



# wwPDB X-ray Structure Validation Summary Report ⓘ

Feb 1, 2016 – 10:39 AM GMT

PDB ID : 3ML8  
Title : Discovery of the Highly Potent PI3K/mTOR Dual Inhibitor PF-04691502  
through Structure Based Drug Design  
Authors : Knighton, D.R.  
Deposited on : 2010-04-16  
Resolution : 2.70 Å(reported)

This is a wwPDB X-ray Structure Validation Summary Report for a publicly released PDB entry.  
We welcome your comments at [validation@mail.wwpdb.org](mailto:validation@mail.wwpdb.org)  
A user guide is available at  
<http://wwpdb.org/validation/2016/XrayValidationReportHelp>  
with specific help available everywhere you see the ⓘ symbol.

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

MolProbity : 4.02b-467  
Mogul : 1.7 (RC4), CSD as536be (2015)  
Xtriage (Phenix) : 1.9-1692  
EDS : rb-20026688  
Percentile statistics : 20151230.v01 (using entries in the PDB archive December 30th 2015)  
Refmac : 5.8.0135  
CCP4 : 6.5.0  
Ideal geometry (proteins) : Engh & Huber (2001)  
Ideal geometry (DNA, RNA) : Parkinson et al. (1996)  
Validation Pipeline (wwPDB-VP) : trunk26865

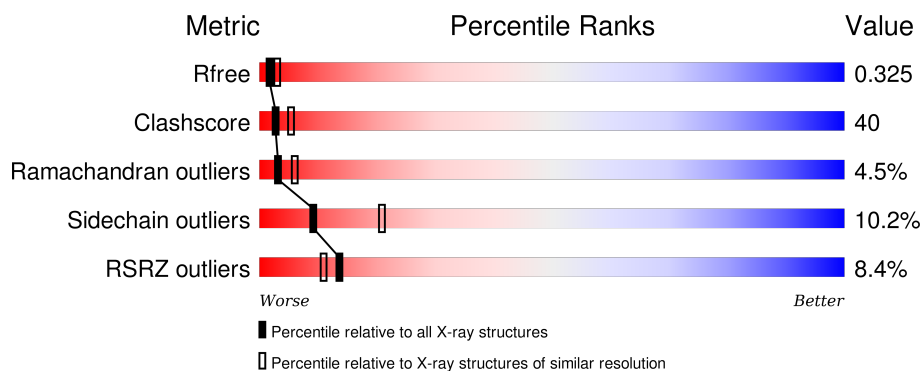
# 1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

## *X-RAY DIFFRACTION*

The reported resolution of this entry is 2.70 Å.

Percentile scores (ranging between 0-100) for global validation metrics of the entry are shown in the following graphic. The table shows the number of entries on which the scores are based.



Metric	Whole archive (#Entries)	Similar resolution (#Entries, resolution range(Å))
$R_{free}$	91344	2103 (2.70-2.70)
Clashscore	102246	2422 (2.70-2.70)
Ramachandran outliers	100387	2382 (2.70-2.70)
Sidechain outliers	100360	2382 (2.70-2.70)
RSRZ outliers	91569	2107 (2.70-2.70)

The table below summarises the geometric issues observed across the polymeric chains and their fit to the electron density. The red, orange, yellow and green segments on the lower bar indicate the fraction of residues that contain outliers for  $\geq 3$ , 2, 1 and 0 types of geometric quality criteria. A grey segment represents the fraction of residues that are not modelled. The numeric value for each fraction is indicated below the corresponding segment, with a dot representing fractions  $\leq 5\%$ . The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density. The numeric value is given above the bar.

Mol	Chain	Length	Quality of chain
1	A	966	<div> <div>7%</div> <div>36%</div> <div>44%</div> <div>7%</div> <div>13%</div> </div>

## 2 Entry composition

There are 2 unique types of molecules in this entry. The entry contains 6858 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.

