



Full wwPDB X-ray Structure Validation Report ⓘ

Jul 14, 2016 – 08:28 PM EDT

PDB ID : 4YTH
Title : Discovery of VX-509 (Decernotinib): A Potent and Selective Janus kinase (JAK) 3 Inhibitor for the Treatment of Autoimmune Diseases
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Deposited on : 2015-03-17
Resolution : 2.04 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-20027790
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-20027790

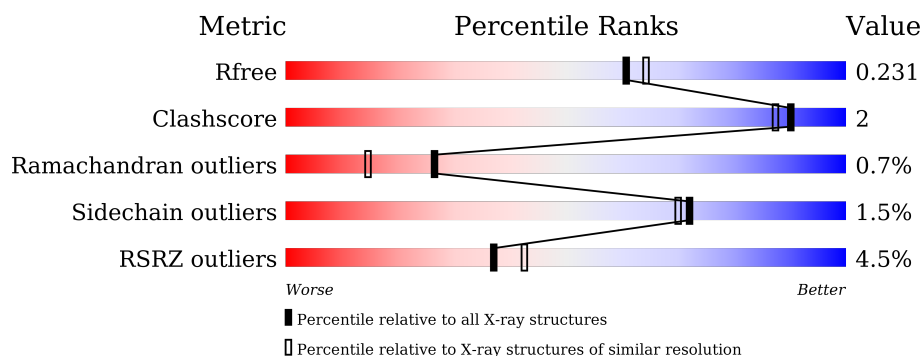
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.04 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	1192 (2.04-2.04)
Clashscore	102246	1269 (2.04-2.04)
Ramachandran outliers	100387	1258 (2.04-2.04)
Sidechain outliers	100360	1258 (2.04-2.04)
RSRZ outliers	91569	1194 (2.04-2.04)

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	296	<div> <div>4%</div> <div>91%</div> <div>6%</div> </div>

2 Entry composition [i](#)

There are 3 unique types of molecules in this entry. The entry contains 2565 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.

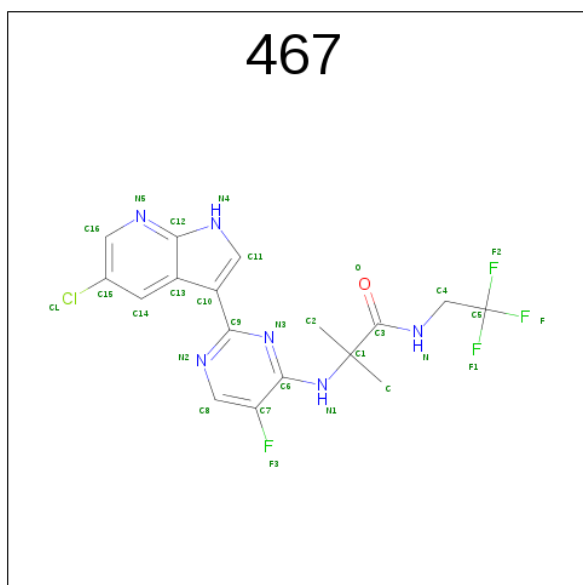
- Molecule 1 is a protein called Tyrosine-protein kinase JAK2.

Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
			Total	C	N	O	P	S			
1	A	289	2404	1525	415	448	2	14	0	2	0

There are 5 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	837	GLY	-	expression tag	UNP O60674
A	838	SER	-	expression tag	UNP O60674
A	839	HIS	-	expression tag	UNP O60674
A	840	ASN	-	expression tag	UNP O60674
A	841	MET	-	expression tag	UNP O60674

- Molecule 2 is N²-[2-(5-chloro-1H-pyrrolo[2,3-b]pyridin-3-yl)-5-fluoropyrimidin-4-yl]-2-methyl-N-(2,2,2-trifluoroethyl)-D-alaninamide (three-letter code: 467) (formula: C₁₇H₁₅ClF₄N₆O).

