

Supplementary Information

Structural mechanism of TRPV3 channel inhibition by the anesthetic dyclonine

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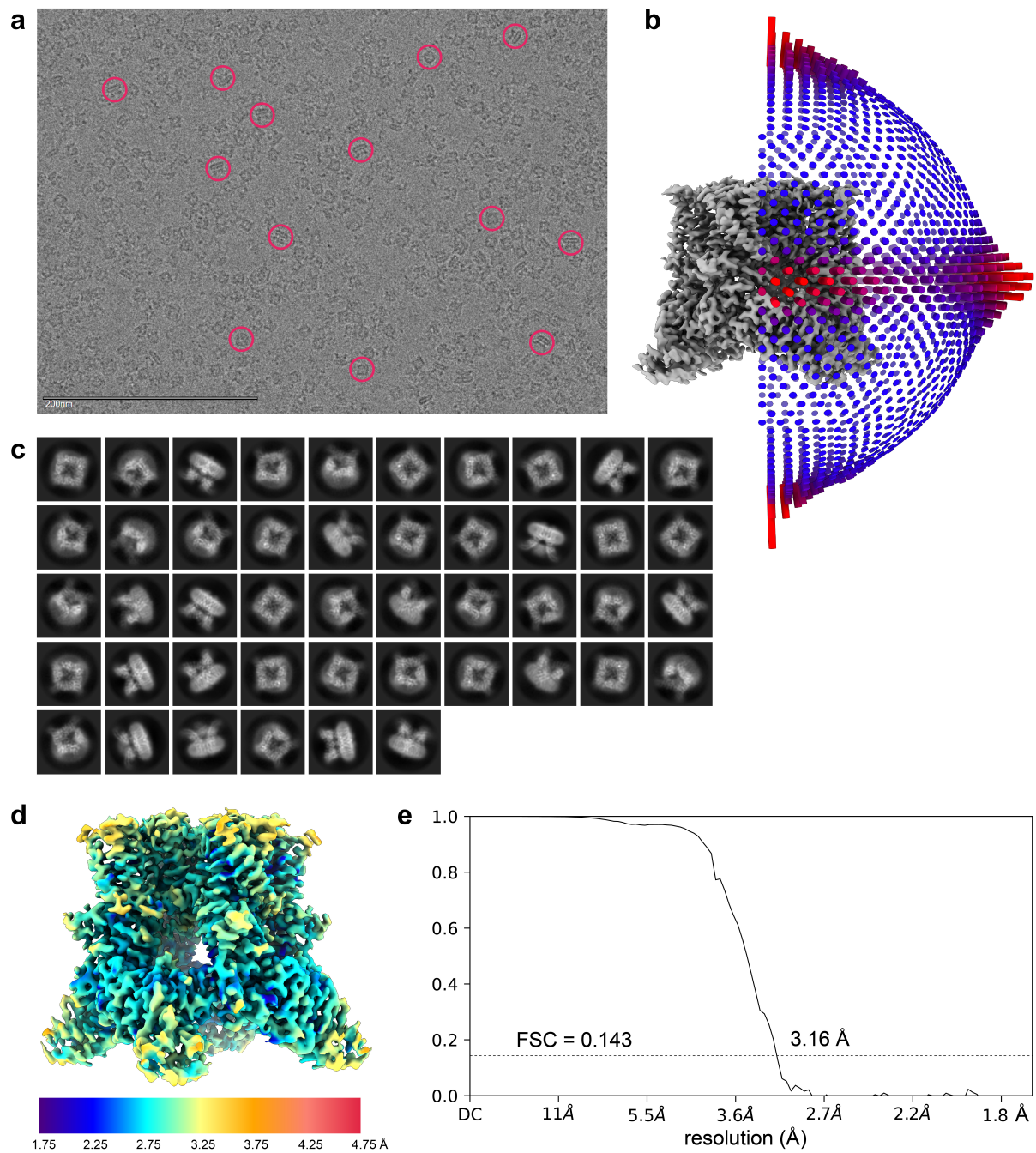
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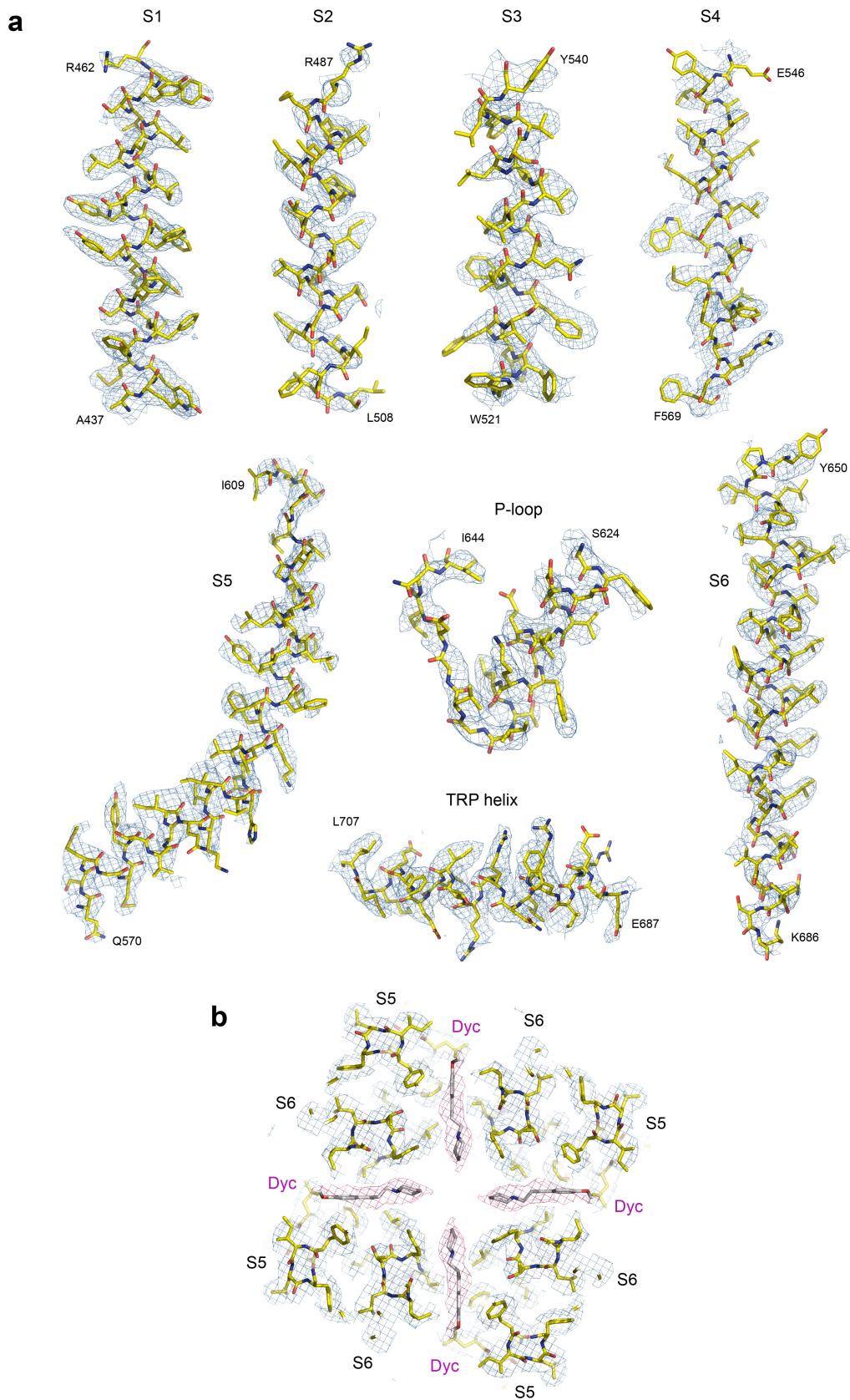
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Supplementary Figures 1-2

