Full wwPDB X-ray Structure Validation Report ⓘ

Oct 5, 2023 – 07:15 AM EDT

PDB ID	:	6V34
Title	:	Crystal structure of BRAF V600E oncogenic mutant in complex with TAK-580
Authors	:	Gonzalez Del-Pino, G.; Li, K.; Eck, M.J.
Deposited on	:	2019-11-25
Resolution	:	3.15 Å(reported)

This is a Full wwPDB X-ray Structure Validation Report for a publicly released PDB entry.

We welcome your comments at *validation@mail.wwpdb.org*
A user guide is available at
https://www.wwpdb.org/validation/2017/XrayValidationReportHelp
with specific help available everywhere you see the ⓘ symbol.

The types of validation reports are described at
http://www.wwpdb.org/validation/2017/FAQs#types.

The following versions of software and data (see references ⓘ) were used in the production of this report:

MolProbity	:	FAILED
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	FAILED
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.35.1

1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure:
X-RAY DIFFRACTION

The reported resolution of this entry is 3.15 Å.

There are no overall percentile quality scores available for this entry.

MolProbity and EDS failed to run properly - the sequence quality summary graphics cannot be shown.

2 Entry composition (i)

There are 2 unique types of molecules in this entry. The entry contains 4087 atoms, of which 0 are hydrogens and 0 are deuteriums.

In the tables below, the ZeroOcc column contains the number of atoms modelled with zero occupancy, the AltConf column contains the number of residues with at least one atom in alternate conformation and the Trace column contains the number of residues modelled with at most 2 atoms.

- Molecule 1 is a protein called Serine/threonine-protein kinase B-raf.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	256	Total	C	N	O	S	0	0	0
			2041	1295	363	370	13			
1	B	247	Total	C	N	O	S	0	0	0
			1982	1263	349	357	13			

There are 48 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	441	GLY	-	expression tag	UNP A0A2R8Y8E0
A	442	GLY	-	expression tag	UNP A0A2R8Y8E0
A	443	GLY	-	expression tag	UNP A0A2R8Y8E0
A	444	ARG	-	expression tag	UNP A0A2R8Y8E0
A	445	ASP	-	expression tag	UNP A0A2R8Y8E0
A	446	ALA	-	expression tag	UNP A0A2R8Y8E0
A	447	ALA	-	expression tag	UNP A0A2R8Y8E0
A	543	ALA	ILE	engineered mutation	UNP A0A2R8Y8E0
A	544	SER	ILE	engineered mutation	UNP A0A2R8Y8E0
A	551	LYS	ILE	engineered mutation	UNP A0A2R8Y8E0
A	562	ARG	GLN	engineered mutation	UNP A0A2R8Y8E0
A	588	ASN	LEU	engineered mutation	UNP A0A2R8Y8E0
A	600	GLU	VAL	engineered mutation	UNP A0A2R8Y8E0
A	630	SER	LYS	engineered mutation	UNP A0A2R8Y8E0
A	667	GLU	PHE	engineered mutation	UNP A0A2R8Y8E0
A	673	SER	TYR	engineered mutation	UNP A0A2R8Y8E0
A	688	ARG	ALA	engineered mutation	UNP A0A2R8Y8E0
A	706	SER	LEU	engineered mutation	UNP A0A2R8Y8E0
A	709	ARG	GLN	engineered mutation	UNP A0A2R8Y8E0
A	713	GLU	SER	engineered mutation	UNP A0A2R8Y8E0
A	716	GLU	LEU	engineered mutation	UNP A0A2R8Y8E0
A	720	GLU	SER	engineered mutation	UNP A0A2R8Y8E0
A	722	SER	-	expression tag	UNP A0A2R8Y8E0
A	723	GLY	-	expression tag	UNP A0A2R8Y8E0
B	441	GLY	-	expression tag	UNP A0A2R8Y8E0