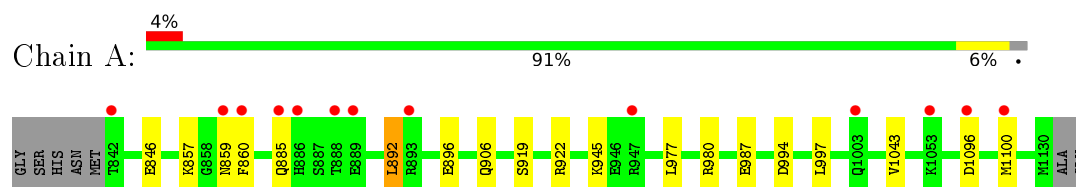


Mol	Chain	Residues	Atoms						ZeroOcc	AltConf
2	A	1	Total	C	Cl	F	N	O	0	0
			29	17	1	4	6	1		

- Molecule 3 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	A	132	Total	O	0	0
			132	132		

- Molecule 1: Tyrosine-protein kinase JAK2



4 Data and refinement statistics

Property	Value	Source
Space group	C 2 2 21	Depositor
Cell constants a, b, c, α , β , γ	95.77Å 99.93Å 68.62Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	69.14 – 2.04 69.14 – 2.04	Depositor EDS
% Data completeness (in resolution range)	99.7 (69.14-2.04) 99.8 (69.14-2.04)	Depositor EDS
R_{merge}	(Not available)	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	3.04 (at 2.05Å)	Xtriage
Refinement program	BUSTER 2.11.5	Depositor
R, R_{free}	0.184 , 0.215 0.192 , 0.231	Depositor DCC
R_{free} test set	1093 reflections (5.42%)	DCC
Wilson B-factor (Å ²)	26.6	Xtriage
Anisotropy	0.075	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.37 , 48.4	EDS
L-test for twinning ²	$\langle L \rangle = 0.48$, $\langle L^2 \rangle = 0.32$	Xtriage
Estimated twinning fraction	0.036 for -k,-h,-l 0.018 for -1/2*h-1/2*k+l,-1/2*h-1/2*k-l,1/2 *h-1/2*k 0.019 for -1/2*h-1/2*k-l,-1/2*h-1/2*k+l,-1/ 2*h+1/2*k 0.029 for -1/2*h+1/2*k-l,1/2*h-1/2*k-l,-1/2 *h-1/2*k 0.016 for -1/2*h+1/2*k+l,1/2*h-1/2*k+l,1/ 2*h+1/2*k	Xtriage
F_o, F_c correlation	0.95	EDS
Total number of atoms	2565	wwPDB-VP
Average B, all atoms (Å ²)	33.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 5.63% of the height of the origin peak. No significant pseudotranslation is detected.*

¹ Intensities estimated from amplitudes.

² 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.

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: 467, PTR

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	0.77	0/2426	0.84	0/3264

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	A	2404	0	2377	11	0
2	A	29	0	15	1	0
3	A	132	0	0	1	0
All	All	2565	0	2392	11	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 2.

All (11) 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:857:LYS:HE2	1:A:885:GLN:OE1	1.67	0.94

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:846:GLU:HB2	1:A:919:SER:HB2	1.57	0.84
1:A:846:GLU:HB2	1:A:919:SER:CB	2.22	0.69
1:A:892:LEU:O	1:A:896:GLU:HG3	2.06	0.55
1:A:896:GLU:OE2	1:A:922:ARG:NH1	2.33	0.54
1:A:859:ASN:O	1:A:860:PHE:HB2	2.09	0.51
1:A:987:GLU:HG3	3:A:4181:HOH:O	2.12	0.48
1:A:980:ARG:O	2:A:4000:467:H8	2.15	0.47
1:A:977:LEU:HG	1:A:1043:VAL:HG21	1.97	0.46
1:A:859:ASN:HD21	1:A:997:LEU:CD2	2.28	0.46
1:A:859:ASN:HD21	1:A:997:LEU:HD21	1.83	0.44

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	287/296 (97%)	280 (98%)	5 (2%)	2 (1%)	26	15

All (2) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	945	LYS
1	A	994	ASP

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	A	264/267 (99%)	260 (98%)	4 (2%)	72 70

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

Mol	Chain	Res	Type
1	A	892	LEU
1	A	906	GLN
1	A	1096	ASP
1	A	1100	MET

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (3) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	859	ASN
1	A	906	GLN
1	A	1072	GLN

5.3.3 RNA ⓘ

There are no RNA molecules in this entry.

