

**Supplementary Figure 1 | Distributions of distances and angles for transmembrane helices.** (**a**) Distribution of the radial distance *r* for the pore-lining helix (PLH) bundle in 39 unique ion channel structures. (**b**) Distribution of the tilt angle *θ* for 171 transmembrane helices in 26 membrane proteins. (**c**) Distribution of *θ* for the PLH bundles of the 39 channel structures. (**d**) Distribution of the contact distances of 128 helix pairs in the 26 membrane proteins. (**e**) Distribution of the contact distances between PLHs and their nearest neighboring helices (not necessarily pore-lining) in the 39 channel structures. (**f**) Distribution of the contact distances between neighboring PLHs in the 39 channel structures.



**Supplementary Figure 2 | The W-shaped accessible region in the** *r***-***θ***- space.** (**a**) The accessible region for trimeric models, along with the conformations of 4 actual porelining helix (PLH) bundles. The *r* values of the plausible models are displayed according to the color scale at the top. Each black dot represents an actual PLH bundle. The closed-state P2X4 receptor and ASIC1a are within the accessible region, but their openstate counterparts are either near the border of the accessible region (4DW1 for P2X4 receptor) or well outside (4FZ1 for ASIC1a). (**b & c**) Corresponding results for hexamers and heptamers. The hexameric calcium release-activated calcium channel (4HKR) and heptameric MscS (2OAU for closed and 2VV5 for open) are within their respective Wshaped accessible regions.



**Supplementary Figure 3 | The W-shaped accessible region in the** *r***-***θ***- space for tetrameric models.** The ranges of parameters are  $5 \text{ Å} < r < 16 \text{ Å}$ ,  $0^{\circ} < \theta < 80^{\circ}$ , and  $-$ 180° <  $\phi$  < 180°. Conformations of pore-lining helix bundles in channel structures are displayed as black dots.



**Supplementary Figure 4 | Minimum pore radii of the plausible models.** (**a**) Hexamers. (**b**) Heptamers. (**c**) Octamers. In each panel, the  $R_0$  values of the plausible models are displayed according to the color scale at the top.



**Supplementary Figure 5 | Average** *R***<sup>0</sup> when only one of the three coordinates is fixed, for oligomeric states.** (**a**) Averaging at fixed *r*. (**b**) Averaging at fixed *θ*. (**c**) Averaging at fixed  $\phi$ . Error bars representing standard deviations are displayed for pentamers, to indicate the significant variations in  $R_0$  when only one coordinate is fixed. In (**b**) the dashed curve displays the prediction of Spencer and Rees for a model of infinite cylinders with a diameter of 7.8 Å.



**Supplementary Figure 6 | Comparison of the open model proposed in this study for MscL (red) with a model proposed by Sukharev et al. (green).** Both top and side views are shown.

