

	Ligand-free	cAMP
Data acquisition		
Microscope	Krios	Krios
Voltage (kV)	300	300
Defocus range (μm)	-1.5 to -3.3	-1.5 to -3.3
Pixel size (\AA)	1.3	1.3
Total electron dose ($\text{e}^-/\text{\AA}^2$)	50	89
Exposure time (s)	10	15
Reconstruction (RELION)		
Particle number	55870	125339
Resolution (unmasked, \AA)	4.17	4.10
Resolution (masked, \AA)	3.50	3.51
Refinement (Refmac)		
Resolution limit (\AA)	3.50	3.51
Map sharpening B-factor (\AA^2)	-80	-100
Refinement weight	0.001	0.0005
Rms deviations		
Bond length (\AA)	0.008	0.007
Bond angle ($^\circ$)	1.207	1.198
Ramachandran plot		
Favored (%)	95.38	96.89
Allowed (%)	4.62	3.11
Validation		
EMRinger score	2.90	2.73
MolProbity score	1.37 (100 th)	1.16 (100 th)
Clashscore	2.59 (100 th)	2.04 (100 th)

Table S1. Summary of data acquisition parameters and refinement statistics, Related to Figures 1, 6 and 7