# Full wwPDB NMR Structure Validation Report (i)

Jun 6, 2020 – 04:13 am BST

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|---|---|---|
| PDB ID | : | 6OVC |
| Title | : | hMcl1 inhibitor complex |
| Authors | : | Poppe, L. |
| Deposited on | : | 2019-05-07 |

This is a Full wwPDB NMR 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/NMRValidationReportHelp
with specific help available everywhere you see the (i) symbol.

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The following versions of software and data (see references (1)) were used in the production of this report:

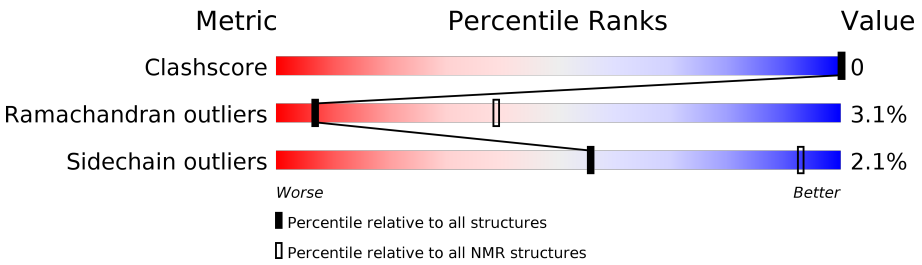
| | | |
|---|---|---|
| Cyrange | : | Kirchner and Güntert (2011) |
| NmrClust | : | Kelley et al. (1996) |
| MolProbity | : | 4.02b-467 |
| Mogul | : | 1.8.5 (274361), CSD as541be (2020) |
| buster-report | : | 1.1.7 (2018) |
| Percentile statistics | : | 20191225.v01 (using entries in the PDB archive December 25th 2019) |
| RCI | : | v_1n_11_5_13_A (Berjanski et al., 2005) |
| PANAV | : | Wang et al. (2010) |
| ShiftChecker | : | 2.11 |
| Ideal geometry (proteins) | : | Engh & Huber (2001) |
| Ideal geometry (DNA, RNA) | : | Parkinson et al. (1996) |
| Validation Pipeline (wwPDB-VP) | : | 2.11 |

# 1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure:
*SOLUTION NMR*

The overall completeness of chemical shifts assignment is 78%.

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) | NMR archive (#Entries) |
|---|---|---|
| Clashscore | 158937 | 12864 |
| Ramachandran outliers | 154571 | 11451 |
| Sidechain outliers | 154315 | 11428 |

The table below summarises the geometric issues observed across the polymeric chains and their fit to the experimental data. The red, orange, yellow and green segments indicate the fraction of residues that contain outliers for >=3, 2, 1 and 0 types of geometric quality criteria. A cyan segment indicates the fraction of residues that are not part of the well-defined cores, and 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 <=5%

| Mol | Chain | Length | Quality of chain |
|---|---|---|---|
| 1 | A | 164 | 95% |

# 2 Ensemble composition and analysis (i)

This entry contains 1 models. Identification of well-defined residues and clustering analysis are not possible.

# 3 Entry composition (i)

There are 2 unique types of molecules in this entry. The entry contains 2705 atoms, of which 1341 are hydrogens and 0 are deuteriums.

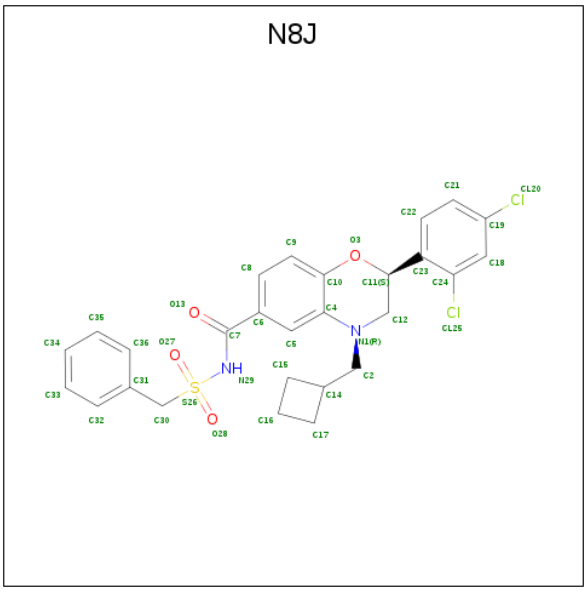
- Molecule 1 is a protein called Induced myeloid leukemia cell differentiation protein Mcl-1.