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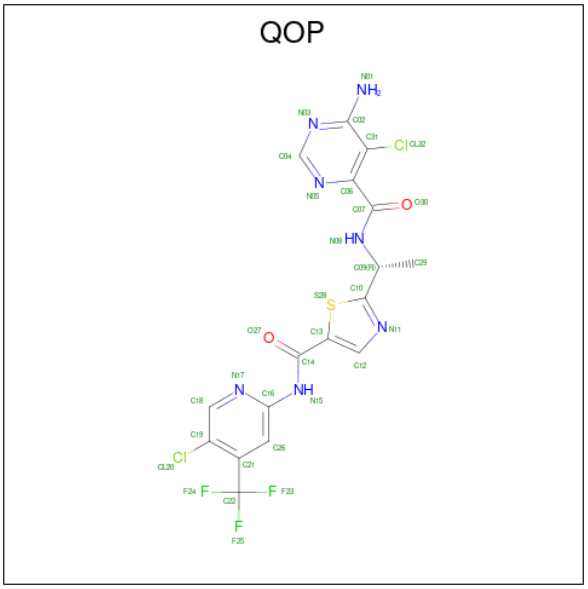
Chain	Residue	Modelled	Actual	Comment	Reference
B	442	GLY	-	expression tag	UNP A0A2R8Y8E0
B	443	GLY	-	expression tag	UNP A0A2R8Y8E0
B	444	ARG	-	expression tag	UNP A0A2R8Y8E0
B	445	ASP	-	expression tag	UNP A0A2R8Y8E0
B	446	ALA	-	expression tag	UNP A0A2R8Y8E0
B	447	ALA	-	expression tag	UNP A0A2R8Y8E0
B	543	ALA	ILE	engineered mutation	UNP A0A2R8Y8E0
B	544	SER	ILE	engineered mutation	UNP A0A2R8Y8E0
B	551	LYS	ILE	engineered mutation	UNP A0A2R8Y8E0
B	562	ARG	GLN	engineered mutation	UNP A0A2R8Y8E0
B	588	ASN	LEU	engineered mutation	UNP A0A2R8Y8E0
B	600	GLU	VAL	engineered mutation	UNP A0A2R8Y8E0
B	630	SER	LYS	engineered mutation	UNP A0A2R8Y8E0
B	667	GLU	PHE	engineered mutation	UNP A0A2R8Y8E0
B	673	SER	TYR	engineered mutation	UNP A0A2R8Y8E0
B	688	ARG	ALA	engineered mutation	UNP A0A2R8Y8E0
B	706	SER	LEU	engineered mutation	UNP A0A2R8Y8E0
B	709	ARG	GLN	engineered mutation	UNP A0A2R8Y8E0
B	713	GLU	SER	engineered mutation	UNP A0A2R8Y8E0
B	716	GLU	LEU	engineered mutation	UNP A0A2R8Y8E0
B	720	GLU	SER	engineered mutation	UNP A0A2R8Y8E0
B	722	SER	-	expression tag	UNP A0A2R8Y8E0
B	723	GLY	-	expression tag	UNP A0A2R8Y8E0

- Molecule 2 is 6-amino-5-chloro-N-[(1R)-1-(5-{[5-chloro-4-(trifluoromethyl)pyridin-2-yl]carbamoyl}-1,3-thiazol-2-yl)ethyl]pyrimidine-4-carboxamide (three-letter code: QOP) (formula: $C_{17}H_{12}Cl_2F_3N_7O_2S$) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms							ZeroOcc	AltConf
2	A	1	Total	C	Cl	F	N	O	S	0	0
			32	17	2	3	7	2	1		
2	B	1	Total	C	Cl	F	N	O	S	0	0
			32	17	2	3	7	2	1		

MolProbity and EDS failed to run properly - this section is therefore empty.

3 Data and refinement statistics (i)

EDS failed to run properly - this section is therefore incomplete.

