C, $P=6.0\times 10^{-15}$; V972C, $P=6.0\times 10^{-15}$; L975C, $P=0.8612$; V976C, $P=6.0\times 10^{-15}$; M978C, $P=0.9675$. **e**, Representative I-V plots of WT and cysteine mutants showing basal currents (black), 2mM AITC (deep blue), and 2mM AITC with 20 μ M Cd²⁺(red). **f**, Cd²⁺ inhibition of 2mM AITC-evoked current at +160mV. $n=8$ (WT), $n=5$ (V972C, V976C). *** $P<0.001$, one-way ANOVA with Dunnett's multiple-comparisons test. Adjusted P values (WT vs mutant): V972C, $P=<1.0\times 10^{-15}$; V976C, $P=<1.0\times 10^{-15}$. **g**, G-V relationships of WT and cysteine mutants of mTRPM8, obtained from peak tail currents and fitted with Boltzmann functions: at 22°C [$n=8$ (WT), $n=4$ (V972C), $n=11$ (L975C)], 7°C [$n=4$ (WT), $n=3$ (L971C, V972C, V976C), $n=6$ (L975C)], and 200 μ M menthol [$n=7$ (WT, L971C), $n=4$ (V972C), $n=3$ (L975C), $n=11$ (V976C)]. **h**, Representative I-V plots of L971C showing basal currents (black), cold (7°C) with 200 μ M menthol (blue), and co-application of cold, 200 μ M menthol and 20 μ M Cd²⁺(red). Cd²⁺ inhibition of currents evoked by cold, menthol, or both at +160mV. $n=4$ (menthol), $n=6$ (cold, menthol+cold). *** $P<0.001$, one-way ANOVA with Dunnett's multiple-comparisons test. $P=2.6\times 10^{-12}$ (cold vs menthol), $P=9.7\times 10^{-10}$ (cold vs menthol+cold). **i, j**, Representative WT currents at -60mV and +60mV induced by 200 μ M menthol (**i**) or 7°C cooling (**j**), followed by 50 μ M RR (black). Dots indicate individual biological replicates where shown. Data are mean $\pm$ SEM. Source data are provided as a Source Data file.

