

# Full wwPDB X-ray Structure Validation Report (i)

#### Oct 25, 2021 – 10:15 AM EDT

PDB ID	:	6XRN
Title	:	Crystal structure of human PI3K-gamma in complex with Compound 17
Authors	:	Walker, N.P.; Jeffrey, J.L.
Deposited on	:	2020-07-13
Resolution	:	2.96 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 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	:	2.23.2
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)	:	2.23.2

# 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 2.96 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.



Motria	Whole archive	Similar resolution
Metric	$(\# {\rm Entries})$	$(\# { m Entries},  { m resolution}  { m range}({ m \AA}))$
$R_{free}$	130704	3104 (3.00-2.92)
Clashscore	141614	3462(3.00-2.92)
Ramachandran outliers	138981	3340 (3.00-2.92)
Sidechain outliers	138945	3343 (3.00-2.92)
RSRZ outliers	127900	2986 (3.00-2.92)

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	949	8%	<u> </u>	13%



# 2 Entry composition (i)

There are 2 unique types of molecules in this entry. The entry contains 13537 atoms, of which 6807 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	А	824	Total 13475	C 4306	Н 6779	N 1138	O 1217	S 35	1143	0	0

There is a discrepancy between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
А	143	MET	-	initiating methionine	UNP P48736

• Molecule 2 is 2-amino-5-{2-[(1S)-1-cyclopropylethyl]-7-methyl-1-oxo-2,3-dihydro-1H-isoindo l-5-yl}-N-(trans-3-hydroxycyclobutyl)pyrazolo[1,5-a]pyrimidine-3-carboxamide (three-letter code: V84) (formula: C<sub>25</sub>H<sub>28</sub>N<sub>6</sub>O<sub>3</sub>) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms			ZeroOcc	AltConf		
2	А	1	Total	С	Η	Ν	Ο	3	0
		1	62	25	28	6	3	5	



# 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 gamma isoform





## 4 Data and refinement statistics (i)

Property	Value	Source
Space group	C 1 2 1	Depositor
Cell constants	144.21Å 68.17Å 106.80Å	Deperitor
a, b, c, $\alpha$ , $\beta$ , $\gamma$	$90.00^{\circ}$ $95.26^{\circ}$ $90.00^{\circ}$	Depositor
Bosolution(A)	44.78 - 2.96	Depositor
Resolution (A)	44.74 - 2.96	EDS
% Data completeness	97.3 (44.78-2.96)	Depositor
(in resolution range)	97.3(44.74-2.96)	EDS
$R_{merge}$	0.05	Depositor
$R_{sym}$	(Not available)	Depositor
$< I/\sigma(I) > 1$	$2.08 (at 2.96 \text{\AA})$	Xtriage
Refinement program	REFMAC 5.8.0258	Depositor
D D	0.224 , $0.270$	Depositor
$n, n_{free}$	0.249 , $0.277$	DCC
$R_{free}$ test set	531 reflections $(2.51\%)$	wwPDB-VP
Wilson B-factor $(Å^2)$	84.4	Xtriage
Anisotropy	0.181	Xtriage
Bulk solvent $k_{sol}(e/Å^3), B_{sol}(Å^2)$	0.35, $94.7$	EDS
L-test for twinning <sup>2</sup>	$ < L >=0.49, < L^2>=0.32$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
$F_o, F_c$ correlation	0.92	EDS
Total number of atoms	13537	wwPDB-VP
Average B, all atoms $(Å^2)$	129.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: The largest off-origin peak in the Patterson function is 5.66% of the height of the origin peak. No significant pseudotranslation is detected.

<sup>&</sup>lt;sup>2</sup>Theoretical 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.



<sup>&</sup>lt;sup>1</sup>Intensities 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:  $\mathbf{V84}$ 

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		
IVIOI	Chain	RMSZ	# Z  > 5	RMSZ	# Z  > 5	
1	А	0.40	0/6835	0.58	1/9237~(0.0%)	

There are no bond length outliers.

All (1) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Ζ	$Observed(^{o})$	$Ideal(^{o})$
1	А	947	ARG	NE-CZ-NH1	6.00	123.30	120.30

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	6696	6779	6744	1	0
2	А	34	28	0	0	0
All	All	6730	6807	6744	1	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 0.

