

Full wwPDB X-ray Structure Validation Report (i)

Nov 13, 2023 - 05:41 PM EST

PDB ID	:	8TS9
Title	:	Human PI3K p85alpha/p110alpha H1047R bound to compound 1 $$
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Deposited on	:	2023-08-11
Resolution	:	2.83 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 (i) 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 (1)) were used in the production of this report:

MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.36
buster-report	:	1.1.7(2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.36

1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure: $X\text{-}RAY \, DIFFRACTION$

The reported resolution of this entry is 2.83 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	Similar resolution
	$(\# { m Entries})$	$(\# { m Entries}, { m resolution} { m range}({ m \AA}))$
R_{free}	130704	$1031 \ (2.86-2.82)$
Clashscore	141614	1078 (2.86-2.82)
Ramachandran outliers	138981	$1050 \ (2.86-2.82)$
Sidechain outliers	138945	1051 (2.86-2.82)
RSRZ outliers	127900	1019 (2.86-2.82)

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 of the lower bar indicate the fraction of residues that contain outliers for >=3, 2, 1 and 0 types of geometric quality criteria respectively. 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% 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	А	1060	91%	• 5%
2	В	300	9% 84%	7% 9%



2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 21092 atoms, of which 10550 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 alpha isoform.

Mol	Chain	Residues		Atoms				ZeroOcc	AltConf	Trace	
1	А	1004	Total 16435	C 5241	Н 8239	N 1403	0 1484	S 68	25	0	0

Chain	Residue	Modelled	Actual	Comment	Reference
А	-9	GLY	-	expression tag	UNP P42336
А	-8	SER	-	expression tag	UNP P42336
А	-7	PRO	-	expression tag	UNP P42336
А	-6	GLY	-	expression tag	UNP P42336
А	-5	ILE	-	expression tag	UNP P42336
А	-4	SER	-	expression tag	UNP P42336
А	-3	GLY	-	expression tag	UNP P42336
А	-2	GLY	-	expression tag	UNP P42336
А	-1	GLY	-	expression tag	UNP P42336
А	0	GLY	-	expression tag	UNP P42336
А	1	GLY	-	expression tag	UNP P42336
А	1047	ARG	HIS	engineered mutation	UNP P42336

There are 12 discrepancies between the modelled and reference sequences:

• Molecule 2 is a protein called Phosphatidylinositol 3-kinase regulatory subunit alpha.

Mol	Chain	Residues	Atoms				ZeroOcc	AltConf	Trace		
2	В	272	$\begin{array}{c} \text{Total} \\ 4607 \end{array}$	C 1451	Н 2293	N 412	0 444	${f S}{7}$	76	0	0

There are 2 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
В	316	GLY	-	expression tag	UNP P27986
В	317	PRO	-	expression tag	UNP P27986



• Molecule 3 is 5-[3-fluoro-5-(trifluoromethyl)benzamido]-N-methyl-6-(2-methylanilino)pyridi ne-3-carboxamide (three-letter code: UE9) (formula: $C_{22}H_{18}F_4N_4O_2$) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms			ZeroOcc	AltConf			
3	А	1	Total 50	C 22	F 4	Н 18	N 4	O 2	0	0



3 Residue-property plots (i)

These plots are drawn for all protein, RNA, DNA and oligosaccharide chains in the entry. The first graphic for a chain summarises the proportions of the various outlier classes 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 alpha isoform





4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants	86.24Å 120.47Å 191.34Å	Depositor
a, b, c, α , β , γ	90.00° 90.00° 90.00°	Depositor
Bosolution (Å)	95.67 - 2.83	Depositor
Resolution (A)	95.67 - 2.83	EDS
% Data completeness	99.9 (95.67-2.83)	Depositor
(in resolution range)	99.9 (95.67 - 2.83)	EDS
R_{merge}	0.09	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) > 1$	$1.15 (at 2.82 \text{\AA})$	Xtriage
Refinement program	PHENIX 1.20.1_4487	Depositor
P. P.	0.230 , 0.252	Depositor
n, n_{free}	0.229 , 0.245	DCC
R_{free} test set	1575 reflections (3.28%)	wwPDB-VP
Wilson B-factor $(Å^2)$	99.5	Xtriage
Anisotropy	0.228	Xtriage
Bulk solvent $k_{sol}(e/A^3), B_{sol}(A^2)$	$0.35 \;, 67.3$	EDS
L-test for $twinning^2$	$ < L >=0.50, < L^2>=0.33$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o, F_c correlation	0.94	EDS
Total number of atoms	21092	wwPDB-VP
Average B, all atoms $(Å^2)$	124.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: The largest off-origin peak in the Patterson function is 3.13% of the height of the origin peak. No significant pseudotranslation is detected.

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.



¹Intensities estimated from amplitudes.

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: UE9

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).

Mal	Chain	Bond	lengths	Bond angles		
	Unam	RMSZ	# Z > 5	RMSZ	# Z > 5	
1	А	0.25	0/8375	0.48	0/11314	
2	В	0.25	0/2354	0.49	0/3153	
All	All	0.25	0/10729	0.48	0/14467	

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

There are no planarity outliers.