| Mol | Chain | Residues | Atoms | | | | | | Trace |
|---|---|---|---|---|---|---|---|---|---|
| | | | Total | C | H | N | O | S | |
| 1 | A | 164 | 2644 | 829 | 1316 | 249 | 246 | 4 | 0 |

There are 8 discrepancies between the modelled and reference sequences:

| Chain | Residue | Modelled | Actual | Comment | Reference |
|---|---|---|---|---|---|
| A | 1 | MET | - | initiating methionine | UNP Q07820 |
| A | 117 | SER | CYS | conflict | UNP Q07820 |
| A | 159 | HIS | - | expression tag | UNP Q07820 |
| A | 160 | HIS | - | expression tag | UNP Q07820 |
| A | 161 | HIS | - | expression tag | UNP Q07820 |
| A | 162 | HIS | - | expression tag | UNP Q07820 |
| A | 163 | HIS | - | expression tag | UNP Q07820 |
| A | 164 | HIS | - | expression tag | UNP Q07820 |

- Molecule 2 is (2S)-N-(benzylsulfonyl)-4-(cyclobutylmethyl)-2-(2,4-dichlorophenyl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide (three-letter code: N8J) (formula: $C_{27}H_{26}Cl_2N_2O_4S$) (labeled as "Ligand of Interest" by author).

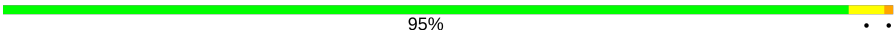


| Mol | Chain | Residues | Atoms | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Total | C | Cl | H | N | O | S |
| 2 | A | 1 | 61 | 27 | 2 | 25 | 2 | 4 | 1 |

# 4 Residue-property plots (i)

These plots are provided for all protein, RNA and DNA chains in the entry. The first graphic is the same as shown in the summary in section 1 of this report. The second graphic shows the sequence where residues are colour-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. Stretches of 2 or more consecutive residues without any outliers are shown as green connectors. Residues which are classified as ill-defined in the NMR ensemble, are shown in cyan with an underline colour-coded according to the previous scheme. Residues which were present in the experimental sample, but not modelled in the final structure are shown in grey.

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

Chain A: 

# 5 Refinement protocol and experimental data overview (i)

The models were refined using the following method: *simulated annealing*.

Of the 1 calculated structures, 1 were deposited, based on the following criterion: *structures with the lowest energy*.

The following table shows the software used for structure solution, optimisation and refinement.

| Software name | Classification | Version |
|---|---|---|
| Matlab | structure calculation | |
| MOE | refinement | |

The following table shows chemical shift validation statistics as aggregates over all chemical shift files. Detailed validation can be found in section 6 of this report.

| Chemical shift file(s) | input_cs.cif |
|---|---|
| Number of chemical shift lists | 1 |
| Total number of shifts | 1876 |
| Number of shifts mapped to atoms | 1876 |
| Number of unparsed shifts | 0 |
| Number of shifts with mapping errors | 0 |
| Number of shifts with mapping warnings | 0 |
| Assignment completeness (well-defined parts) | 78% |

No validations of the models with respect to experimental NMR restraints is performed at this time.

COVALENT-GEOMETRY INFOmissingINFO

## 5.1 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 each 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 averaged over the ensemble.

| Mol | Chain | Non-H | H(model) | H(added) | Clashes |
|---|---|---|---|---|---|
| All | All | 1364 | 1341 | 1313 | - |

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 -.

There are no clashes.