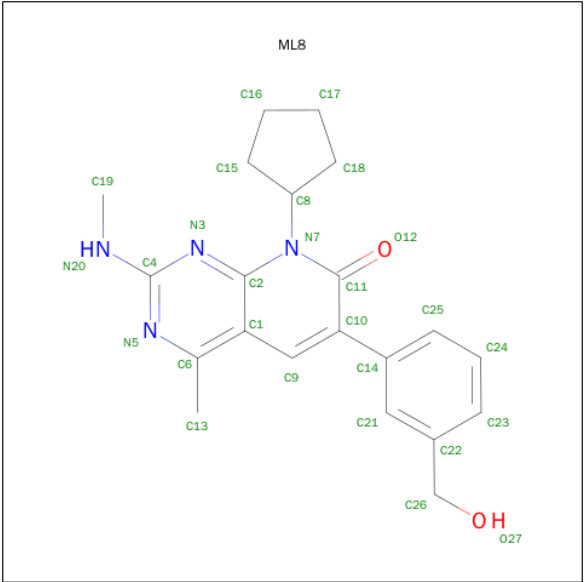
- Molecule 1 is a protein called Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma isoform.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	843	Total	C	N	O	S	0	0	0
			6831	4392	1162	1242	35			

There are 8 discrepancies between the modelled and reference sequences:

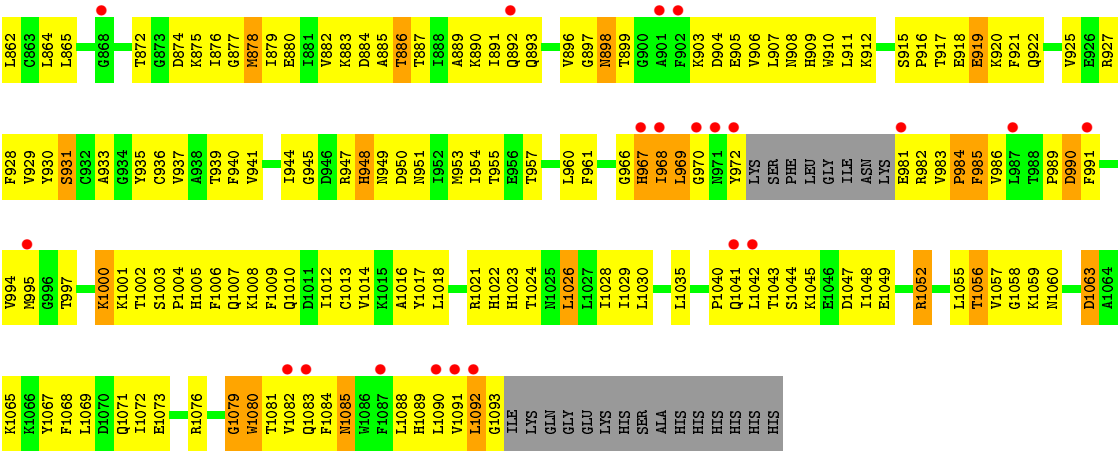
Chain	Residue	Modelled	Actual	Comment	Reference
A	143	MET	-	EXPRESSION TAG	UNP P48736
A	459	ARG	GLN	CONFLICT	UNP P48736
A	1103	HIS	-	EXPRESSION TAG	UNP P48736
A	1104	HIS	-	EXPRESSION TAG	UNP P48736
A	1105	HIS	-	EXPRESSION TAG	UNP P48736
A	1106	HIS	-	EXPRESSION TAG	UNP P48736
A	1107	HIS	-	EXPRESSION TAG	UNP P48736
A	1108	HIS	-	EXPRESSION TAG	UNP P48736

- Molecule 2 is 8-CYCLOPENTYL-6-[3-(HYDROXYMETHYL)PHENYL]-4-METHYL-2-(METHYLAMINO)PYRIDO[2,3-D]PYRIMIDIN-7(8H)-ONE (three-letter code: ML8) (formula: C<sub>21</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub>).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
2	A	1	Total	C	N	O	0	0
			27	21	4	2		