Supplementary Table 1



Supplementary Fig. 1. Overview of cryo-EM data for TRPV3_{Dyc}. **a**, Representative micrograph with example particles circled in pink. **b**, Euler angle distribution of particles contributing to the final reconstruction with larger red cylinders representing orientations comprising more particles. **c**, Reference-free 2D class averages. **d**, Local resolution presented as coloring of the TRPV3_{Dyc} cryo-EM map. **e**, FSC curve.



Supplementary Fig. 2. Cryo-EM density of TRPV3_{Dyc}. **a**, Fragments of TRPV3_{Dyc} cryo-EM map (blue mesh) for the membrane segments and TRP helix. **b**, The central slice of the map at the plane of dyclonine molecules. Density that corresponds to dyclonine molecules is shown as pink mesh.

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

Structure	TRPV3 _{Dyc}
EMDB accession code	EMD-26488
PDB accession code	7UGG
Data collection and processing	
Magnification	105,000x
Voltage (kV)	300
Electron exposure (e ⁻ Å ⁻²)	60
Defocus range (μm)	-0.8 to -2.0
Reported pixel size (Å)	0.86
Exposures (no.)	6,856
Processing software	
Platform software for particle picking	cryoSPARC v3.1
Motion correction	cryoSPARC v3.1
CTF estimation	cryoSPARC v3.1
Software for 2D/3D class. & refinements	cryoSPARC v3.1
Symmetry imposed	C4
Initial particle images (no.)	4,985,077
Final particle images (no.)	87,876
Map resolution (Å)	3.16
FSC 0.143	
Refinement	
Initial models used (PDB code)	This study
Model resolution (Å)	3.16
FSC threshold	0.143
Map sharpening <i>B</i> factor (Å ²)	-132.9
Model composition	
Non-hydrogen atoms	21,670
Protein residues	2480
Ligands	30
Water	124
<i>B</i> factors (Å²)	
Protein	63.11
Ligands	17.75
R.m.s. deviations	
Bond lengths (Å)	0.008
Bond angles (°)	1.241
Validation	
MolProbity score	1.60
Clash score, all atoms	3.36
Poor rotamers (%)	0.54
Ramachandran plot	
Favoured (%)	92.51
Allowed (%)	7.17
Disallowed (%)	0.33