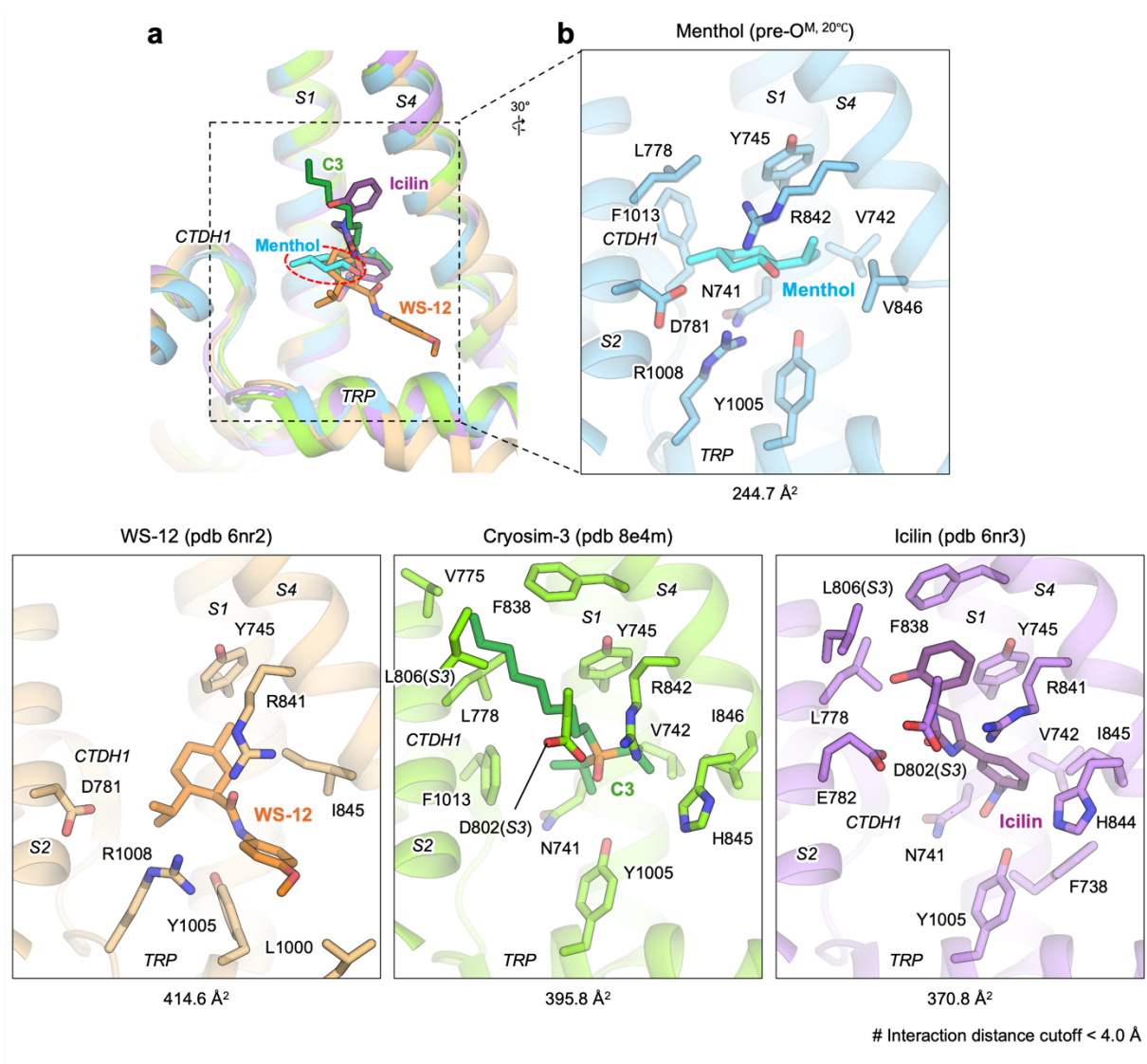


Supplementary Fig. 9 | Density comparison between pre-O^M, 20°C and O^M, 4°C. **a**, Overall EM densities of pre-O^M, 20°C (sky blue) and O^M, 4°C (blue) are shown side by side at three contour levels (sdLevel = 6, 8, and 10; top to bottom) for fair comparison. Difference maps between pre-O^M, 20°C and O^M, 4°C (blue) are displayed at the same contour levels in side (left) and top (right) views. Conformational differences are predominantly observed in the pore region relative to the cytoplasmic regions. **b**, Cα traces of S5-PH-S6 in pre-O^M, 20°C and O^M, 4°C are shown as cartoons overlaid with transparent EM density, highlighting the pronounced tilt of PH. Due to limited local resolution in this region, EM densities are shown from unsharpened maps.



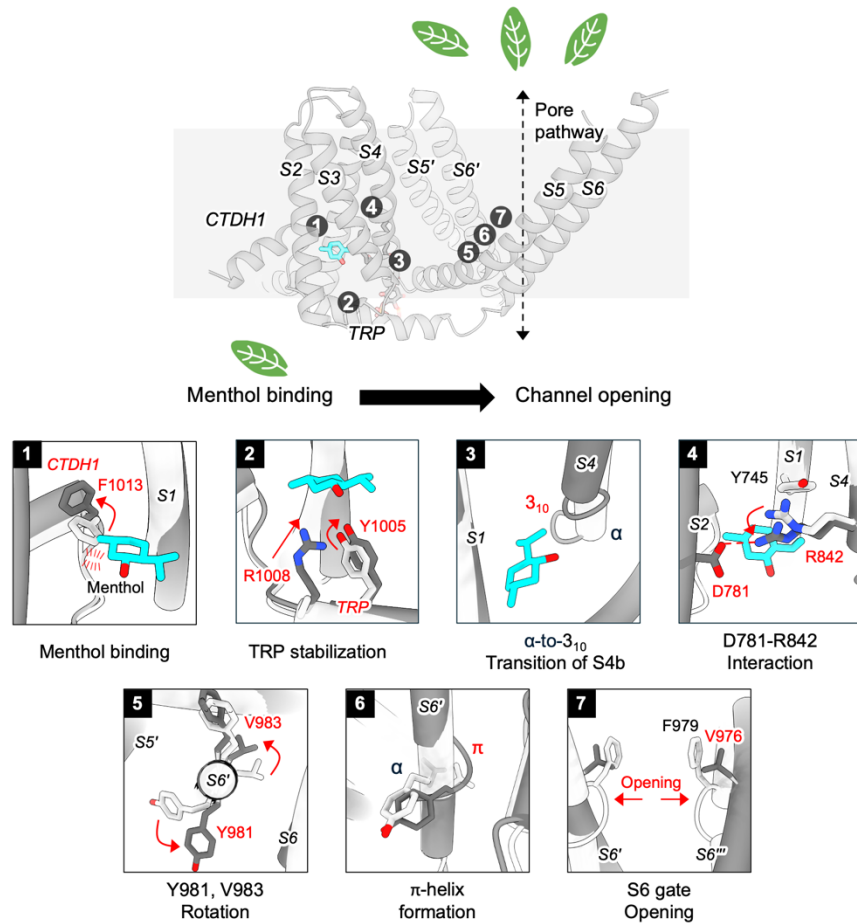
Supplementary Fig. 10 | Specificity of menthol binding on TRPM8. **a**, Representative currents of the mTRPM8 WT and menthol binding site mutants at -60mV and +60mV. Colored lines indicate application of 200μM menthol (green). **b**, Menthol-evoked inward current densities (pA/pF) for WT and menthol site mutants. $n=4$ (Y745A, F1013A), $n=5$ (WT, N741A, V742A, L778A, D781A, R842A, R1008A), $n=7$ (Y1005A). Cells transfected with same amounts of cDNA.