## 4 Data and refinement statistics

Property	Value	Source
Space group	C 1 2 1	Depositor
Cell constants a, b, c, $\alpha$ , $\beta$ , $\gamma$	144.24Å 67.39Å 106.88Å 90.00° 95.12° 90.00°	Depositor
Resolution (Å)	37.54 – 2.70 44.72 – 2.52	Depositor EDS
% Data completeness (in resolution range)	95.2 (37.54-2.70) 94.6 (44.72-2.52)	Depositor EDS
$R_{merge}$	0.05	Depositor
$R_{sym}$	0.05	Depositor
$\langle I/\sigma(I) \rangle$ <sup>1</sup>	0.00 (at 2.51Å)	Xtriage
Refinement program	CNX 2005	Depositor
R, $R_{free}$	0.246 , 0.324 0.242 , 0.325	Depositor DCC
$R_{free}$ test set	1400 reflections (5.45%)	DCC
Wilson B-factor (Å <sup>2</sup> )	68.2	Xtriage
Anisotropy	0.261	Xtriage
Bulk solvent $k_{sol}$ (e/Å <sup>3</sup> ), $B_{sol}$ (Å <sup>2</sup> )	0.33 , 54.9	EDS
Estimated twinning fraction	No twinning to report.	Xtriage
L-test for twinning <sup>2</sup>	$\langle  L  \rangle = 0.49$ , $\langle L^2 \rangle = 0.32$	Xtriage
Outliers	0 of 34301 reflections	Xtriage
$F_o, F_c$ correlation	0.93	EDS
Total number of atoms	6858	wwPDB-VP
Average B, all atoms (Å <sup>2</sup> )	71.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 5.47% of the height of the origin peak. No significant pseudotranslation is detected.*

<sup>1</sup>Intensities estimated from amplitudes.

<sup>2</sup>Theoretical values of  $\langle |L| \rangle$ ,  $\langle L^2 \rangle$  for acentric reflections are 0.5, 0.375 respectively for untwinned datasets, and 0.333, 0.2 for perfectly twinned datasets.

## 5 Model quality [i](#)

### 5.1 Standard geometry [i](#)

Bond lengths and bond angles in the following residue types are not validated in this section: ML8

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  $|Z| > 5$  is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Chain	Bond lengths		Bond angles	
		RMSZ	$\# Z  > 5$	RMSZ	$\# Z  > 5$
1	A	0.41	0/6979	0.57	0/9443

Chiral center outliers are detected by calculating the chiral volume of a chiral center and verifying if the center is modelled as a planar moiety or with the opposite hand. A planarity outlier is detected by checking planarity of atoms in a peptide group, atoms in a mainchain group or atoms of a sidechain that are expected to be planar.

Mol	Chain	#Chirality outliers	#Planarity outliers
1	A	0	2

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

All (2) planarity outliers are listed below:

Mol	Chain	Res	Type	Group
1	A	497	PHE	Peptide
1	A	524	CYS	Peptide

### 5.2 Too-close contacts [i](#)

In the following table, the Non-H and H(model) columns list the number of non-hydrogen atoms and hydrogen atoms in the chain respectively. The H(added) column lists the number of hydrogen atoms added and optimized by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, whereas Symm-Clashes lists symmetry related clashes.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	6831	0	6871	552	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
2	A	27	0	24	3	0
All	All	6858	0	6895	553	0

The all-atom clashscore is defined as the number of clashes found per 1000 atoms (including hydrogen atoms). The all-atom clashscore for this structure is 40.

The worst 5 of 553 close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:524:CYS:HB2	1:A:525:HIS:HA	1.28	1.09
1:A:524:CYS:CB	1:A:525:HIS:HA	1.87	1.04
1:A:351:THR:HG23	1:A:526:PRO:HB2	1.40	1.04
1:A:527:ILE:HA	1:A:528:ALA:HB2	1.36	1.02
1:A:291:GLN:HA	1:A:291:GLN:HE21	1.26	0.98

There are no symmetry-related clashes.