<b>PDB</b>	r	$\theta$ (°)	$\phi$ <sup>(°)</sup>	Residues of	Aligned	Ideal	rmsd	Description	Ref.
entry	$(\AA)$			PLHs	segment	helix	$(\AA)$		
<b>Trimers</b>									
				$A-C$ :					$\mathbf{1}$
3HGC	4.5	44.7	147.0	V427-E451	427-450	$1 - 24$	1.5	ASIC1 desensitized state	
				$A-C$ :					
4FZ1	12.7	12.5	153.5	V427-L450	427-450	$1 - 24$	$2.0\,$	ASIC1-psalmotoxin 1 at high pH	2
				$A-C$ :					
4DW0	6.4	49.9	144.5	1335-1359	335-358	$1 - 24$	1.4	P2X4R apo	3
				$A-C$ :					
4DW1	8.6	45.3	$-159.5$	1335-1359	335-358	$1 - 24$	1.1	P2X4R with ATP	3
						<i>Tetramers</i>			
				$A-D$ :					
1BL8	6.8	32.9	$-25.1$	L86-Q119	94-117	$1 - 24$	0.7	KcsA	$\overline{4}$
1K4C								$KcsA + Fab$	5
2ITC								$KcsA + Fab$ in NaCl	6
2NLJ								KcsA M96V mutant in KCl	6
								KcsA in $150$ mM $Li+$ and 3 mM	
3IGA								$K^+$	$\tau$
								KcsA closed inactivated. E71H	
3HPL								and F103A	$\,$ 8 $\,$
3OR7								KcsA E71I	9
3OR6								KcsAE71Q	9
3STL								KcsAY82C with cadmium	10
								KcsA open conductive. Open 20	
3FB8								Å	11
3EFF								Full length KcsA closed	12
3PJS								Full length KcsA open	13
3F7Y								KcsA partially open. Open 17 Å	11
				$A-D$ :					
3FB6	7.8	40.0	$-4.0$	L86-F114	94-114	$1 - 21$	0.6	KcsA partially open. Open 16 Å	11
3FB5								KcsA partially open. Open 14.5 Å	11
				$A-D$ :				KcsA open inactivated. Open 32	
3F5W	9.8	56.1	11.8	L86-Q117	94-117	$1 - 24$	1.7	Å	11
3FB7								KcsA in open state with $Rb^+$	8
								KcsA open inactivated. Open 23	
3F7V								Å	11
				$A-D$ :					
2A0L	9.2	57.8	0.4	P207-K237	214-237	$1 - 24$	1.4	$KvAP + Fv$ fragment	14
1ORQ								$KvAP + Fab$	15
				$A-D$ :					
2A79	7.7	48.4	8.6	I385-T421	394-417	$1 - 24$	1.6	Kv1.2	16
3LUT								Full length Kv1.2	17
2R9R								Kv1.2/Kv2.1	18
3LNM								Kv1.2/Kv2.1 F233W	19
				$A-D$ :					
4H33	6.2	33.8	4.1	P68-T102	79-102	$1 - 24$	1.1	KvLm closed	20
								KvLm in $K^+$ condition	20
4H37									
				$A-D$ :					21
3LDC	10.2	55.9	2.6	P70-I99	76-99	$1 - 24$	1.7	Mth $K K^+$ channel	22
1LNQ								MthK $K^+$ channel, $Ca^{2+}$ gated	23
4HYO								MthK $K^+$ channel. S68H & V77C	
				$A-D$ :					24
4GX5	12.1	28.0	$-53.0$	S78-F108	79-99	$1 - 21$	1.4	GsuK wild-type	24
4GX0								GsuK L97D	24
4GX1								GsuK L97D with ADP	24
4GX2								GsuK L97D with NAD <sup>+</sup>	
$3\mathrm{JYC}$	9.6	35.8	$-37.9$	$A-D$ :	160-183	$1 - 24$	0.6	Kir2.2	25

**Supplementary Table 1 | Oligomeric arrangements of pore-lining helix bundles in channel structures**







Only entries shown in black were deemed "unique"; entries in gray were deemed similar to the preceding entries in black. There are a total of 138 entries, of which 39 are unique.