## 5.2 Torsion angles (i)

### 5.2.1 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 PDB entries followed by that with respect to all NMR entries. 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 | 162/164 (99%) | 145 (90%) | 12 (7%) | 5 (3%) | 7 39 |
| All | All | 162/164 (99%) | 145 (90%) | 12 (7%) | 5 (3%) | 7 39 |

All 5 Ramachandran outliers are listed below. They are sorted by the frequency of occurrence in the ensemble.

| Mol | Chain | Res | Type |
|---|---|---|---|
| 1 | A | 163 | HIS |
| 1 | A | 89 | VAL |
| 1 | A | 34 | GLY |
| 1 | A | 26 | ASP |
| 1 | A | 159 | HIS |

### 5.2.2 Protein sidechains (i)

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all PDB entries followed by that with respect to all NMR entries. 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 | 143/143 (100%) | 140 (98%) | 3 (2%) | 56 93 |
| All | All | 143/143 (100%) | 140 (98%) | 3 (2%) | 56 93 |

All 3 residues with a non-rotameric sidechain are listed below. They are sorted by the frequency of occurrence in the ensemble.

| Mol | Chain | Res | Type |
|---|---|---|---|
| 1 | A | 25 | LYS |
| 1 | A | 133 | LYS |
| 1 | A | 18 | ARG |

#### 5.2.3 RNA (i)

There are no RNA molecules in this entry.

### 5.3 Non-standard residues in protein, DNA, RNA chains (i)

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

### 5.4 Carbohydrates (i)

There are no carbohydrates in this entry.

### 5.5 Ligand geometry (i)

1 ligand is modelled in this entry.

In the following table, the Counts columns list the number of bonds for which Mogul statistics could be retrieved, the number of bonds that are observed in the model and the number of bonds 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 is the number of standard deviations the observed value is removed from the expected value. A bond length with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the average root-mean-square of all Z scores of the bond lengths.

| Mol | Type | Chain | Res | Link | Bond lengths | | |
|---|---|---|---|---|---|---|---|
| | | | | | Counts | RMSZ | #Z>2 |
| 2 | N8J | A | 201 | - | 39,40,40 | 1.00 | 0 (0%) |

In the following table, the Counts columns list the number of angles for which Mogul statistics could be retrieved, the number of angles that are observed in the model and the number of 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 angle is the number of standard deviations the observed value is removed from the expected value. A bond angle with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the average root-mean-square of all Z scores of the bond angles.

| Mol | Type | Chain | Res | Link | Bond angles | | |
|---|---|---|---|---|---|---|---|
| | | | | | Counts | RMSZ | #Z>2 |
| 2 | N8J | A | 201 | - | 50,58,58 | 1.51 | 0 (0%) |

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 | N8J | A | 201 | - | - | 2,22,40,40 | 0,5,5,5 |

There are no bond-length outliers.

There are no bond-angle outliers.

There are no chirality outliers.

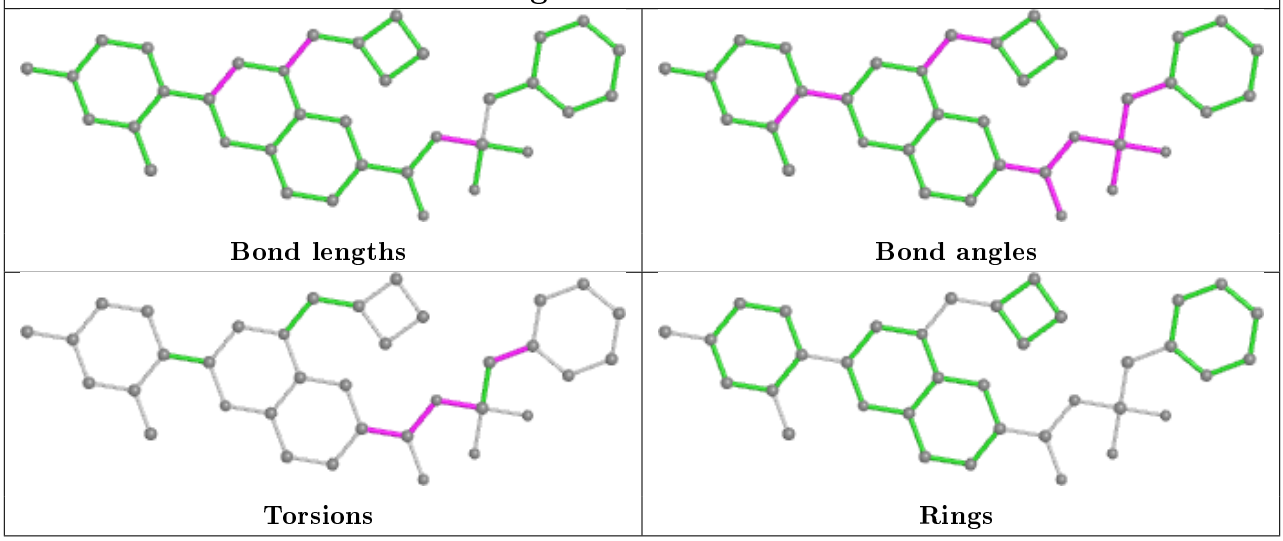
All torsion outliers are listed below.