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	А	8196	8239	8231	18	0
2	В	2314	2293	2292	8	0
3	А	32	18	0	1	0
All	All	10542	10550	10523	26	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 (26) close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.



Atom 1	Atom 2	Interatomic	Clash
Atom-1	Atom-2	distance (Å)	overlap (Å)
1:A:913:ILE:HG22	1:A:913:ILE:O	2.02	0.60
2:B:356:LEU:HD23	2:B:357:VAL:N	2.18	0.58
1:A:992:ARG:NH1	1:A:1027:ALA:O	2.37	0.56
2:B:390:TYR:N	2:B:398:PHE:O	2.44	0.49
1:A:29:GLY:HA3	2:B:501:GLN:HA	1.95	0.47
3:A:1101:UE9:C10	3:A:1101:UE9:N18	2.76	0.47
1:A:638:VAL:HG23	1:A:649:LEU:HD21	1.98	0.44
1:A:136:VAL:HG13	1:A:686:LEU:HD11	1.99	0.43
1:A:807:LEU:HD12	1:A:846:GLY:HA3	2.00	0.43
1:A:338:ILE:HD12	1:A:338:ILE:N	2.33	0.43
1:A:376:VAL:HG13	1:A:377:PRO:HD2	2.01	0.43
2:B:343:VAL:HG11	2:B:358:ARG:HD3	2.01	0.42
1:A:208:THR:C	1:A:209:LEU:HD12	2.41	0.42
2:B:354:THR:HG22	2:B:426:TYR:HB2	2.02	0.41
1:A:412:ARG:NE	1:A:412:ARG:HA	2.36	0.41
1:A:573:LYS:HG3	1:A:575:ASN:OD1	2.20	0.41
1:A:37:LEU:H	1:A:37:LEU:HD22	1.86	0.41
1:A:264:LYS:O	1:A:264:LYS:HG3	2.20	0.41
1:A:873:ASN:O	1:A:876:THR:HG22	2.21	0.41
1:A:392:TYR:HD1	1:A:394:PRO:HD2	1.86	0.41
2:B:562:ARG:O	2:B:566:ILE:HD13	2.21	0.40
1:A:139:PHE:CZ	1:A:143:ILE:HD13	2.56	0.40
2:B:594:LEU:HA	2:B:597:TRP:CD2	2.56	0.40
1:A:199:SER:N	1:A:200:PRO:CD	2.85	0.40
1:A:342:THR:O	1:A:471:PRO:HA	2.22	0.40
2:B:434:ASP:OD1	2:B:434:ASP:N	2.55	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	А	994/1060~(94%)	966 (97%)	27 (3%)	1 (0%)	51	75

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Mol	Chain	Analysed	Favoured	Allowed	Outliers	Perce	ntiles
2	В	270/300~(90%)	260 (96%)	10 (4%)	0	100	100
All	All	1264/1360~(93%)	1226 (97%)	37 (3%)	1 (0%)	51	75

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	А	264	LYS

5.3.2 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 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	Percen	tiles
1	А	920/960~(96%)	912~(99%)	8 (1%)	78	89
2	В	253/277~(91%)	247~(98%)	6(2%)	49	72
All	All	1173/1237~(95%)	1159 (99%)	14 (1%)	71	85

All (14) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	А	187	LYS
1	А	349	ARG
1	А	392	TYR
1	А	418	GLU
1	А	523	LEU
1	А	798	GLU
1	А	851	VAL
1	А	888	GLU
2	В	328	LEU
2	В	396	LEU
2	В	433	GLN
2	В	579	GLN
2	В	583	TRP
2	В	595	ASN



Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. There are no such sidechains identified.

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 monosaccharides 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).

Mal	Type	Chain	Dog	Link	Bond lengths			Bond angles		
	туре	Ullaili	nes		Counts	RMSZ	# Z >2	Counts	RMSZ	# Z > 2
3	UE9	А	1101	-	33,34,34	2.27	6 (18%)	47,49,49	1.34	6 (12%)

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
3	UE9	А	1101	-	-	4/24/24/24	0/3/3/3

All (6) bond length outliers are listed below:



Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	А	1101	UE9	C03-N02	9.33	1.45	1.33
3	А	1101	UE9	C08-N09	5.80	1.46	1.36
3	А	1101	UE9	C19-N18	3.62	1.45	1.35
3	А	1101	UE9	C10-N09	2.37	1.46	1.39
3	А	1101	UE9	O04-C03	-2.17	1.18	1.23
3	А	1101	UE9	O20-C19	-2.17	1.18	1.23

All (6) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms		$Observed(^{o})$	$Ideal(^{o})$
3	А	1101	UE9	C17-N18-C19	-2.93	118.89	126.93
3	А	1101	UE9	C10-N09-C08	-2.87	122.45	129.63
3	А	1101	UE9	C25-C23-C22	-2.80	119.98	123.52
3	А	1101	UE9	C14-C15-C10	2.74	120.03	117.44
3	А	1101	UE9	C05-C03-N02	2.54	120.27	116.89
3	А	1101	UE9	C06-N07-C08	2.26	120.58	116.05

There are no chirality outliers.