## Supplementary References

- <span id="page-10-0"></span>1. Gonzales, E.B., Kawate, T. & Gouaux, E. Pore architecture and ion sites in acidsensing ion channels and P2X receptors. *Nature* **460**, 599-604 (2009).
- <span id="page-10-1"></span>2. Baconguis, I. & Gouaux, E. Structural plasticity and dynamic selectivity of acidsensing ion channel-spider toxin complexes. *Nature* **489**, 400-5 (2012).
- <span id="page-10-2"></span>3. Hattori, M. & Gouaux, E. Molecular mechanism of ATP binding and ion channel activation in P2X receptors. *Nature* **485**, 207-12 (2012).
- <span id="page-10-3"></span>4. Doyle, D.A. et al. The structure of the potassium channel: molecular basis of K+ conduction and selectivity. *Science* **280**, 69-77 (1998).
- <span id="page-10-4"></span>5. Zhou, Y., Morais-Cabral, J.H., Kaufman, A. & MacKinnon, R. Chemistry of ion coordination and hydration revealed by a K+ channel-Fab complex at 2.0 A resolution. *Nature* **414**, 43-8 (2001).
- <span id="page-10-5"></span>6. Lockless, S.W., Zhou, M. & MacKinnon, R. Structural and thermodynamic properties of selective ion binding in a K+ channel. *PLoS Biol* **5**, e121 (2007).
- <span id="page-10-6"></span>7. Thompson, A.N. et al. Mechanism of potassium-channel selectivity revealed by Na(+) and Li(+) binding sites within the KcsA pore. *Nat Struct Mol Biol* **16**, 1317-24 (2009).
- <span id="page-10-7"></span>8. Cuello, L.G. et al. Structural basis for the coupling between activation and inactivation gates in K(+) channels. *Nature* **466**, 272-5 (2010).
- <span id="page-10-8"></span>9. Chakrapani, S. et al. On the structural basis of modal gating behavior in  $K(+)$ channels. *Nat Struct Mol Biol* **18**, 67-74 (2011).
- <span id="page-10-9"></span>10. Raghuraman, H. et al. Mechanism of Cd2+ coordination during slow inactivation in potassium channels. *Structure* **20**, 1332-42 (2012).
- <span id="page-10-10"></span>11. Cuello, L.G., Jogini, V., Cortes, D.M. & Perozo, E. Structural mechanism of Ctype inactivation in K(+) channels. *Nature* **466**, 203-8 (2010).
- <span id="page-10-11"></span>12. Uysal, S. et al. Crystal structure of full-length KcsA in its closed conformation. *Proc Natl Acad Sci U S A* **106**, 6644-9 (2009).
- <span id="page-10-12"></span>13. Uysal, S. et al. Mechanism of activation gating in the full-length KcsA K+ channel. *Proc Natl Acad Sci U S A* **108**, 11896-9 (2011).
- <span id="page-10-13"></span>14. Lee, S.Y., Lee, A., Chen, J. & MacKinnon, R. Structure of the KvAP voltage-

