Crystal structure of the *Vibrio cholerae* VqmA–ligand–DNA complex provides insight into ligand-binding mechanisms relevant for drug design

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List of the supplementary data

TABLES

Table S1. Data collection and refinement statistics

	VqmA complex	Se-Met
Data collection		
Space group	$P2_12_12_1$	$I2_12_12_1$
a, b, c(Å)	52.78 108.98 214.32	52.73 105.54 209.36
α, β, γ(°)	90.00 90.00 90.00	90.00 90.00 90.00
Wavelength(Å)	0.97915	0.97915
Resolution(Å)	43.33 - 2.51(2.58 - 2.51)	52.34 - 2.85(2.92 – 2.85)
$CC_{1/2}$	0.998(0.790)	0.999(0.760)
Unique reflections	43223(3120)	14020(1030)
R_{meas}(%)[a]	7.7(175.3)	12.5(190.7)
Mean $I/\sigma(I)$[a]	18.9(1.8)	17.1(2.1)
Completeness(%)[a]	99.6(99.6)	99.2(99.1)
Multiplicity [a]	13.1(13.2)	19.0(20.6)
Refinement		
Resolution(Å)	43.33 – 2.51	
R_{work}/R_{free}[b]	0.1915/0.2294	
No.atoms		
Protein	3575	
DNA/Ligand	732/18	
Water	6	
Average *B* factors (Å^2)		
Protein	90.69	
DNA	125.29	
Ligand	69.14	
Water	69.95	
Wilson *B* factor (Å^2)	78.30	
R.m.s. deviations		
Bond lengths(Å)	0.005	
Bond angles(°)	0.689	
Ramachandran plot		
Favored (%)	97.31	
Allowed (%)	2.47	
Outliers (%)	0.22	

[a] The values in parentheses are for the outermost shell.

[b] R_{free} is the R_{work} based on 5% of the data excluded from the refinement.

$R_{\mathrm{meas}} = \sum_{hkl}\sqrt{n/(n-1)}\sum_{i=1}^{n}|\mathrm{I_i}(hkl) - \langle \mathrm{I}(hkl)\rangle| \,/\, \sum_{hkl}\sum_i \mathrm{I_i}(hkl)$, where $\langle \mathrm{I}(hkl)\rangle$ is the mean intensity of a set of equivalent reflections.

$R_{\mathrm{work}} = \sum_{hkl}||\mathrm{F_{obs}}| - |\mathrm{F_{calc}}|| \,/\, \sum_{hkl} |\mathrm{F_{obs}}|$ where F_{obs} and F_{calc} are observed and calculated structure factors, respectively.

Table S2. Target dsDNA sequences of different lengths

Sequence name	DNA sequence
vqmR18	5'- AGGGGGGATTTCCCCCCT -3'
vqmR20	5'- AAGGGGGGATTTCCCCCCTT -3'

Table S3. DPO-binding capacity of WT and mutant VqmA

VqmA	K_d (μM)	Δ*H* (kJ/mol)	Δ*G* (kJ/mol)	-*T*Δ*S* (kJ/mol)
WT	2.56	-46.3	-31.9	14.4
Y36F	7.86	-54.2	-29.2	25.0
F67A	No binding	N/A	N/A	N/A
F67I	22.7	-39.8	-26.5	13.2
Q70A	No binding	N/A	N/A	N/A
F99A	35.2	-22.4	-25.5	-3.08
F99I	3.56	-43.1	-31.1	12.0
K101	No binding	N/A	N/A	N/A
S229A	23.0	-61.5	-26.5	35.0

The VqmA–DPO binding affnity was determined using the ITC assay and is represented by the dissociation constant, K_d.

Table S4. Target dsDNA-binding capacity of Apo and DPO-binding VqmA

VqmA	K_d (nM)	Δ*H* (kJ/mol)	Δ*G* (kJ/mol)	-*T*Δ*S* (kJ/mol)
Apo	9.73	-111	-45.8	65.6
DPO-binding	10.3	-137	-45.6	91.7

The VqmA–dsDNA binding affnity was determined using the ITC assay and is represented by the dissociation constant, K_d.