Dots indicate biological replicates. *** $P < 0.001$, one-way ANOVA with Dunnett's multiple-comparisons test. Adjusted P values provided in the Source Data file. Data are mean $\pm$ SEM. **c**, Sequence alignment of human TRPM channels. Residues with 100% and 80% conservation are shaded in green and light grey, respectively. Menthol binding residues within the VSLD are marked with red asterisks. D781 and F1013, in red, are uniquely conserved in TRPM8 among the TRPM family. **d**, Structural alignment of mTRPM8 (C₁^{M,4°C'}) menthol binding site against human TRPM2 (PDB 6PUO), mouse TRPM3 (PDB 9B2A) and human TRPM4 (PDB 6BQV), as indicated. Only F1013 and D781 differ in sequence (**c**), being P1077 and E827 in hTRPM4, respectively. **e**, Representative currents of the WT and mutants of hTRPM2 and mTRPM3 at -60mV and +60mV in HEK293T cells. The mTRPM8 trace from **a** is included for comparison. Colored lines indicate the application of 200 μ M menthol (green). **f**, Currents elicited between -100mV and +160mV in 20mV steps with hTRPM4 WT and E827D/P1077F double-mutant. Holding potential is -60mV. Representative traces obtained in the absence or presence of 200 μ M menthol and 3mM Ca²⁺, with condition color-codes: black for control, green for menthol alone, red for Ca²⁺ alone, and purple for both menthol+ Ca²⁺. **g**, Currents elicited between -100mV and +160mV in 20mV steps with hTRPM4 WT (left) and E827D/P1077F double-mutant (right). Holding potential is -60mV. I-V curves testing effects of 200 μ M menthol and 3mM Ca²⁺ on WT ($n=5$ (hM4, menthol, Ca²⁺, menthol+Ca²⁺)) and E827D/P1077F double-mutant hTRPM4 ($n=5$ (hM4, menthol), $n=4$ (Ca²⁺, menthol+Ca²⁺)) with condition color-codes: black for hM4 (absence of menthol and Ca²⁺), green for menthol alone, red for Ca²⁺ alone, and purple for menthol+Ca²⁺. Data are mean $\pm$ SEM. Source data are provided as a Source Data file.