dependent K+ channel and its dependence on the lipid membrane. *Proc Natl Acad Sci U S A* **102**, 15441-6 (2005).

- <span id="page-11-0"></span>15. Jiang, Y. et al. X-ray structure of a voltage-dependent K+ channel. *Nature* **423**, 33-41 (2003).
- <span id="page-11-1"></span>16. Long, S.B., Campbell, E.B. & Mackinnon, R. Crystal structure of a mammalian voltage-dependent Shaker family K+ channel. *Science* **309**, 897-903 (2005).
- <span id="page-11-2"></span>17. Chen, X., Wang, Q., Ni, F. & Ma, J. Structure of the full-length Shaker potassium channel Kv1.2 by normal-mode-based X-ray crystallographic refinement. *Proc Natl Acad Sci U S A* **107**, 11352-7 (2010).
- <span id="page-11-3"></span>18. Long, S.B., Tao, X., Campbell, E.B. & MacKinnon, R. Atomic structure of a voltage-dependent K+ channel in a lipid membrane-like environment. *Nature* **450**, 376-82 (2007).
- <span id="page-11-4"></span>19. Tao, X., Lee, A., Limapichat, W., Dougherty, D.A. & MacKinnon, R. A gating charge transfer center in voltage sensors. *Science* **328**, 67-73 (2010).
- <span id="page-11-5"></span>20. Santos, J.S. et al. Crystal structure of a voltage-gated K+ channel pore module in a closed state in lipid membranes. *J Biol Chem* **287**, 43063-70 (2012).
- <span id="page-11-6"></span>21. Ye, S., Li, Y. & Jiang, Y. Novel insights into K+ selectivity from high-resolution structures of an open K+ channel pore. *Nat Struct Mol Biol* **17**, 1019-23 (2010).
- <span id="page-11-7"></span>22. Jiang, Y. et al. Crystal structure and mechanism of a calcium-gated potassium channel. *Nature* **417**, 515-22 (2002).
- <span id="page-11-8"></span>23. Posson, D.J., McCoy, J.G. & Nimigean, C.M. The voltage-dependent gate in MthK potassium channels is located at the selectivity filter. *Nat Struct Mol Biol* **20**, 159-66 (2013).
- <span id="page-11-9"></span>24. Kong, C. et al. Distinct gating mechanisms revealed by the structures of a multiligand gated K(+) channel. *Elife* **1**, e00184 (2012).
- <span id="page-11-10"></span>25. Tao, X., Avalos, J.L., Chen, J. & MacKinnon, R. Crystal structure of the eukaryotic strong inward-rectifier K+ channel Kir2.2 at 3.1 A resolution. *Science* **326**, 1668-74 (2009).
- <span id="page-11-11"></span>26. Hansen, S.B., Tao, X. & MacKinnon, R. Structural basis of PIP2 activation of the classical inward rectifier K+ channel Kir2.2. *Nature* **477**, 495-8 (2011).
- <span id="page-11-12"></span>27. Nishida, M., Cadene, M., Chait, B.T. & MacKinnon, R. Crystal structure of a