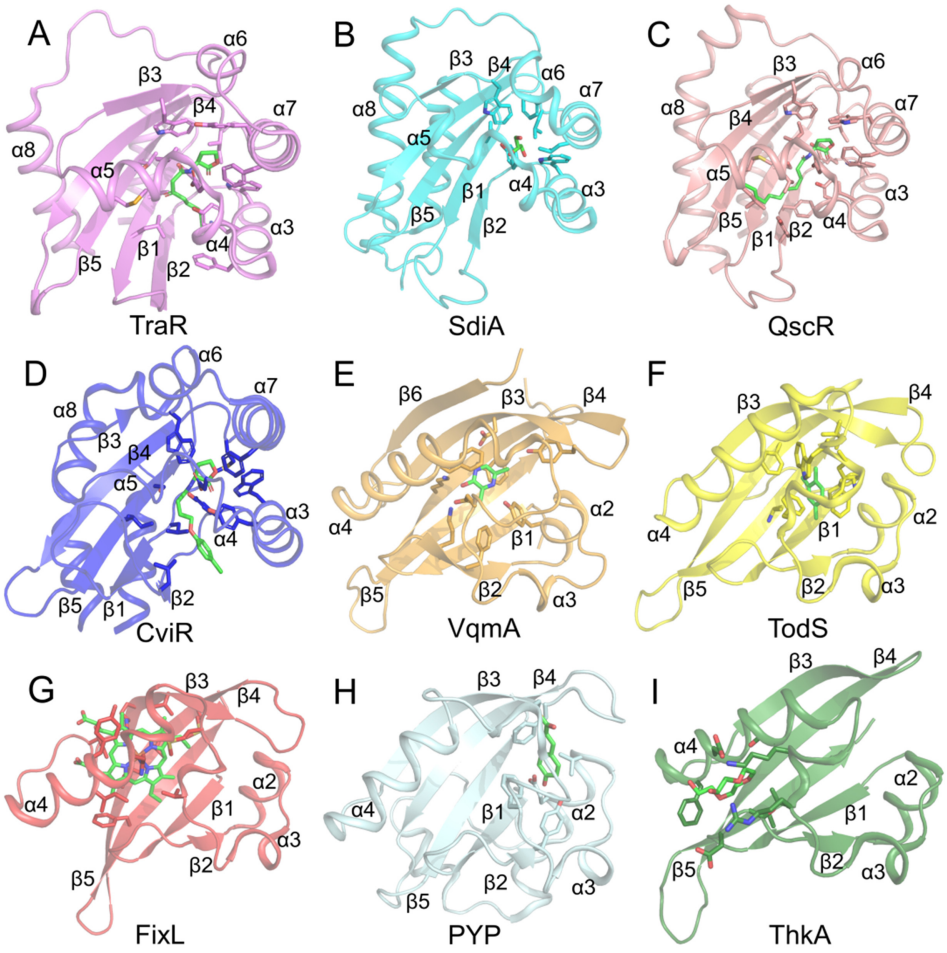

Figure S1. Structural comparison of the PAS domain of VqmA and other PAS domains. Ligands are represented as green stick models, and residues involved in ligand interaction are shown as stick models. (A) The PAS domain of TraR (PDB ID: 1L3L) is in violet. (B) The PAS domain of SdiA (PDB ID: 4LGW) is in cyan. (C) The PAS domain of QscR (PDB ID: 6CC0) is in pink. (D) The PAS domain of CviR (PDB ID: 3QP5) is in blue. (E) The PAS domain of VqmA is in orange. (F) The PAS domain of TodS (PDB ID: 5HWW) is in yellow. (G) The PAS domain of FixL (PDB ID: 1DP6) is in red. (H) The PAS domain of PYP (PDB ID: 1F98) is in silver. (I) The PAS domain of ThkA (PDB ID: 3A0S) is in dark green.