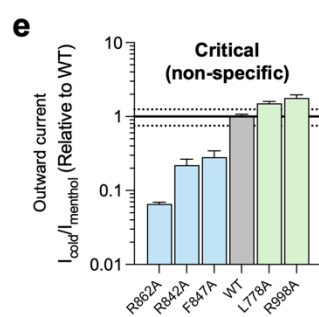
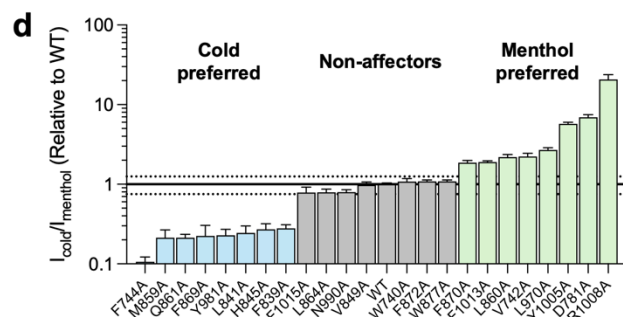
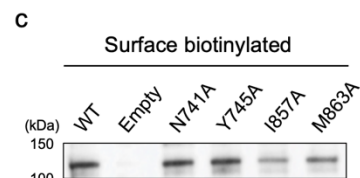
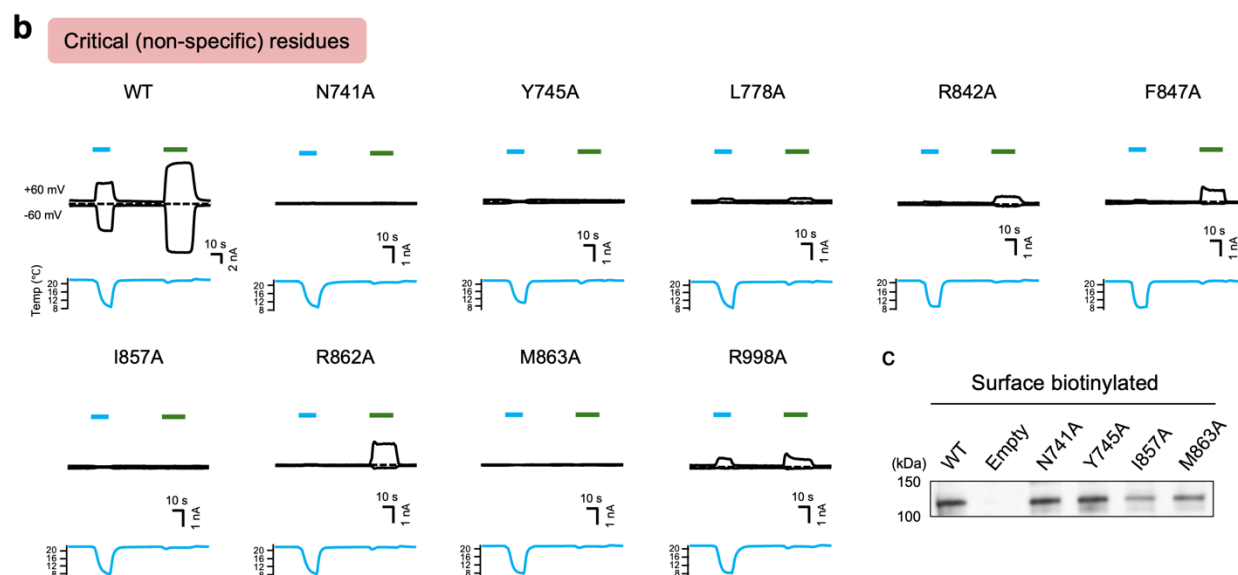
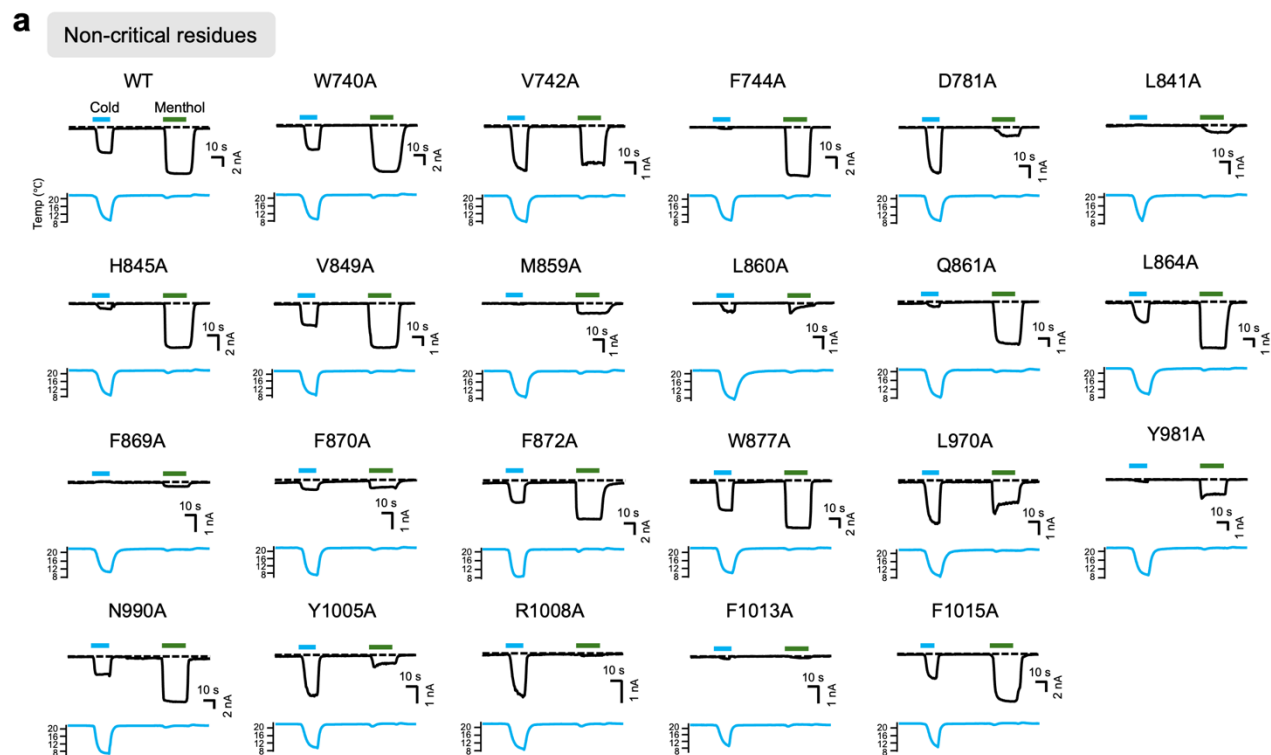


Supplementary Fig. 11 | Different cooling agonists bound within the VSLD cavity of TRPM8.