All (4) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
3	А	1101	UE9	C17-C08-N09-C10
3	А	1101	UE9	N07-C08-N09-C10
3	А	1101	UE9	C08-C17-N18-C19
3	А	1101	UE9	C32-C17-N18-C19

There are no ring outliers.

1 monomer is involved in 1 short contact:

Μ	ol	Chain	Res	Type	Clashes	Symm-Clashes
	}	А	1101	UE9	1	0

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.



Ligand UE9 A 1101 Bond lengths Bond angles Torsions Rings

The outliers are highlighted in purple. The color gray indicates Mogul did not find sufficient equivalents in the CSD to analyse the geometry.

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^{th} 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	А	1004/1060~(94%)	0.73	61 (6%) 21	15	63, 101, 145, 202	2~(0%)
2	В	272/300~(90%)	0.66	26 (9%) 8	4	79, 139, 201, 227	6 (2%)
All	All	1276/1360~(93%)	0.71	87 (6%) 17	11	63, 106, 174, 227	8 (0%)

All (87) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
2	В	591	GLN	5.3
1	А	6	SER	5.1
1	А	7	SER	4.6
1	А	312	SER	4.4
2	В	447	LYS	4.1
1	А	500	VAL	3.8
1	А	481	SER	3.5
2	В	372	LEU	3.5
1	А	200	PRO	3.4
1	А	498	TRP	3.4
2	В	353	GLY	3.3
1	А	181	ILE	3.2
1	А	881	LEU	3.2
2	В	595	ASN	3.2
1	А	880	TRP	3.2
1	А	14	HIS	3.2
1	А	11	TRP	3.1
1	А	738	GLN	3.0
1	А	559	VAL	3.0
1	А	715	LEU	3.0
2	В	534	ARG	3.0
1	А	367	LEU	2.9
1	A	99	LEU	2.9
1	A	548	LYS	2.8

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Mol	Chain	Res	Type	RSRZ	
2	В	424	LEU	2.8	
2	В	381	ILE	2.8	
1	А	551	LEU	2.8	
2	В	587	LYS	2.7	
2	В	589	VAL	2.7	
2	В	443	GLU	2.7	
2	В	431	TYR	2.7	
1	А	37	LEU	2.7	
1	А	731	GLN	2.7	
2	В	418	PRO	2.7	
1	А	34	LEU	2.6	
1	А	568	LEU	2.6	
2	В	449	LEU	2.6	
1	A	725	ASP	2.6	
1	А	62	LEU	2.6	
1	А	71	VAL	2.6	
1	А	718	ILE	2.5	
1	А	771	ILE	2.5	
2	В	363	LYS	2.5	
1	А	985	TYR	2.5	
1	А	473	LEU	2.5	
1	А	734	PHE	2.5	
2	В	333	TRP	2.5	
1	А	201	ASN	2.5	
1	А	45	ILE	2.4	
1	А	777	ARG	2.4	
2	В	401	VAL	2.4	
1	А	528	LYS	2.4	
1	А	279	LEU	2.4	
1	А	877	LEU	2.4	
1	А	429	LEU	2.4	
2	В	538	ILE	2.4	
1	А	117	ILE	2.3	
1	А	49	LEU	2.3	
1	А	128	PHE	2.3	
1	А	362	HIS	2.3	
1	А	277	ILE	2.3	
1	А	455	LEU	2.3	
1	A	577	ARG	2.3	
2	В	408	TYR	2.3	
1	А	906	VAL	2.2	
1	А	302	PHE	2.2	

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Mol	Chain	Res	Type	RSRZ
1	А	392	TYR	2.2
2	В	593	LYS	2.2
1	А	440	LYS	2.2
1	А	929	LEU	2.2
1	А	735	LEU	2.1
2	В	392	PHE	2.1
1	А	479	TRP	2.1
2	В	355	PHE	2.1
2	В	592	LYS	2.1
2	В	419	LYS	2.1
2	В	357	VAL	2.1
1	А	635	LEU	2.1
1	А	83	PHE	2.1
1	А	15	LEU	2.0
1	А	883	ASP	2.0
1	А	726	GLU	2.0
1	А	89	LEU	2.0
1	А	422	LEU	2.0
1	А	443	LEU	2.0
2	В	413	LEU	2.0
1	А	396	LEU	2.0

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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 monosaccharides 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. The B-factors column lists the minimum, median, 95^{th} 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	$B-factors(Å^2)$	Q < 0.9
3	UE9	А	1101	32/32	0.94	0.27	78,96,126,128	0



The following is a graphical depiction of the model fit to experimental electron density of all instances of the Ligand of Interest. In addition, ligands with molecular weight > 250 and outliers as shown on the geometry validation Tables will also be included. Each fit is shown from different orientation to approximate a three-dimensional view.



6.5 Other polymers (i)

There are no such residues in this entry.