Kir3.1-prokaryotic Kir channel chimera. *EMBO J* **26**, 4005-15 (2007).

- <span id="page-12-0"></span>28. Whorton, M.R. & MacKinnon, R. X-ray structure of the mammalian GIRK2 betagamma G-protein complex. *Nature* **498**, 190-7 (2013).
- <span id="page-12-1"></span>29. Whorton, M.R. & MacKinnon, R. Crystal structure of the mammalian GIRK2  $K^+$ channel and gating regulation by G proteins, PIP2, and sodium. *Cell* **147**, 199-208 (2011).
- <span id="page-12-2"></span>30. Kuo, A. et al. Crystal structure of the potassium channel KirBac1.1 in the closed state. *Science* **300**, 1922-6 (2003).
- <span id="page-12-3"></span>31. Clarke, O.B. et al. Domain reorientation and rotation of an intracellular assembly regulate conduction in Kir potassium channels. *Cell* **141**, 1018-29 (2010).
- <span id="page-12-4"></span>32. Bavro, V.N. et al. Structure of a KirBac potassium channel with an open bundle crossing indicates a mechanism of channel gating. *Nat Struct Mol Biol* **19**, 158-63 (2012).
- <span id="page-12-5"></span>33. Clayton, G.M., Altieri, S., Heginbotham, L., Unger, V.M. & Morais-Cabral, J.H. Structure of the transmembrane regions of a bacterial cyclic nucleotide-regulated channel. *Proc Natl Acad Sci U S A* **105**, 1511-5 (2008).
- <span id="page-12-6"></span>34. Shi, N., Ye, S., Alam, A., Chen, L. & Jiang, Y. Atomic structure of a Na+- and K+ conducting channel. *Nature* **440**, 570-4 (2006).
- <span id="page-12-7"></span>35. Alam, A., Shi, N. & Jiang, Y. Structural insight into Ca2+ specificity in tetrameric cation channels. *Proc Natl Acad Sci U S A* **104**, 15334-9 (2007).
- <span id="page-12-8"></span>36. Irie, K., Shimomura, T. & Fujiyoshi, Y. The C-terminal helical bundle of the tetrameric prokaryotic sodium channel accelerates the inactivation rate. *Nat Commun* **3**, 793 (2012).
- <span id="page-12-9"></span>37. Alam, A. & Jiang, Y. High-resolution structure of the open NaK channel. *Nat Struct Mol Biol* **16**, 30-4 (2009).
- <span id="page-12-10"></span>38. Derebe, M.G., Zeng, W., Li, Y., Alam, A. & Jiang, Y. Structural studies of ion permeation and Ca2+ blockage of a bacterial channel mimicking the cyclic nucleotide-gated channel pore. *Proc Natl Acad Sci U S A* **108**, 592-7 (2011).
- <span id="page-12-11"></span>39. Derebe, M.G. et al. Tuning the ion selectivity of tetrameric cation channels by changing the number of ion binding sites. *Proc Natl Acad Sci U S A* **108**, 598-602 (2011).
- <span id="page-13-0"></span>40. Sauer, D.B., Zeng, W., Raghunathan, S. & Jiang, Y. Protein interactions central to stabilizing the K+ channel selectivity filter in a four-sited configuration for selective K+ permeation. *Proc Natl Acad Sci U S A* **108**, 16634-9 (2011).
- <span id="page-13-1"></span>41. Payandeh, J., Scheuer, T., Zheng, N. & Catterall, W.A. The crystal structure of a voltage-gated sodium channel. *Nature* **475**, 353-8 (2011).
- <span id="page-13-2"></span>42. Zhang, X. et al. Crystal structure of an orthologue of the NaChBac voltage-gated sodium channel. *Nature* **486**, 130-4 (2012).
- <span id="page-13-3"></span>43. Shaya, D. et al. Structure of a prokaryotic sodium channel pore reveals essential gating elements and an outer ion binding site common to eukaryotic channels. *J Mol Biol* **426**, 467-83 (2014).
- <span id="page-13-4"></span>44. Payandeh, J., Gamal El-Din, T.M., Scheuer, T., Zheng, N. & Catterall, W.A. Crystal structure of a voltage-gated sodium channel in two potentially inactivated states. *Nature* **486**, 135-9 (2012).
- <span id="page-13-5"></span>45. McCusker, E.C. et al. Structure of a bacterial voltage-gated sodium channel pore reveals mechanisms of opening and closing. *Nat Commun* **3**, 1102 (2012).
- <span id="page-13-6"></span>46. Sobolevsky, A.I., Rosconi, M.P. & Gouaux, E. X-ray structure, symmetry and mechanism of an AMPA-subtype glutamate receptor. *Nature* **462**, 745-56 (2009).
- <span id="page-13-7"></span>47. Sharma, M. et al. Insight into the mechanism of the influenza A proton channel from a structure in a lipid bilayer. *Science* **330**, 509-12 (2010).
- <span id="page-13-8"></span>48. Schnell, J.R. & Chou, J.J. Structure and mechanism of the M2 proton channel of influenza A virus. *Nature* **451**, 591-5 (2008).
- <span id="page-13-9"></span>49. Stouffer, A.L. et al. Structural basis for the function and inhibition of an influenza virus proton channel. *Nature* **451**, 596-9 (2008).
- <span id="page-13-10"></span>50. Acharya, R. et al. Structure and mechanism of proton transport through the transmembrane tetrameric M2 protein bundle of the influenza A virus. *Proc Natl Acad Sci U S A* **107**, 15075-80 (2010).
- <span id="page-13-11"></span>51. Wang, J. et al. Structure and inhibition of the drug-resistant S31N mutant of the M2 ion channel of influenza A virus. *Proc Natl Acad Sci U S A* **110**, 1315-20 (2013).
- <span id="page-13-12"></span>52. Wang, J., Pielak, R.M., McClintock, M.A. & Chou, J.J. Solution structure and functional analysis of the influenza B proton channel. *Nat Struct Mol Biol* **16**,

1267-71 (2009).