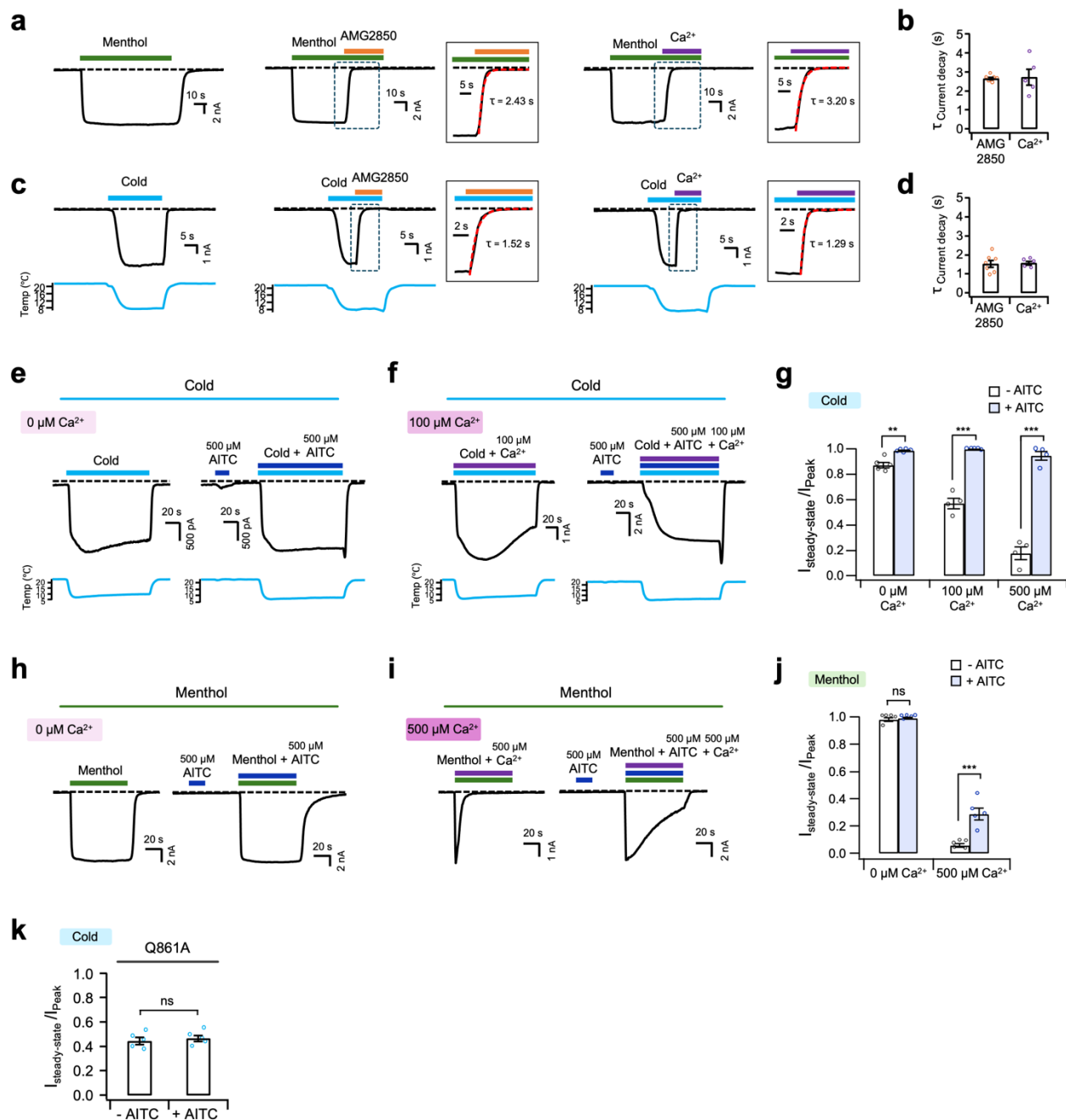
a, Comparison of binding modes for different cooling agonists within the VSLD cavity. The VSLD regions of menthol (pre-O^M, 20°C; sky blue), WS-12 (PDB 6NR2; orange), Cryosim-3 (PDB 8E4M; green), and icilin (PDB 6NR3; purple) bound structures are shown as cartoons and overlaid. S2, S2–S3, and S3 segments are omitted for clarity. The red dashed circle indicates that menthol is positioned deeper around CTDH1 compared to other agonists. **b**, Residues interacting with each agonist within ~4 Å are shown as sticks and labeled. The interaction surface area between each agonist and the surrounding protein is indicated below.



Supplementary Fig. 12 | Mechanistic model for cold- and menthol-induced TRPM8 activation. Serial conformational changes within the VSLD cavity induced by menthol binding at 4°C propagate towards the S6 gate to invoke pore opening with interaction changes at the interface between neighboring protomers.