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

2 non-standard protein/DNA/RNA residues are 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	$\# Z > 2$
1	PTR	A	1007	1	13,16,17	2.35	7 (53%)	19,22,24	1.78	7 (36%)
1	PTR	A	1008	1	13,16,17	1.96	4 (30%)	19,22,24	2.11	9 (47%)

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
1	PTR	A	1007	1	-	0/9/11/13	0/1/1/1
1	PTR	A	1008	1	-	0/9/11/13	0/1/1/1

All (11) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	1007	PTR	CE2-CD2	2.21	1.43	1.38
1	A	1007	PTR	CD1-CG	2.50	1.44	1.38
1	A	1008	PTR	CE1-CZ	2.62	1.44	1.38
1	A	1008	PTR	CD1-CG	2.65	1.44	1.38
1	A	1007	PTR	CE1-CD1	2.72	1.44	1.38
1	A	1007	PTR	CB-CA	3.11	1.60	1.53
1	A	1008	PTR	CB-CA	3.20	1.60	1.53
1	A	1007	PTR	CE2-CZ	3.31	1.45	1.38
1	A	1007	PTR	CE1-CZ	3.70	1.46	1.38
1	A	1007	PTR	CD2-CG	3.94	1.47	1.38
1	A	1008	PTR	CD2-CG	4.02	1.47	1.38

All (16) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	1008	PTR	CG-CB-CA	-3.37	106.36	114.12
1	A	1008	PTR	O3P-P-OH	-3.28	95.01	105.47
1	A	1007	PTR	CG-CB-CA	-3.06	107.07	114.12
1	A	1007	PTR	O2P-P-OH	-2.90	96.24	105.47
1	A	1008	PTR	O-C-CA	-2.62	118.69	125.72
1	A	1008	PTR	OH-CZ-CE1	-2.52	111.36	119.22
1	A	1007	PTR	CE1-CD1-CG	-2.46	117.56	121.02
1	A	1007	PTR	OH-CZ-CE2	-2.36	111.88	119.22
1	A	1008	PTR	CE1-CD1-CG	-2.28	117.82	121.02
1	A	1008	PTR	CB-CG-CD1	-2.24	116.39	120.91
1	A	1007	PTR	O-C-CA	-2.20	119.83	125.72
1	A	1008	PTR	OH-CZ-CE2	2.15	125.92	119.22
1	A	1008	PTR	O2P-P-O1P	2.33	118.23	110.63
1	A	1007	PTR	OH-CZ-CE1	2.35	126.53	119.22
1	A	1007	PTR	CD2-CG-CD1	2.75	122.69	118.15
1	A	1008	PTR	O2P-P-OH	3.88	117.83	105.47

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

No monomer is involved in short contacts.

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	467	A	4000	-	27,31,31	2.03	9 (33%)	32,47,47	1.21	2 (6%)

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	467	A	4000	-	-	0/16/21/21	0/3/3/3

All (9) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	4000	467	C8-N2	2.08	1.38	1.34
2	A	4000	467	C1-N1	2.26	1.51	1.47
2	A	4000	467	C16-N5	2.43	1.36	1.31
2	A	4000	467	C6-N3	2.54	1.39	1.34
2	A	4000	467	C8-C7	3.12	1.41	1.37
2	A	4000	467	C16-C15	3.15	1.44	1.38
2	A	4000	467	C6-N1	3.43	1.40	1.35
2	A	4000	467	C9-N2	4.26	1.41	1.34
2	A	4000	467	C12-N4	4.54	1.41	1.35

All (2) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	4000	467	C8-C7-C6	-3.31	117.72	121.26
2	A	4000	467	C14-C15-C16	2.73	122.83	120.42

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	4000	467	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	287/296 (96%)	0.13	13 (4%) 37 42	16, 29, 57, 73	0

All (13) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	886	HIS	5.1
1	A	860	PHE	4.9
1	A	889	GLU	3.3
1	A	885	GLN	3.3
1	A	1096	ASP	2.9
1	A	1003	GLN	2.7
1	A	859	ASN	2.7
1	A	947	ARG	2.6
1	A	842	THR	2.4
1	A	1100	MET	2.3
1	A	1053	LYS	2.2
1	A	893	ARG	2.2
1	A	888	THR	2.0

6.2 Non-standard residues in protein, DNA, RNA chains [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
1	PTR	A	1007	16/17	0.91	0.14	-	28,38,54,55	0
1	PTR	A	1008	16/17	0.90	0.15	-	27,38,51,51	0

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(\AA^2)	Q<0.9
2	467	A	4000	29/29	0.96	0.11	-0.38	16,23,28,29	0

6.5 Other polymers [i](#)

There are no such residues in this entry.