



Full wwPDB X-ray Structure Validation Report ⓘ

Sep 5, 2016 – 02:29 PM EDT

PDB ID : 5IS5
Title : Discovery and Pharmacological Characterization of Novel Quinazoline-based PI3K delta-selective Inhibitors
Authors : Gutmann, S.; Rummel, G.; Shrestha, B.
Deposited on : 2016-03-15
Resolution : 2.85 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

<http://wwpdb.org/validation/2016/XrayValidationReportHelp>

with specific help available everywhere you see the ⓘ symbol.

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

MolProbity : 4.02b-467
Mogul : 1.7.1 (RC1), CSD as537be (2016)
Xtriage (Phenix) : 1.9-1692
EDS : rb-20027939
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) : rb-20027939

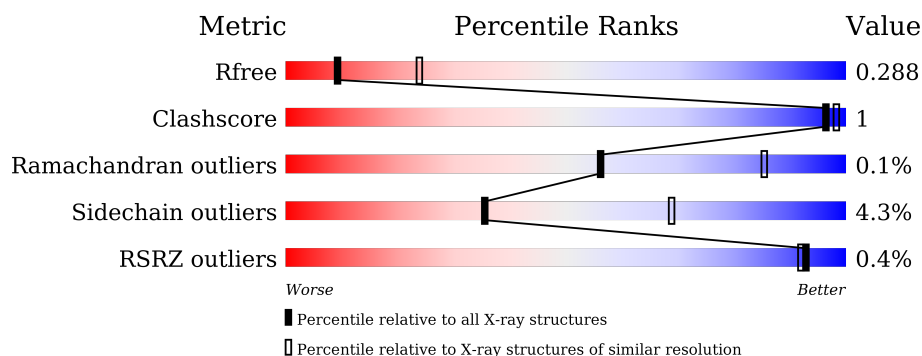
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.85 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	2228 (2.90-2.82)
Clashscore	102246	2499 (2.90-2.82)
Ramachandran outliers	100387	2439 (2.90-2.82)
Sidechain outliers	100360	2442 (2.90-2.82)
RSRZ outliers	91569	2236 (2.90-2.82)

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. 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	1044	

The following table lists non-polymeric compounds, carbohydrate monomers and non-standard residues in protein, DNA, RNA chains that are outliers for geometric or electron-density-fit criteria:

Mol	Type	Chain	Res	Chirality	Geometry	Clashes	Electron density
2	6CY	A	1101	-	-	-	X

2 Entry composition [i](#)

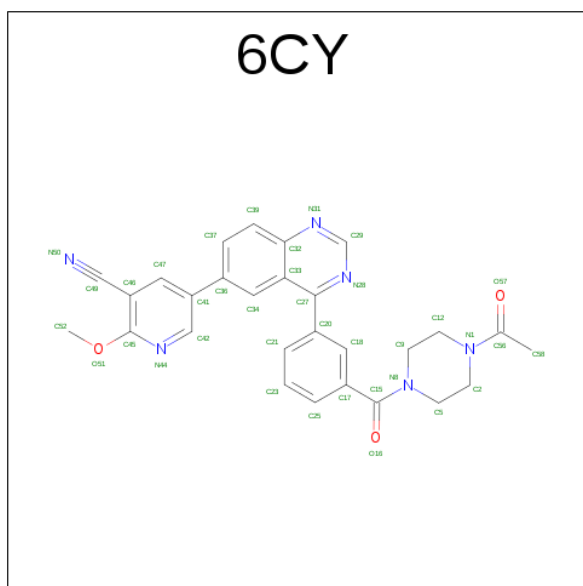
There are 3 unique types of molecules in this entry. The entry contains 5917 atoms, of which 0 are hydrogens and 0 are deuteriums.

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 delta isoform.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	785	Total	C	N	O	S	0	0	0
			5648	3615	983	1000	50			

- Molecule 2 is 5-{4-[3-(4-acetylpiperazine-1-carbonyl)phenyl]quinazolin-6-yl}-2-methoxypyridine-3-carbonitrile (three-letter code: 6CY) (formula: C₂₈H₂₄N₆O₃).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
2	A	1	Total	C	N	O	0	0
			37	28	6	3		