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	48.80Å 85.24Å 122.91Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	24.92 – 3.15	Depositor
% Data completeness (in resolution range)	97.0 (24.92-3.15)	Depositor
R_{merge}	0.25	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	2.04 (at 3.17Å)	Xtriage
Refinement program	PHENIX 1.17.1_3660	Depositor
R, R_{free}	0.255 , 0.286	Depositor
Wilson B-factor (Å^2)	70.9	Xtriage
Anisotropy	0.569	Xtriage
L-test for twinning[2]	$< \|L\| > = 0.50$, $< L^2 > = 0.34$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
Total number of atoms	4087	wwPDB-VP
Average B, all atoms (Å^2)	81.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 7.25% of the height of the origin peak. No significant pseudotranslation is detected.*

[1] Intensities estimated from amplitudes.

[2] Theoretical values of $< |L| >$, $< L^2 >$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 0.2 for perfectly twinned datasets.

4 Model quality

4.1 Standard geometry

MolProbity failed to run properly - this section is therefore empty.

4.2 Too-close contacts

MolProbity failed to run properly - this section is therefore empty.

4.3 Torsion angles

4.3.1 Protein backbone

MolProbity failed to run properly - this section is therefore empty.

4.3.2 Protein sidechains

MolProbity failed to run properly - this section is therefore empty.

4.3.3 RNA

MolProbity failed to run properly - this section is therefore empty.

4.4 Non-standard residues in protein, DNA, RNA chains

There are no non-standard protein/DNA/RNA residues in this entry.

4.5 Carbohydrates

There are no monosaccharides in this entry.

4.6 Ligand geometry

2 ligands are modelled in this entry.

In the following table, the Counts columns list the number of bonds (or angles) for which Mogul statistics could be retrieved, the number of bonds (or angles) that are observed in the model and the number of bonds (or angles) that are defined in the Chemical Component Dictionary. The Link column lists molecule types, if any, to which the group is linked. The Z score for a bond

length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\#\|Z\| > 2$	Counts	RMSZ	$\#\|Z\| > 2$
2	QOP	A	801	-	29,34,34	2.59	12 (41%)	34,50,50	2.08	9 (26%)
2	QOP	B	801	-	29,34,34	2.60	12 (41%)	34,50,50	2.08	9 (26%)

In the following table, the Chirals column lists the number of chiral outliers, the number of chiral centers analysed, the number of these observed in the model and the number defined in the Chemical Component Dictionary. Similar counts are reported in the Torsion and Rings columns. '-' means no outliers of that kind were identified.

Mol	Type	Chain	Res	Link	Chirals	Torsions	Rings
2	QOP	A	801	-	-	3/18/26/26	0/3/3/3
2	QOP	B	801	-	-	3/18/26/26	0/3/3/3

All (24) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	B	801	QOP	C12-N11	7.53	1.47	1.36
2	A	801	QOP	C12-N11	7.51	1.47	1.36
2	B	801	QOP	C07-N08	5.42	1.46	1.34
2	A	801	QOP	C07-N08	5.33	1.45	1.34
2	B	801	QOP	C02-N01	4.58	1.45	1.34
2	A	801	QOP	C02-N01	4.57	1.45	1.34
2	A	801	QOP	C14-N15	3.89	1.46	1.35
2	B	801	QOP	C14-N15	3.81	1.45	1.35
2	A	801	QOP	C10-S28	-3.40	1.63	1.73
2	B	801	QOP	C10-S28	-3.37	1.63	1.73
2	B	801	QOP	C31-C02	-3.14	1.39	1.41
2	A	801	QOP	C31-C02	-3.11	1.39	1.41
2	B	801	QOP	C31-CL32	2.96	1.79	1.72
2	A	801	QOP	C31-CL32	2.92	1.79	1.72
2	B	801	QOP	C12-C13	2.67	1.42	1.37
2	A	801	QOP	C12-C13	2.61	1.42	1.37
2	A	801	QOP	C16-N15	2.45	1.45	1.40
2	B	801	QOP	C16-N15	2.37	1.45	1.40
2	B	801	QOP	C19-CL20	2.25	1.79	1.73
2	A	801	QOP	O30-C07	-2.22	1.18	1.23
2	B	801	QOP	O30-C07	-2.19	1.18	1.23
2	A	801	QOP	C19-CL20	2.19	1.78	1.73
2	B	801	QOP	O27-C14	-2.18	1.18	1.23