## 5.3 Torsion angles [i](#)

### 5.3.1 Protein backbone [i](#)

In the following table, the Percentiles column shows the percent Ramachandran outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the backbone conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles
1	A	825/966 (85%)	684 (83%)	104 (13%)	37 (4%)	<b>3</b> <b>6</b>

5 of 37 Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	164	ASP
1	A	227	SER
1	A	230	SER
1	A	231	GLN
1	A	288	LYS

### 5.3.2 Protein sidechains ⓘ

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the sidechain conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Rotameric	Outliers	Percentiles
1	A	758/864 (88%)	681 (90%)	77 (10%)	9 21

5 of 77 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	647	LYS
1	A	766	GLN
1	A	1052	ARG
1	A	653	ASP
1	A	729	LEU

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 23 such sidechains are listed below:

Mol	Chain	Res	Type
1	A	737	GLN
1	A	766	GLN
1	A	1083	GLN
1	A	743	GLN
1	A	773	ASN

### 5.3.3 RNA ⓘ

There are no RNA molecules in this entry.

## 5.4 Non-standard residues in protein, DNA, RNA chains ⓘ

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

## 5.5 Carbohydrates ⓘ

There are no carbohydrates in this entry.

## 5.6 Ligand geometry ⓘ

1 ligand is 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	ML8	A	9999	-	29,30,30	2.37	10 (34%)	28,43,43	1.76	5 (17%)

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	ML8	A	9999	-	-	0/8/19/19	0/4/4/4

The worst 5 of 10 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	9999	ML8	C6-C1	-2.02	1.40	1.43
2	A	9999	ML8	C8-N7	2.13	1.52	1.49
2	A	9999	ML8	C25-C14	2.14	1.43	1.39
2	A	9999	ML8	C9-C1	2.22	1.46	1.42
2	A	9999	ML8	C21-C14	2.67	1.44	1.39

All (5) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	9999	ML8	C19-N20-C4	-4.65	117.83	123.07
2	A	9999	ML8	N3-C4-N5	-2.99	121.64	126.22
2	A	9999	ML8	C9-C1-C2	3.36	120.14	117.00
2	A	9999	ML8	N20-C4-N3	3.52	121.02	116.94
2	A	9999	ML8	C4-N3-C2	4.02	119.93	115.09

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 3 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	9999	ML8	3	0

## 5.7 Other polymers [i](#)

There are no such residues in this entry.

## 5.8 Polymer linkage issues [i](#)

There are no chain breaks in this entry.

## 6 Fit of model and data [i](#)

### 6.1 Protein, DNA and RNA chains [i](#)

In the following table, the column labelled ‘#RSRZ> 2’ contains the number (and percentage) of RSRZ outliers, followed by percent RSRZ outliers for the chain as percentile scores relative to all X-ray entries and entries of similar resolution. The OWAB column contains the minimum, median, 95<sup>th</sup> percentile and maximum values of the occupancy-weighted average B-factor per residue. The column labelled ‘Q< 0.9’ lists the number of (and percentage) of residues with an average occupancy less than 0.9.

Mol	Chain	Analysed	<RSRZ>	#RSRZ>2	OWAB(Å <sup>2</sup> )	Q<0.9
1	A	843/966 (87%)	0.56	71 (8%) 14 11	29, 70, 105, 121	0

The worst 5 of 71 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	971	ASN	7.1
1	A	409	LEU	6.0
1	A	1090	LEU	5.2
1	A	244	ILE	5.1
1	A	216	ALA	5.0

### 6.2 Non-standard residues in protein, DNA, RNA chains [i](#)

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

### 6.3 Carbohydrates [i](#)

There are no carbohydrates in this entry.

### 6.4 Ligands [i](#)

In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. LLDF column lists the quality of electron density of the group with respect to its neighbouring residues in protein, DNA or RNA chains. The B-factors column lists the minimum, median, 95<sup>th</sup> percentile and maximum values of B factors of atoms in the group. The column labelled ‘Q< 0.9’ lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	LLDF	B-factors(Å <sup>2</sup> )	Q<0.9
2	ML8	A	9999	27/27	0.94	0.26	1.20	47,51,58,59	0

## 6.5 Other polymers [i](#)

There are no such residues in this entry.