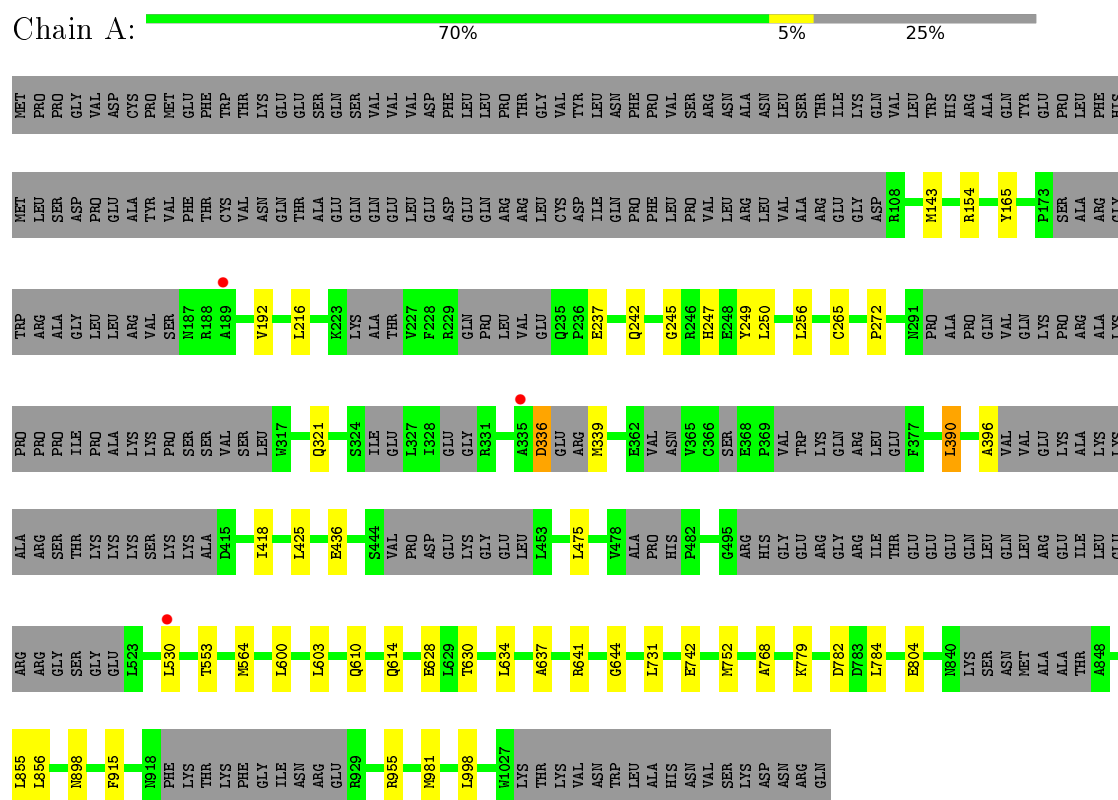
- Molecule 3 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	A	232	Total	O	0	0
			232	232		

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: Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform



4 Data and refinement statistics

Property	Value	Source
Space group	C 1 2 1	Depositor
Cell constants a, b, c, α , β , γ	141.46Å 64.32Å 116.64Å 90.00° 103.20° 90.00°	Depositor
Resolution (Å)	65.95 – 2.85 65.93 – 2.85	Depositor EDS
% Data completeness (in resolution range)	97.8 (65.95-2.85) 97.8 (65.93-2.85)	Depositor EDS
R_{merge}	0.23	Depositor
R_{sym}	0.10	Depositor
$\langle I/\sigma(I) \rangle$ ¹	3.61 (at 2.86Å)	Xtriage
Refinement program	BUSTER-TNT	Depositor
R, R_{free}	(Not available) , 0.271 0.237 , 0.288	Depositor DCC
R_{free} test set	1181 reflections (5.26%)	DCC
Wilson B-factor (Å ²)	45.8	Xtriage
Anisotropy	0.695	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.30 , 70.2	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.32$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o, F_c correlation	0.89	EDS
Total number of atoms	5917	wwPDB-VP
Average B, all atoms (Å ²)	50.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 4.60% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

²Theoretical values of $\langle |L| \rangle$, $\langle L^2 \rangle$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 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: 6CY

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	0.40	0/5763	0.59	0/7833

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	321	GLN	Mainchain
1	A	475	LEU	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	5648	0	4949	15	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
2	A	37	0	0	1	0
3	A	232	0	0	0	0
All	All	5917	0	4949	15	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 1.

