



Full wwPDB X-ray Structure Validation Report

Feb 28, 2014 – 09:46 AM GMT

PDB ID : 4HW4
Title : Discovery of potent Mcl-1 inhibitors using fragment-based methods and structure-based design
Authors : Friberg, A.; Zhao, B.
Deposited on : 2012-11-07
Resolution : 1.53 Å(reported)

This is a full wwPDB validation report for a publicly released PDB entry.
We welcome your comments at validation@mail.wwpdb.org
A user guide is available at <http://wwpdb.org/ValidationPDFNotes.html>

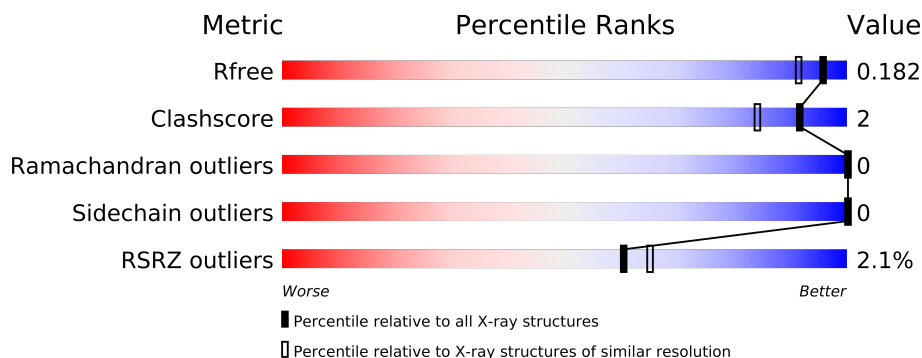
The following versions of software and data (see [references](#)) were used in the production of this report:

MolProbity : 4.02b-467
Mogul : 1.15 2013
Xtriage (Phenix) : dev-1323
EDS : stable22639
Percentile statistics : 21963
Refmac : 5.8.0049
CCP4 : 6.3.0 (Settle)
Ideal geometry (proteins) : Engh & Huber (2001)
Ideal geometry (DNA, RNA) : Parkinson et. al. (1996)
Validation Pipeline (wwPDB-VP) : stable22683

1 Overall quality at a glance

The reported resolution of this entry is 1.53 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}	66092	1031 (1.56-1.52)
Clashscore	79885	1155 (1.56-1.52)
Ramachandran outliers	78287	1127 (1.56-1.52)
Sidechain outliers	78261	1125 (1.56-1.52)
RSRZ outliers	66119	1031 (1.56-1.52)

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 ≥ 3 , 2, 1 and 0 types of geometric quality criteria. The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density.

Mol	Chain	Length	Quality of chain
1	A	157	
1	B	157	
2	C	18	
2	D	18	

2 Entry composition

There are 3 unique types of molecules in this entry. The entry contains 5727 atoms, of which 2686 are hydrogens and 0 are deuterium.

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 Induced myeloid leukemia cell differentiation protein Mcl-1.

Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
1	A	154	Total	C	H	N	O	S	0	3	0
			2506	780	1263	231	228	4			
1	B	141	Total	C	H	N	O	S	0	2	0
			2314	724	1165	212	210	3			

There are 2 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	171	GLY	-	EXPRESSION TAG	UNP Q07820
B	171	GLY	-	EXPRESSION TAG	UNP Q07820

- Molecule 2 is a protein called Mcl-1 BH3 peptide.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
2	C	18	Total	C	H	N	O	0	0	1
			260	77	129	30	24			
2	D	18	Total	C	H	N	O	0	0	1
			260	77	129	30	24			

- Molecule 3 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	A	212	Total	O	0	0
			212	212		
3	B	119	Total	O	0	0
			119	119		
3	C	32	Total	O	0	0
			32	32		
3	D	24	Total	O	0	0
			24	24		

3 Residue-property plots

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of errors displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and electron density. Residues are color-coded according to the number of geometric quality criteria for which they contain at least one outlier: green = 0, yellow = 1, orange = 2 and red = 3 or more. A red dot above a residue indicates a poor fit to the electron density ($RSRZ > 2$). Stretches of 2 or more consecutive residues without any outlier are shown as a green connector. Residues present in the sample, but not in the model, are shown in grey.

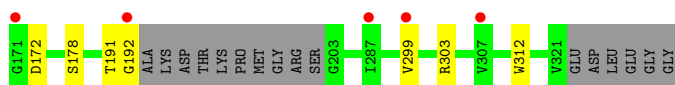
- Molecule 1: Induced myeloid leukemia cell differentiation protein Mcl-1

Chain A: 



- Molecule 1: Induced myeloid leukemia cell differentiation protein Mcl-1

Chain B: 



- Molecule 2: Mcl-1 BH3 peptide

Chain C: 



- Molecule 2: Mcl-1 BH3 peptide

Chain D: 

There are no outlier residues recorded for this chain.