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Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	801	QOP	O27-C14	-2.14	1.18	1.23

All (18) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	A	801	QOP	C18-N17-C16	4.90	122.80	117.82
2	B	801	QOP	C18-N17-C16	4.84	122.73	117.82
2	B	801	QOP	C31-C02-N01	-4.46	120.33	122.94
2	A	801	QOP	N05-C04-N03	-4.42	121.70	128.60
2	B	801	QOP	N05-C04-N03	-4.32	121.84	128.60
2	A	801	QOP	C31-C02-N01	-4.20	120.48	122.94
2	B	801	QOP	C13-C14-N15	3.48	119.36	113.93
2	A	801	QOP	C19-C18-N17	-3.38	119.93	122.84
2	B	801	QOP	C19-C18-N17	-3.18	120.11	122.84
2	A	801	QOP	C13-C14-N15	3.10	118.77	113.93
2	B	801	QOP	C29-C09-C10	-2.80	107.72	110.95
2	B	801	QOP	C04-N05-C06	2.54	121.67	116.42
2	A	801	QOP	F23-C22-C21	-2.51	108.32	112.70
2	A	801	QOP	C04-N05-C06	2.51	121.61	116.42
2	A	801	QOP	C29-C09-C10	-2.51	108.06	110.95
2	B	801	QOP	C16-N15-C14	-2.40	121.43	128.07
2	B	801	QOP	F24-C22-C21	-2.19	108.89	112.70
2	A	801	QOP	F25-C22-C21	-2.08	109.07	112.70

There are no chirality outliers.

All (6) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	B	801	QOP	N17-C16-N15-C14
2	B	801	QOP	C26-C16-N15-C14
2	A	801	QOP	N17-C16-N15-C14
2	A	801	QOP	C26-C16-N15-C14
2	B	801	QOP	C31-C06-C07-O30
2	A	801	QOP	C31-C06-C07-O30

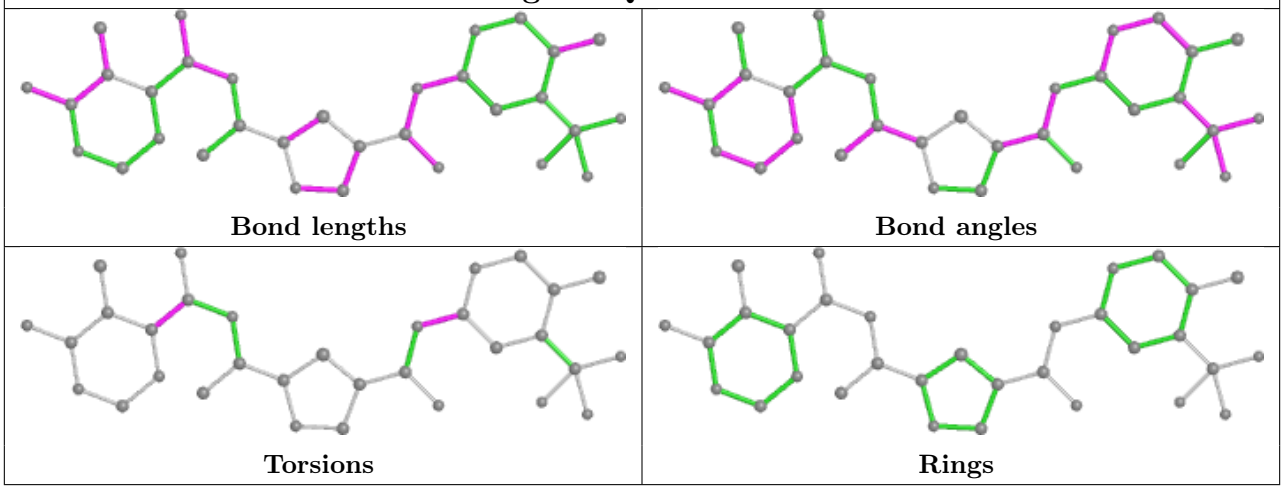
There are no ring outliers.