| Mol | Chain | Res | Type | Atoms |
|---|---|---|---|---|
| 2 | A | 201 | N8J | C6-C7-N29-S26 |
| 2 | A | 201 | N8J | O13-C7-N29-S26 |

There are no ring outliers.

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 N8J A 201**



## 5.6 Other polymers (i)

There are no such molecules in this entry.

## 5.7 Polymer linkage issues (i)

There are no chain breaks in this entry.

# 6 Chemical shift validation (i)

The completeness of assignment taking into account all chemical shift lists is 78% for the well-defined parts and 78% for the entire structure.

## 6.1 Chemical shift list 1

File name: input_cs.cif

Chemical shift list name: *assigned_chem_shift_list_1*

### 6.1.1 Bookkeeping (i)

The following table shows the results of parsing the chemical shift list and reports the number of nuclei with statistically unusual chemical shifts.

| | |
|---|---|
| Total number of shifts | 1876 |
| Number of shifts mapped to atoms | 1876 |
| Number of unparsed shifts | 0 |
| Number of shifts with mapping errors | 0 |
| Number of shifts with mapping warnings | 0 |
| Number of shift outliers (ShiftChecker) | 5 |

### 6.1.2 Chemical shift referencing (i)

The following table shows the suggested chemical shift referencing corrections.

| Nucleus | # values | Correction ± precision, *ppm* | Suggested action |
|---|---|---|---|
| $^{13}C_{\alpha}$ | 159 | -0.61 ± 0.10 | Should be applied |
| $^{13}C_{\beta}$ | 146 | 0.43 ± 0.07 | None needed (< 0.5 ppm) |
| $^{13}C'$ | 0 | — | None (insufficient data) |
| $^{15}N$ | 155 | 0.36 ± 0.26 | None needed (< 0.5 ppm) |

### 6.1.3 Completeness of resonance assignments (i)

The following table shows the completeness of the chemical shift assignments for the well-defined regions of the structure. The overall completeness is 78%, i.e. 1646 atoms were assigned a chemical shift out of a possible 2099. 27 out of 27 assigned methyl groups (LEU and VAL) were assigned stereospecifically.

| | Total | $^{1}H$ | $^{13}C$ | $^{15}N$ |
|---|---|---|---|---|
| Backbone | 630/816 (77%) | 316/326 (97%) | 159/328 (48%) | 155/162 (96%) |
| Sidechain | 906/1095 (83%) | 558/640 (87%) | 330/393 (84%) | 18/62 (29%) |

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| | Total | $^{1}$H | $^{13}$C | $^{15}$N |
|---|---|---|---|---|
| Aromatic | 110/188 (59%) | 66/101 (65%) | 42/71 (59%) | 2/16 (12%) |
| Overall | 1646/2099 (78%) | 940/1067 (88%) | 531/792 (67%) | 175/240 (73%) |

The following table shows the completeness of the chemical shift assignments for the full structure. The overall completeness is 78%, i.e. 1646 atoms were assigned a chemical shift out of a possible 2099. 27 out of 27 assigned methyl groups (LEU and VAL) were assigned stereospecifically.