4 Data and refinement statistics

Property	Value	Source
Space group	P 1 21 1	Depositor
Cell constants a, b, c, α , β , γ	50.07Å 48.35Å 68.18Å 90.00° 93.83° 90.00°	Depositor
Resolution (Å)	34.74 – 1.53 49.96 – 1.53	Depositor EDS
% Data completeness (in resolution range)	99.9 (34.74-1.53) 100.0 (49.96-1.53)	Depositor EDS
R_{merge}	0.05	Depositor
R_{sym}	0.04	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.75 (at 1.53Å)	Xtriage
Refinement program	PHENIX (phenix.refine: 1.8.1069)	Depositor
R, R_{free}	0.137 , 0.184 0.138 , 0.182	Depositor DCC
R_{free} test set	2494 reflections (5.06%)	DCC
Wilson B-factor (Å ²)	17.1	Xtriage
Anisotropy	0.629	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.43 , 43.3	EDS
Estimated twinning fraction	No twinning to report.	Xtriage
L-test for twinning	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.32$	Xtriage
Outliers	0 of 49304 reflections	Xtriage
F_o, F_c correlation	0.97	EDS
Total number of atoms	5727	wwPDB-VP
Average B, all atoms (Å ²)	21.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 8.81% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

5 Model quality

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: ACE, NH2

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	0.46	0/1272	0.58	0/1710
1	B	0.38	0/1173	0.49	0/1576
2	C	0.45	0/128	1.13	2/171 (1.2%)
2	D	0.45	0/128	0.69	0/171
All	All	0.43	0/2701	0.59	2/3628 (0.1%)

There are no bond length outliers.

All (2) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	C	0	ACE	O-C-N	10.55	139.57	122.70
2	C	0	ACE	C-N-CA	6.61	138.22	121.70

There are no chirality outliers.

There are no planarity outliers.

5.2 Close contacts

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 hydrogens added by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, and the number in parentheses is this value normalized per 1000 atoms of the molecule in the chain. The Symm-Clashes column gives symmetry related clashes, in the same way as for the Clashes column.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	1243	1263	0	5	0
1	B	1149	1165	0	4	0
2	C	131	129	0	0	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
2	D	131	129	0	0	0
3	A	212	0	0	0	1
3	B	119	0	0	0	1
3	C	32	0	0	0	1
3	D	24	0	0	0	1
All	All	3041	2686	0	9	2

Clashscore is defined as the number of clashes calculated for the entry per 1000 atoms (including hydrogens) of the entry. The overall clashscore for this entry is 2.

All (9) close contacts within the same asymmetric unit are listed below.

Atom-1	Atom-2	Distance(Å)	Clash(Å)
1:A:178:SER:HG	1:A:312:TRP:HE1	1.40	0.68
1:B:178:SER:HG	1:B:312:TRP:HE1	1.40	0.68
1:B:191:THR:OG1	1:B:192:GLY:N	2.27	0.67
1:B:172:ASP:OD2	1:B:303:ARG:NH2	2.43	0.50
1:B:299:VAL:O	1:B:303:ARG:HB2	2.16	0.45
1:A:239:ASN:HA	1:A:286:CYS:HG	1.82	0.44
1:A:214:ARG:O	1:A:218:ASP:HB2	2.18	0.44
1:A:190:ALA:O	1:A:279:LYS:HD3	2.19	0.43
1:A:246:LEU:HG	1:A:250:MET:HE2	2.03	0.40

All (2) symmetry-related close contacts are listed below. The label for Atom-2 includes the symmetry operator and encoded unit-cell translations to be applied.

Atom-1	Atom-2	Distance(Å)	Clash(Å)
3:B:515:HOH:O	3:D:124:HOH:O[2_454]	1.45	0.75
3:A:575:HOH:O	3:C:116:HOH:O[2_455]	1.81	0.39

5.3 Torsion angles

5.3.1 Protein backbone ⓘ

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	155/157 (99%)	153 (99%)	2 (1%)	0	100 100

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Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles	
1	B	139/157 (88%)	138 (99%)	1 (1%)	0	100	100
2	C	16/18 (89%)	16 (100%)	0	0	100	100
2	D	16/18 (89%)	16 (100%)	0	0	100	100
All	All	326/350 (93%)	323 (99%)	3 (1%)	0	100	100

There are no Ramachandran outliers to report.

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	134/135 (99%)	134 (100%)	0	100	100
1	B	125/135 (93%)	125 (100%)	0	100	100
2	C	13/13 (100%)	13 (100%)	0	100	100
2	D	13/13 (100%)	13 (100%)	0	100	100
All	All	285/296 (96%)	285 (100%)	0	100	100

There are no protein residues with a non-rotameric sidechain to report.

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (8) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	177	GLN
1	A	221	GLN
1	B	221	GLN
1	B	229	GLN
1	B	252	HIS
2	C	16	HIS
2	D	15	ASN
2	D	16	HIS

5.3.3 RNA ⓘ

There are no RNA chains 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 ⓘ

There are no ligands in this entry.

5.7 Other polymers ⓘ

There are no such residues in this entry.

5.8 Polymer linkage issues

There are no chain breaks in this entry.

6 Fit of model and data ⓘ

6.1 Protein, DNA and RNA chains ⓘ

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, 95th 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 ²)	Q<0.9
1	A	154/157 (98%)	-0.33	2 (1%) 74 79	7, 14, 27, 47	0
1	B	141/157 (89%)	-0.04	5 (3%) 42 44	10, 21, 43, 54	0
2	C	18/18 (100%)	-0.30	0 100 100	10, 12, 22, 28	0
2	D	18/18 (100%)	-0.55	0 100 100	12, 16, 22, 28	0
All	All	331/350 (94%)	-0.22	7 (2%) 60 65	7, 17, 37, 54	0

All (7) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	B	171	GLY	6.8
1	B	299	VAL	2.8
1	B	307	VAL	2.4
1	B	192	GLY	2.2
1	A	307	VAL	2.2
1	A	198	PRO	2.1
1	B	287	ILE	2.0

6.2 Non-standard residues in protein, DNA, RNA chains ⓘ

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

6.3 Carbohydrates ⓘ

There are no carbohydrates in this entry.

6.4 Ligands ⓘ

There are no ligands in this entry.

6.5 Other polymers ⓘ

There are no such residues in this entry.