All (1) 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:787:TYR:CD1	1:A:868:GLY:HA3	2.56	0.41	

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 Outlier		Percentiles	
1	А	800/949~(84%)	771 (96%)	26~(3%)	3~(0%)	34 69	

All (3) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	А	867	TYR
1	А	916	PRO
1	А	866	PRO

#### 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	Percentiles	
1	А	743/850~(87%)	739 (100%)	4 (0%)	88 95	

All (4) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type				
1	А	865	LEU				
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Mol	Chain	Res	Type
1	А	870	ILE
1	А	959	ASN
1	А	1053	ASP

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (1) such sidechains are listed below:

Mol	Chain	Res	Type
1	А	432	GLN

#### 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	Mol Type Chain Res	Dog	Bond lengths			Bond angles				
Mol Type Chain	Res Link		Counts	RMSZ	# Z  > 2	Counts	RMSZ	# Z  > 2		
2	V84	А	1101	-	32,39,39	0.97	2 (6%)	31,60,60	<b>3.15</b>	7 (22%)

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	V84	А	1101	-	-	1/16/42/42	0/6/6/6

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms		Observed(Å)	Ideal(Å)
2	А	1101	V84	C25-C28	-2.73	1.47	1.51
2	А	1101	V84	C23-N24	2.22	1.39	1.34

All (7) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	$Observed(^{o})$	$Ideal(^{o})$
2	А	1101	V84	C9-C8-N7	11.72	106.08	102.18
2	А	1101	V84	C8-N7-C16	-10.10	108.97	113.12
2	А	1101	V84	C2-N7-C16	5.01	128.29	122.91
2	А	1101	V84	O17-C16-C15	-2.83	125.07	129.09
2	А	1101	V84	C13-C15-C16	2.46	134.81	127.44
2	А	1101	V84	C6-C4-C2	-2.25	114.49	119.32
2	А	1101	V84	C18-N27-C26	2.03	121.12	118.08

There are no chirality outliers.

All (1) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	А	1101	V84	C37-C31-N30-C28

There are no ring outliers.

No monomer is involved in short contacts.

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 sufficient that 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.





## 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	$\langle RSRZ \rangle$	$\#RSRZ{>}2$	$OWAB(Å^2)$	$Q{<}0.9$
1	А	824/949~(86%)	0.76	75 (9%) 9 5	47, 127, 230, 299	138 (16%)

All (75) RSRZ outliers are listed below:

Mol	Chain	Res Type		RSRZ	
1	А	1086	TRP	7.4	
1	А	1087	PHE	4.8	
1	А	216	ALA	4.6	
1	А	226	ARG	4.3	
1	А	373	LEU	4.2	
1	А	752	LEU	4.1	
1	А	997	THR	4.0	
1	А	995	MET	4.0	
1	А	252	MET	4.0	
1	А	1084	PHE	4.0	
1	А	A 220		4.0	
1	А	1088	LEU	3.9	
1	А	225	HIS	3.9	
1	А	778	GLN	3.9	
1	А	231	GLN	3.8	
1	А	948	HIS	3.8	
1	А	545	ALA	3.8	
1	А	1083	GLN	3.7	
1	А	233	ILE	3.6	
1	А	921	PHE	3.6	
1	А	404	PHE	3.5	
1	А	869	CYS	3.4	
1	А	1080	TRP	3.3	
1	А	282	VAL	3.2	
1	А	1009	PHE	3.2	
1	А	1040	PRO	3.2	
1	А	1067	TYR	3.2	

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Mol	Chain	Res	Type	RSRZ
1	А	989	PRO	3.2
1	А	988	THR	3.2
1	А	924	ALA	3.1
1	А	940	PHE	3.0
1	А	749	ILE	3.0
1	А	1014	VAL	2.9
1	А	403	PRO	2.9
1	А	862	LEU	2.9
1	А	320	LYS	2.9
1	А	1075	CYS	2.8
1	А	234	LYS	2.8
1	А	250	THR	2.8
1	А	235	VAL	2.8
1	A	823	LEU	2.8
1	А	777	SER	2.8
1	A	219	CYS	2.8
1	А	222	ILE	2.8
1	А	824	SER	2.7
1	А	275	CYS	2.7
1	А	1004	PRO	2.6
1	А	911	LEU	2.5
1	А	981	GLU	2.5
1	А	459	GLN	2.5
1	А	834	HIS	2.4
1	А	1001	LYS	2.4
1	А	990	ASP	2.4
1	А	522	ASN	2.3
1	А	1006	PHE	2.3
1	А	406	GLU	2.3
1	А	1091	VAL	2.3
1	A	751	SER	2.2
1	А	868	GLY	2.2
1	A	939	THR	2.1
1	A	271	VAL	2.1
1	A	1068	PHE	2.1
1	А	496	SER	2.1
1	A	280	TYR	2.1
1	A	610	LEU	2.1
1	А	864	LEU	2.1
1	А	1089	HIS	2.1
1	А	922	GLN	2.1
1	А	241	PRO	2.1

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Mol	Chain	Res	Type	RSRZ
1	А	357	CYS	2.0
1	А	903	LYS	2.0
1	А	966	GLY	2.0
1	А	846	GLN	2.0
1	А	242	GLY	2.0
1	А	576	TRP	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	$\mathbf{B} ext{-factors}(\mathrm{\AA}^2)$	Q<0.9
2	V84	А	1101	34/34	0.93	0.19	64,88,134,135	3

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.