| | Total | $^{1}$H | $^{13}$C | $^{15}$N |
|---|---|---|---|---|
| Backbone | 630/816 (77%) | 316/326 (97%) | 159/328 (48%) | 155/162 (96%) |
| Sidechain | 906/1095 (83%) | 558/640 (87%) | 330/393 (84%) | 18/62 (29%) |
| Aromatic | 110/188 (59%) | 66/101 (65%) | 42/71 (59%) | 2/16 (12%) |
| Overall | 1646/2099 (78%) | 940/1067 (88%) | 531/792 (67%) | 175/240 (73%) |

### 6.1.4 Statistically unusual chemical shifts (i)

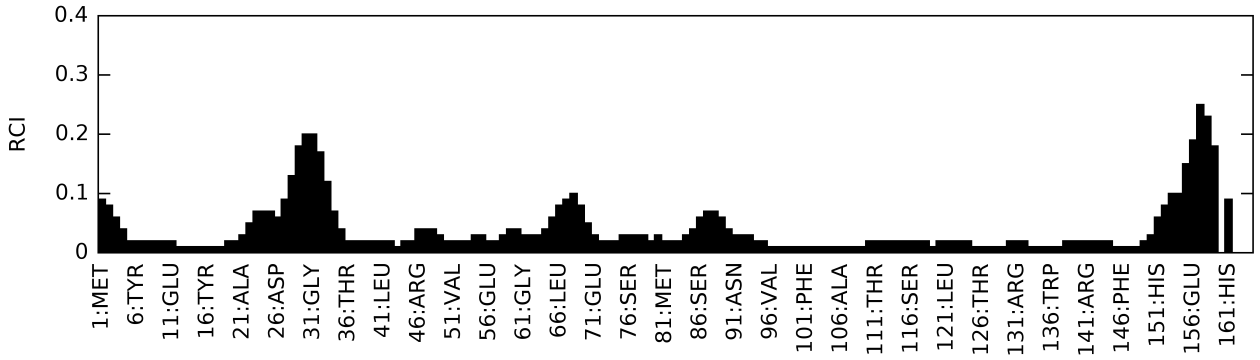
The following table lists the statistically unusual chemical shifts. These are statistical measures, and large deviations from the mean do not necessarily imply incorrect assignments. Molecules containing paramagnetic centres or hemes are expected to give rise to anomalous chemical shifts.

| Mol | Chain | Res | Type | Atom | Shift, *ppm* | Expected range, *ppm* | Z-score |
|---|---|---|---|---|---|---|---|
| 1 | A | 140 | GLN | HG3 | -0.05 | 3.75 – 0.85 | -8.1 |
| 1 | A | 90 | THR | HG21 | -0.49 | 2.29 – -0.01 | -7.1 |
| 1 | A | 90 | THR | HG22 | -0.49 | 2.29 – -0.01 | -7.1 |
| 1 | A | 90 | THR | HG23 | -0.49 | 2.29 – -0.01 | -7.1 |
| 1 | A | 140 | GLN | HG2 | 0.93 | 3.67 – 0.97 | -5.2 |

### 6.1.5 Random Coil Index (RCI) plots (i)

The image below reports *random coil index* values for the protein chains in the structure. The height of each bar gives a probability of a given residue to be disordered, as predicted from the available chemical shifts and the amino acid sequence. A value above 0.2 is an indication of significant predicted disorder. The colour of the bar shows whether the residue is in the well-defined core (black) or in the ill-defined residue ranges (cyan), as described in section 2 on ensemble composition.

Random coil index (RCI) for chain A:


RCI
0.4
0.3
0.2
0.1
0
1:MET
6:TYR
11:GLU
16:TYR
21:ALA
26:ASP
31:GLY
36:THR
41:LEU
46:ARG
51:VAL
56:GLU
61:GLY
66:LEU
71:GLU
76:SER
81:MET
86:SER
91:ASN
96:VAL
101:PHE
106:ALA
111:THR
116:SER
121:LEU
126:THR
131:ARG
136:TRP
141:ARG
146:PHE
151:HIS
156:GLU
161:HIS