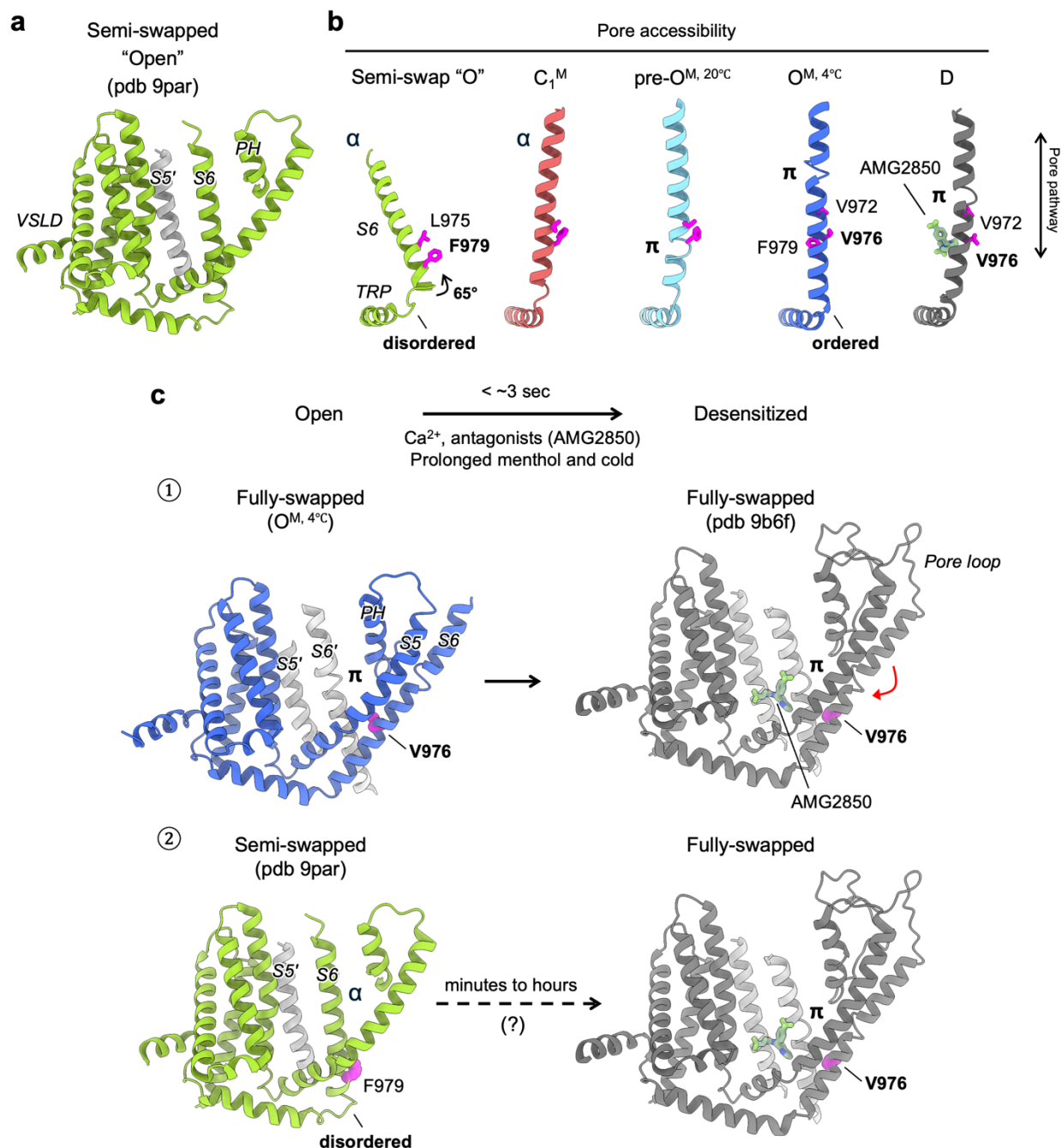


Supplementary Fig. 13 | Extensive electrophysiological analysis to identify residues involved in cold and menthol activation. **a**, Representative inward current traces of mTRPM8 WT and alanine mutants, elicited by cold and 200 μ M menthol at -60 mV. Horizontal colored lines represent the application of cold (sky blue) and 200 μ M menthol (green), as indicated. **b**, Representative currents of mTRPM8 WT and alanine-substituted critical (non-specific) mutants lacking inward-current activity to both menthol and cold. Recordings in HEK293T cells at -60 mV and $+60$ mV in response to cold (sky blue) and 200 μ M menthol (green), as indicated. **c**, Western blot analysis of surface-biotinylated HEK293T cells transfected with WT TRPM8 and completely non-functional mutants N741A, Y745A, I857A, and M863A, demonstrating their proper trafficking to the plasma membrane. The uncropped blot is found in the Source Data file. **d**, Plot of inward current density ratio for cold:menthol activation for mTRPM8 alanine mutants set relative to WT; $n = 3$ (F869A, F1015A, F870A, F1013A), $n = 4$ (W740A, L970A), $n = 5$ (H845A, N990A, V849A, L860A, V742A), $n = 6$ (Q861A, Y981A, L841A, F839A, L864A, F872A, W877A, R1008A), $n = 7$ (WT, M859A, D781A), $n = 9$ (F744A, Y1005A). An arbitrary threshold of $\pm 25\%$ from WT indicates residues not substantially impacted by mutation to alanine (non-affectors). Mutants below or above these thresholds are cold or menthol dominant, respectively. Data are mean $\pm$ SEM. **e**, The outward current density ratio was used to further categorize five critical (non-specific) mutants as menthol- or cold-preferred. $n = 3$ (R998A), $n = 4$ (R862A, L778A), $n = 6$ (R842A, F847A), $n = 9$ (WT). Data are mean $\pm$ SEM. Source data are provided as a Source Data file.