No monomer is involved in short contacts.

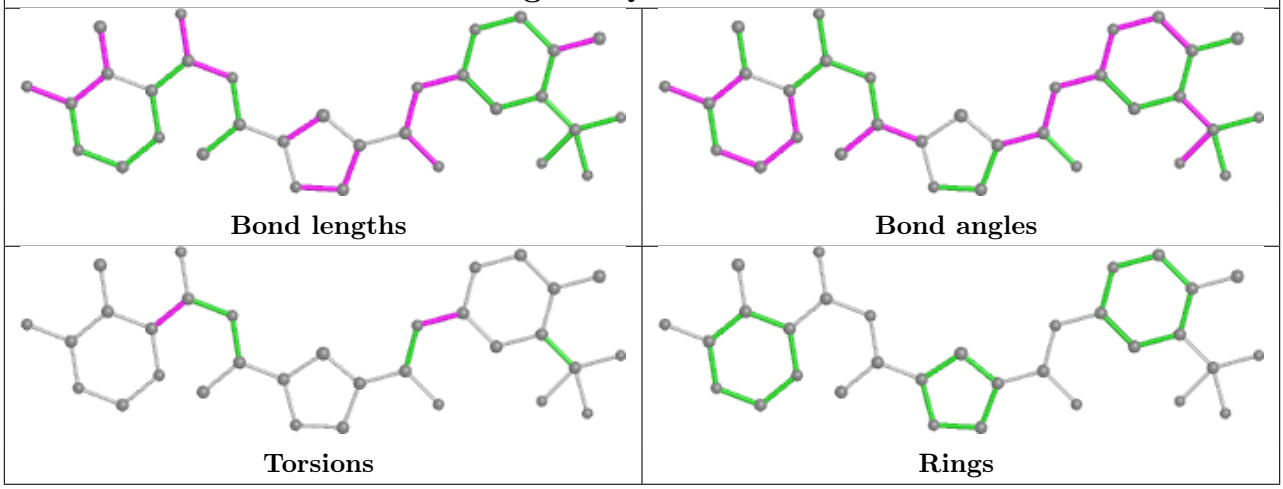
The following is a two-dimensional graphical depiction of Mogul quality analysis of bond lengths, bond angles, torsion angles, and ring geometry for all instances of the Ligand of Interest. In addition, ligands with molecular weight > 250 and outliers as shown on the validation Tables will also be included. For torsion angles, if less then 5% of the Mogul distribution of torsion angles is

within 10 degrees of the torsion angle in question, then that torsion angle is considered an outlier. Any bond that is central to one or more torsion angles identified as an outlier by Mogul will be highlighted in the graph. For rings, the root-mean-square deviation (RMSD) between the ring in question and similar rings identified by Mogul is calculated over all ring torsion angles. If the average RMSD is greater than 60 degrees and the minimal RMSD between the ring in question and any Mogul-identified rings is also greater than 60 degrees, then that ring is considered an outlier. The outliers are highlighted in purple. The color gray indicates Mogul did not find sufficient equivalents in the CSD to analyse the geometry.

Ligand QOP A 801



Ligand QOP B 801



4.7 Other polymers (i)

There are no such residues in this entry.

4.8 Polymer linkage issues (i)

There are no chain breaks in this entry.

5 Fit of model and data

5.1 Protein, DNA and RNA chains

EDS failed to run properly - this section is therefore empty.

5.2 Non-standard residues in protein, DNA, RNA chains

EDS failed to run properly - this section is therefore empty.

5.3 Carbohydrates

EDS failed to run properly - this section is therefore empty.

5.4 Ligands

EDS failed to run properly - this section is therefore empty.

5.5 Other polymers

EDS failed to run properly - this section is therefore empty.