- <span id="page-14-0"></span>53. Pielak, R.M., Oxenoid, K. & Chou, J.J. Structural investigation of rimantadine inhibition of the AM2-BM2 chimera channel of influenza viruses. *Structure* **19**, 1655-63 (2011).
- <span id="page-14-1"></span>54. Liu, Z., Gandhi, C.S. & Rees, D.C. Structure of a tetrameric MscL in an expanded intermediate state. *Nature* **461**, 120-4 (2009).
- <span id="page-14-2"></span>55. Liao, M., Cao, E., Julius, D. & Cheng, Y. Structure of the TRPV1 ion channel determined by electron cryo-microscopy. *Nature* **504**, 107-12 (2013).
- <span id="page-14-3"></span>56. Cao, E., Liao, M., Cheng, Y. & Julius, D. TRPV1 structures in distinct conformations reveal activation mechanisms. *Nature* **504**, 113-8 (2013).
- <span id="page-14-4"></span>57. Chang, G., Spencer, R.H., Lee, A.T., Barclay, M.T. & Rees, D.C. Structure of the MscL homolog from Mycobacterium tuberculosis: a gated mechanosensitive ion channel. *Science* **282**, 2220-6 (1998).
- <span id="page-14-5"></span>58. Hibbs, R.E. & Gouaux, E. Principles of activation and permeation in an anionselective Cys-loop receptor. *Nature* **474**, 54-60 (2011).
- <span id="page-14-6"></span>59. Mowrey, D.D. et al. Open-channel structures of the human glycine receptor alpha1 full-length transmembrane domain. *Structure* **21**, 1897-904 (2013).
- <span id="page-14-7"></span>60. Miyazawa, A., Fujiyoshi, Y. & Unwin, N. Structure and gating mechanism of the acetylcholine receptor pore. *Nature* **423**, 949-55 (2003).
- <span id="page-14-8"></span>61. Unwin, N. Refined structure of the nicotinic acetylcholine receptor at 4A resolution. *J Mol Biol* **346**, 967-89 (2005).
- <span id="page-14-9"></span>62. Unwin, N. & Fujiyoshi, Y. Gating movement of acetylcholine receptor caught by plunge-freezing. *J Mol Biol* **422**, 617-34 (2012).
- <span id="page-14-10"></span>63. Hilf, R.J. & Dutzler, R. X-ray structure of a prokaryotic pentameric ligand-gated ion channel. *Nature* **452**, 375-9 (2008).
- <span id="page-14-11"></span>64. Spurny, R. et al. Pentameric ligand-gated ion channel ELIC is activated by GABA and modulated by benzodiazepines. *Proc Natl Acad Sci U S A* **109**, E3028-34 (2012).
- <span id="page-14-12"></span>65. Gonzalez-Gutierrez, G. et al. Mutations that stabilize the open state of the Erwinia chrisanthemi ligand-gated ion channel fail to change the conformation of the pore domain in crystals. *Proc Natl Acad Sci U S A* **109**, 6331-6 (2012).
- <span id="page-15-0"></span>66. Pan, J. et al. Structure of the pentameric ligand-gated ion channel ELIC cocrystallized with its competitive antagonist acetylcholine. *Nat Commun* **3**, 714 (2012).
- <span id="page-15-1"></span>67. Spurny, R. et al. Multisite binding of a general anesthetic to the prokaryotic pentameric Erwinia chrysanthemi ligand-gated ion channel (ELIC). *J Biol Chem* **288**, 8355-64 (2013).
- <span id="page-15-2"></span>68. Prevost, M.S. et al. A locally closed conformation of a bacterial pentameric proton-gated ion channel. *Nat Struct Mol Biol* **19**, 642-9 (2012).
- <span id="page-15-3"></span>69. Sauguet, L. et al. Crystal structures of a pentameric ligand-gated ion channel provide a mechanism for activation. *Proc Natl Acad Sci U S A* **111**, 966-71 (2014).
- <span id="page-15-4"></span>70. Bocquet, N. et al. X-ray structure of a pentameric ligand-gated ion channel in an apparently open conformation. *Nature* **457**, 111-4 (2009).