All (15) 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:245:GLY:HA3	1:A:768:ALA:HB2	1.78	0.65
1:A:336:ASP:HB3	1:A:339:MET:HB2	1.90	0.54
1:A:553:THR:HG21	1:A:564:MET:HG2	1.92	0.51
1:A:779:LYS:HE3	1:A:782:ASP:HB2	1.92	0.51
1:A:614:GLN:HG3	1:A:981:MET:HG2	1.94	0.50
1:A:600:LEU:HD22	1:A:603:LEU:HD11	1.96	0.46
1:A:396:ALA:HB2	1:A:418:ILE:HD11	1.98	0.45
1:A:752:MET:HG2	2:A:1101:6CY:O16	2.18	0.44
1:A:630:THR:O	1:A:634:LEU:HB2	2.18	0.42
1:A:216:LEU:HD22	1:A:256:LEU:HD21	2.01	0.42
1:A:154:ARG:HD2	1:A:165:TYR:CZ	2.55	0.41
1:A:637:ALA:HB1	1:A:644:GLY:HA2	2.03	0.41
1:A:192:VAL:HG13	1:A:272:PRO:HB2	2.02	0.41
1:A:390:LEU:HD12	1:A:425:LEU:HD21	2.01	0.41
1:A:242:GLN:HG3	1:A:249:TYR:CZ	2.57	0.40

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	751/1044 (72%)	725 (96%)	25 (3%)	1 (0%)	56 85

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	742	GLU

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	487/925 (53%)	466 (96%)	21 (4%)	35 69

All (21) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	143	MET
1	A	237	GLU
1	A	247	HIS
1	A	250	LEU
1	A	265	CYS
1	A	336	ASP
1	A	390	LEU
1	A	436	GLU
1	A	530	LEU
1	A	610	GLN
1	A	628	GLU
1	A	641	ARG
1	A	731	LEU
1	A	784	LEU
1	A	804	GLU
1	A	855	LEU
1	A	856	LEU
1	A	898	ASN
1	A	915	PHE
1	A	955	ARG

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Mol	Chain	Res	Type
1	A	998	LEU

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (6) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	278	HIS
1	A	617	GLN
1	A	773	ASN
1	A	780	ASN
1	A	898	ASN
1	A	976	HIS

5.3.3 RNA [i](#)

There are no RNA molecules in this entry.

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

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

5.5 Carbohydrates [i](#)

There are no carbohydrates in this entry.

5.6 Ligand geometry [i](#)

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	6CY	A	1101	-	41,41,41	1.21	2 (4%)	55,58,58	2.78	16 (29%)

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	6CY	A	1101	-	-	0/23/34/34	0/5/5/5

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	1101	6CY	O51-C45	3.16	1.40	1.35
2	A	1101	6CY	C27-N28	4.07	1.36	1.32

All (16) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	1101	6CY	N31-C29-N28	-10.76	120.42	128.87
2	A	1101	6CY	C46-C45-N44	-7.00	119.00	124.01
2	A	1101	6CY	C33-C27-N28	-6.33	118.73	123.01
2	A	1101	6CY	O16-C15-C17	-3.74	113.06	120.16
2	A	1101	6CY	O57-C56-C58	-2.63	112.82	122.02
2	A	1101	6CY	C2-C5-N8	-2.57	105.02	110.44
2	A	1101	6CY	C41-C42-N44	-2.46	120.32	124.31
2	A	1101	6CY	C5-N8-C9	2.50	117.16	112.57
2	A	1101	6CY	C42-N44-C45	2.57	122.34	116.47
2	A	1101	6CY	C29-N28-C27	2.85	122.49	117.47
2	A	1101	6CY	C2-N1-C12	2.89	117.86	112.57
2	A	1101	6CY	C20-C27-C33	3.83	125.85	122.16
2	A	1101	6CY	C17-C15-N8	4.07	124.17	118.77
2	A	1101	6CY	C58-C56-N1	4.68	124.37	118.21
2	A	1101	6CY	C29-N31-C32	5.62	120.27	115.19
2	A	1101	6CY	O51-C45-C46	6.42	119.72	115.98

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	1101	6CY	1	0

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 [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, 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	785/1044 (75%)	-0.26	3 (0%) 93 92	20, 51, 83, 109	0

All (3) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	189	ALA	2.4
1	A	335	ALA	2.4
1	A	530	LEU	2.3

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, 95th 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 ²)	Q<0.9
2	6CY	A	1101	37/37	0.96	0.23	3.96	29,33,40,41	0

6.5 Other polymers [i](#)

There are no such residues in this entry.