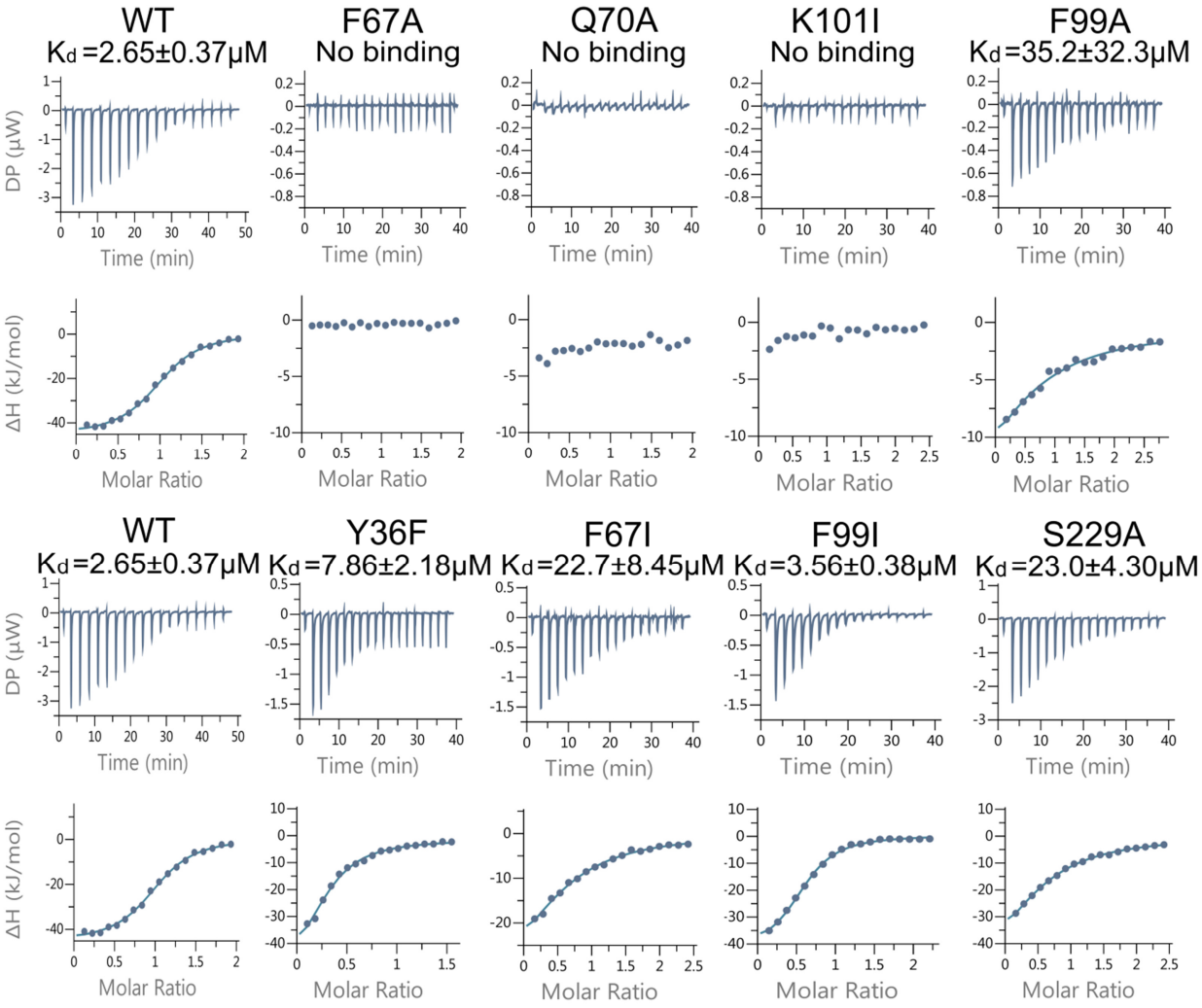

Figure S2. ITC profiles for the interactions of WT VqmA and its mutants (Y36F, F67A, F67I, Q70A, F99A, F99I, K101I, S229A) with DPO. K_d, dissociation constant. In order to better show the differences between WT VqmA and its mutants in ligand binding ability, the ITC profile of WT VqmA, which is shown in figure 5D, is listed in the first line of this figure.