- <span id="page-15-5"></span>71. Hilf, R.J. & Dutzler, R. Structure of a potentially open state of a proton-activated pentameric ligand-gated ion channel. *Nature* **457**, 115-8 (2009).
- <span id="page-15-6"></span>72. Sauguet, L. et al. Structural basis for ion permeation mechanism in pentameric ligand-gated ion channels. *EMBO J* **32**, 728-41 (2013).
- <span id="page-15-7"></span>73. Hilf, R.J. et al. Structural basis of open channel block in a prokaryotic pentameric ligand-gated ion channel. *Nat Struct Mol Biol* **17**, 1330-6 (2010).
- <span id="page-15-8"></span>74. Nury, H. et al. X-ray structures of general anaesthetics bound to a pentameric ligand-gated ion channel. *Nature* **469**, 428-31 (2011).
- <span id="page-15-9"></span>75. Pan, J. et al. Structure of the pentameric ligand-gated ion channel GLIC bound with anesthetic ketamine. *Structure* **20**, 1463-9 (2012).
- <span id="page-15-10"></span>76. Verardi, R., Shi, L., Traaseth, N.J., Walsh, N. & Veglia, G. Structural topology of phospholamban pentamer in lipid bilayers by a hybrid solution and solid-state NMR method. *Proc Natl Acad Sci U S A* **108**, 9101-6 (2011).
- <span id="page-15-11"></span>77. Vostrikov, V.V., Mote, K.R., Verardi, R. & Veglia, G. Structural dynamics and topology of phosphorylated phospholamban homopentamer reveal its role in the regulation of calcium transport. *Structure* **21**, 2119-30 (2013).
- <span id="page-15-12"></span>78. Lunin, V.V. et al. Crystal structure of the CorA Mg2+ transporter. *Nature* **440**, 833-7 (2006).
- <span id="page-16-0"></span>79. Eshaghi, S. et al. Crystal structure of a divalent metal ion transporter CorA at 2.9 angstrom resolution. *Science* **313**, 354-7 (2006).
- <span id="page-16-1"></span>80. Payandeh, J. & Pai, E.F. A structural basis for Mg2+ homeostasis and the CorA translocation cycle. *EMBO J* **25**, 3762-73 (2006).
- <span id="page-16-2"></span>81. Pfoh, R. et al. Structural asymmetry in the magnesium channel CorA points to sequential allosteric regulation. *Proc Natl Acad Sci U S A* **109**, 18809-14 (2012).
- <span id="page-16-3"></span>82. Guskov, A. et al. Structural insights into the mechanisms of Mg2+ uptake, transport, and gating by CorA. *Proc Natl Acad Sci U S A* **109**, 18459-64 (2012).
- <span id="page-16-4"></span>83. Hou, X., Pedi, L., Diver, M.M. & Long, S.B. Crystal structure of the calcium release-activated calcium channel Orai. *Science* **338**, 1308-13 (2012).
- <span id="page-16-5"></span>84. Bass, R.B., Strop, P., Barclay, M. & Rees, D.C. Crystal structure of Escherichia coli MscS, a voltage-modulated and mechanosensitive channel. *Science* **298**, 1582-7 (2002).
- <span id="page-16-6"></span>85. Zhang, X. et al. Structure and molecular mechanism of an anion-selective mechanosensitive channel of small conductance. *Proc Natl Acad Sci U S A* **109**, 18180-5 (2012).
- <span id="page-16-7"></span>86. Lai, J.Y., Poon, Y.S., Kaiser, J.T. & Rees, D.C. Open and shut: crystal structures of the dodecylmaltoside solubilized mechanosensitive channel of small conductance from Escherichia coli and Helicobacter pylori at 4.4 A and 4.1 A resolutions. *Protein Sci* **22**, 502-9 (2013).
- <span id="page-16-8"></span>87. Wang, W. et al. The structure of an open form of an E. coli mechanosensitive channel at 3.45 A resolution. *Science* **321**, 1179-83 (2008).
- <span id="page-16-9"></span>88. Pliotas, C. et al. Conformational state of the MscS mechanosensitive channel in solution revealed by pulsed electron-electron double resonance (PELDOR) spectroscopy. *Proc Natl Acad Sci U S A* **109**, E2675-82 (2012).