Supplementary Fig. 14 | Role of AITC in reducing desensitization of cooling agonist- and cold-activated TRPM8. **a,c**, Representative mTRPM8 WT currents at -60mV . Currents elicited by $200\mu\text{M}$ menthol (**a**) and cold (**c**) are shown on the left and inhibited by application of $1\mu\text{M}$ AMG2850 (orange) and $500\mu\text{M}$ Ca^{2+} (purple). The segments of current traces used for current decay analysis are highlighted with blue boxes and expanded on the right. Red dashed curves indicate single exponential fits to determine the time constants (τ) of current decay. **b, d**, Summary

of τ for inhibition of menthol- (**b**) and cold- (**d**) activated currents by AMG2850 and Ca^{2+} , based on the exponential fitting in **a** and **c**. For **b**, $n=6$ (AMG2850) and $n=5$ (Ca^{2+}). For **d**, $n=7$ (AMG2850) and $n=5$ (Ca^{2+}). **e, f**, Representative currents of the WT at -60mV . Current traces elicited by cold without (left) or with $500\mu\text{M}$ AITC (right) for 2 min in the presence of $0\mu\text{M}$ (**e**) and $100\mu\text{M}$ (**f**) extracellular Ca^{2+} . **g**, Remaining current after desensitization in the presence of $0\mu\text{M}$, $100\mu\text{M}$, and $500\mu\text{M}$ extracellular Ca^{2+} ; $n=5$ ($0\mu\text{M}$ Ca^{2+}), $n=5$ ($0\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$), $n=4$ ($100\mu\text{M}$ Ca^{2+}), $n=5$ ($100\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$), $n=4$ ($500\mu\text{M}$ Ca^{2+}), $n=4$ ($500\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$). $**P<0.01$, $***P<0.001$, two-way ANOVA with Sidak multiple-comparisons test. $P=0.0089$ ($0\mu\text{M}$ Ca^{2+} vs $0\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$), $P=2.1\times 10^{-9}$ ($100\mu\text{M}$ Ca^{2+} vs $100\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$), $P=8.3\times 10^{-14}$ ($500\mu\text{M}$ Ca^{2+} vs $500\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$). **h, i**, Representative currents of the WT at -60mV . Current traces elicited by $200\mu\text{M}$ menthol without (left) or with $500\mu\text{M}$ AITC (right) in the presence of $0\mu\text{M}$ (**h**) or $500\mu\text{M}$ (**i**) extracellular Ca^{2+} . **j**, Remaining current after desensitization in the presence of $0\mu\text{M}$ and $500\mu\text{M}$ extracellular Ca^{2+} ; $n=5$ ($0\mu\text{M}$ Ca^{2+}), $n=5$ ($0\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$), $n=5$ ($500\mu\text{M}$ Ca^{2+}), $n=5$ ($500\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$). $\text{ns}>0.05$, $***P<0.001$, two-way ANOVA with Sidak multiple-comparisons test. $P=0.9396$ ($0\mu\text{M}$ Ca^{2+} vs $0\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$), $P=1.04\times 10^{-5}$ ($500\mu\text{M}$ Ca^{2+} vs $500\mu\text{M}$ $\text{Ca}^{2+}+\text{AITC}$). **k**, Coldspot mutant Q861A current in the absence of Ca^{2+} without or with $500\mu\text{M}$ AITC. $\text{ns}>0.05$ ($P=0.5972$), student's two-tailed unpaired t -test. Dots indicate individual biological replicates. Data are mean $\pm$ SEM. Source data are provided as a Source data file.



Supplementary Fig. 15 | Incompatibility of a semi-swap conformation in TRPM8 gating. a, Protomer structure for the semi-swapped conformation of TRPM8 as recently proposed as an “open” conformation by Choi. K.Y, *et al.* (2026) (PDB 9PAR)²⁸. One protomer TMD is shown in green and the S5' of the adjacent protomer is shown in gray. **b,** Structural comparison of S6 between semi- and fully-swapped architectures. Relative to the fully-swapped conformation, S6 in the semi-swapped conformation is completely α -helical and is dramatically shorter and tilted

by 50° towards the VSLD of same protomer. Consequently, the linker between S6 and TRP helix becomes substantially disordered. Previous studies underscore the importance of the π -bulge and the tight linkage between S6-TRP^{15,16}. For V976 to become the functionally verified pore-lining constriction residue, helical extension and rotation of S6 requires formation and movement of the π -bulge and tightening of the linkage between S6 and the TRP helix. This drastically contrasts with the loose linkage observed between the TRP helix and the short, fully α -helical S6 in the semi-swapped arrangement **c**, TRPM8 desensitization towards a single, functionally and structurally verified fully-swapped conformation is induced by either Ca²⁺ from prolonged menthol or cold activation, or antagonists such as AMG2850. During desensitization, the critical interface comprising S4, the S4-S5 linker, S5', S6' and the TRP helix undergoes structural rearrangement with the π -bulge in S6 stabilizing AMG2850 binding. Notably, V976 is the gate residue in the desensitized state, and TRPM8 inhibitors bind specifically to the desensitized state¹⁵. TRPM8 desensitization and inhibition occur quickly (<3s) (Supplementary Fig. 14a–d), consistent with the occurrence of rather small conformational changes. However, the large structural rearrangements in quaternary structure required for transition between semi-swap to full-swap conformations would necessitate partial disassembly of the TRPM8 tetramer in order to accommodate the drastic rotation of S6, PH, and pore loop, which has been measured to occur over several minutes to hours (bottom)²⁸. Therefore, activation then desensitization (or inhibition) through a semi-swapped conformation is incompatible with the functional data, which supports a fully-swapped architecture of TRPM8.

Supplementary Table 1 | Cryo-EM data collection, refinement and validation statistics.

	Mouse TRPM8 WT			Mouse TRPM8-I846V		Mouse TRPM8-I846V	
	4°C			4°C		20°C	
	AITC (500 µM) C ₁ ^A	Menthol (1 mM) C ₁ ^M	Menthol + AITC (1 mM) (500 µM) C ₁ ^{M'}	Menthol + AITC (1 mM) (500 µM) C ₂ ^M , 4°C	O ^M , 4°C	Menthol (1 mM) C ₂ ^M , 20°C	Menthol + AITC (1 mM) (500 µM) pre-O ^M , 20°C
	(EMD-71919) (PDB 9PWH)	(EMD-74963) (PDB 9ZYR)	(EMD-71916) (PDB 9PWE)	(EMD-72557) (PDB 9Y69)	(EMD-72558) (PDB 9Y6A)	(EMD-71917) (PDB 9PWF)	(EMD-71918) (PDB 9PWG)
Data collection and processing							
Magnification	105,000	105,000	105,000	105,000		105,000	105,000
Voltage (kV)	300	300	300	300		300	300
Electron exposure (e ⁻ /Å ²)	50	50	60	60		50	50
Defocus range (µm)	-2.0 to -0.75	-1.6 to -0.8	-2.2 to -0.7	-2.2 to -0.7		-1.6 to -0.8	-1.9 to -0.9
Pixel size (Å)	0.855	0.855	0.844	0.843		0.855	0.855
Symmetry imposed	C4	C4	C4	C4		C4	C4
Initial particle images (no.)	1,181,585	480,164	313,327	1,750,822		1,008,576	1,029,549
Final particle images (no.)	40,275	28,033	39,702	47,522	18,191	75,451	59,401
Map resolution (Å)	3.6	3.6	3.4	3.3	3.4	3.1	3.4
FSC threshold	0.143	0.143	0.143	0.143	0.143	0.143	0.143
Map sharpening <i>B</i> factor (Å ²)	-105.0	-94.4	-96.9	-113.0	-99.7	-84.1	-93.6
Refinement							
Initial model used (PDB code)	C ₁ (8E4N)	C ₁ (8E4N)	C ₁ (8E4N)	C ₁ (8E4L)	O (8E4L)	C ₁ (8E4L)	O (8E4L)
Model composition							
Nonhydrogen atoms	27,012	29,956	29,736	29,152	29,144	29,140	29,300
Protein residues	3,564	3,848	3,876	3,876	3,860	3,876	3,888
Ligands	8	8	24	8	12	8	12
<i>B</i> factors (Å ²)							
Protein	96.84	206.77	122.89	108.69	217.51	100.92	130.94
Ligand	72.31	163.51	96.57	85.65	150.08	97.82	94.15
R.m.s. deviations							
Bond lengths (Å)	0.009	0.004	0.006	0.003	0.008	0.005	0.006
Bond angles (°)	0.881	0.532	0.438	0.499	0.607	0.579	0.518
Validation							
MolProbity score	1.45	2.19	1.56	1.68	1.89	1.61	1.69
Clashscore	8.02	7.96	6.41	6.31	5.75	6.05	6.79
Poor rotamers (%)	0.47	3.25	0	1.46	2.20	0.88	1.09
Ramachandran plot							
Favored (%)	97.93	94.73	96.70	96.75	95.50	95.92	95.93
Allowed (%)	2.07	5.27	3.30	3.25	4.50	4.08	4.07
Disallowed (%)	0	0	0	0	0	0	0