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5TT7

Discovery of TAK-659, an Orally Available Investigational Inhibitor of Spleen Tyrosine Kinase (SYK)

PDB DOI: <https://doi.org/10.2210/pdb5TT7/pdb>

Classification: **Transferase/Transferase Inhibitor**

Organism(s): **Homo sapiens**

Expression System: **Baculovirus expression vector pFastBac1-HM**

Mutation(s): **No**

Deposited: 2016-11-01 Released: 2016-11-30

Deposition Author(s): **Yano, J., Jennings, A., Lam, B., Hoffman, I.D.**

Experimental Data Snapshot

Method: **X-RAY DIFFRACTION**

Resolution: **1.77 Å**

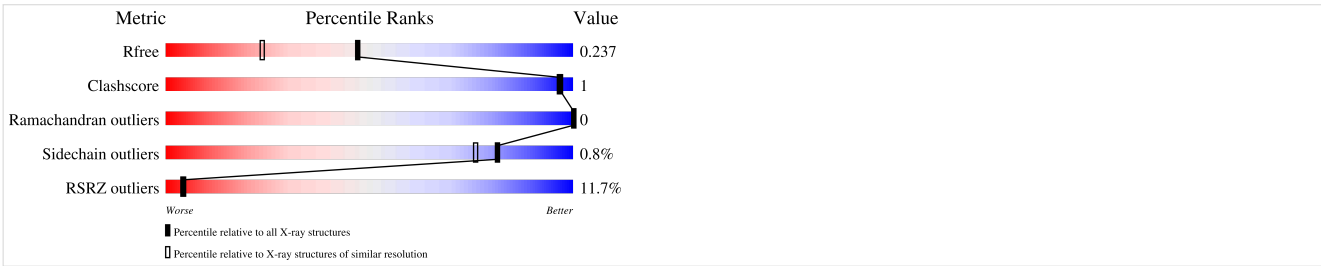
R-Value Free: **0.234**

R-Value Work: **0.206**

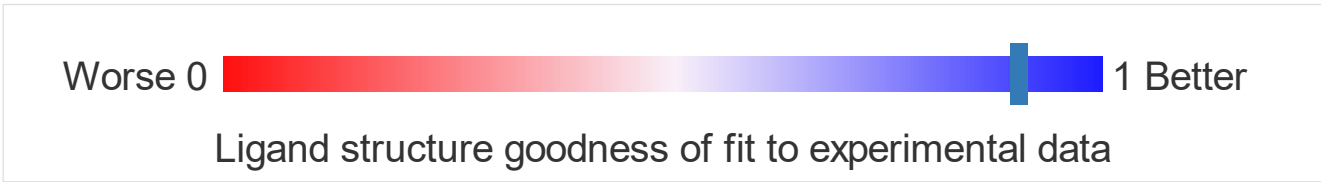
R-Value Observed: **0.208**

wwPDB Validation

3D Report Full Report



Ligand Structure Quality Assessment



This is version 1.3 of the entry. See complete history.

Literature

Discovery of TAK-659 an orally available investigational inhibitor of Spleen Tyrosine Kinase (SYK).
Lam, B., Ariawa, Y., Cramlett, J., Dong, Q., de Jong, R., Feher, V., Grimshaw, C.E., Farrell, P.J., Hoffman, I.D., Jennings, A., Jones, B., Matuszkiewicz, J., Miura, J., Miyake, H., Natalia, S.R., Shi, L., Takahashi, M., Taylor, E., Wyrick, C., Yano, J., Zalevsky, J., Nie, Z.
(2016) Bioorg Med Chem Lett 26: 5947-5950
PubMed: [27839918](https://pubmed.ncbi.nlm.nih.gov/27839918/)
DOI: <https://doi.org/10.1016/j.bmcl.2016.10.087>

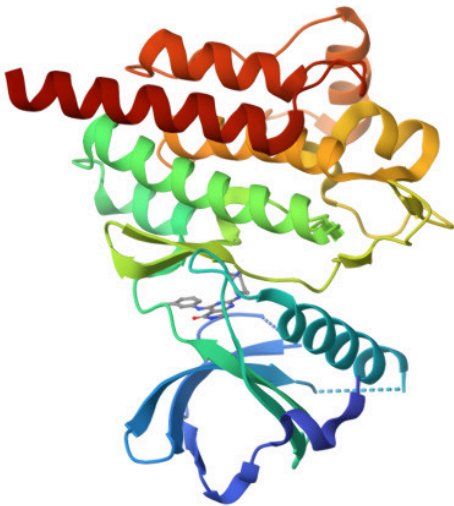
Primary Citation of Related Structures:
5TR6, 5TT7

PubMed Abstract:
Spleen Tyrosine Kinase (SYK) is a non-receptor cytoplasmic tyrosine kinase that is primarily expressed in hematopoietic cells. SYK is a key mediator for a variety of inflammatory cells, including B cells, mast cells, macrophages and neutrophils and therefore, an attractive approach for treatment of both inflammatory diseases and oncology indications. Using in house co-crystal structure information, and structure-based drug design, we designed and optimized a novel series of heteroaromatic...
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Organizational Affiliation:
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Biological Assembly 1



Explore in 3D: Structure | Sequence Annotations | Electron Density | Validation Report | Ligand Interaction (7KF)

Global Symmetry: Asymmetric - C1
Global Stoichiometry: Monomer - A1

[Find Similar Assemblies](#)

Biological assembly 1 assigned by authors and generated by PISA (software)

Macromolecules

Find similar proteins by: Sequence (by identity cutoff) | 3D Structure

Entity ID: 1					
Molecule	Chains	Sequence Length	Organism	Details	Image
Tyrosine-protein kinase SYK	A	289	Homo sapiens	Mutation(s): 0 Gene Names: SYK EC: 2.7.10.2	

UniProt & NIH Common Fund Data Resources

Find proteins for [P43405](#) (*Homo sapiens*)
[Explore](#) [P43405](#)

Go to UniProtKB: [P4340](#)

PHAROS:

P43405

GTEx:

ENSG00000165025

Entity Groups

Sequence Clusters

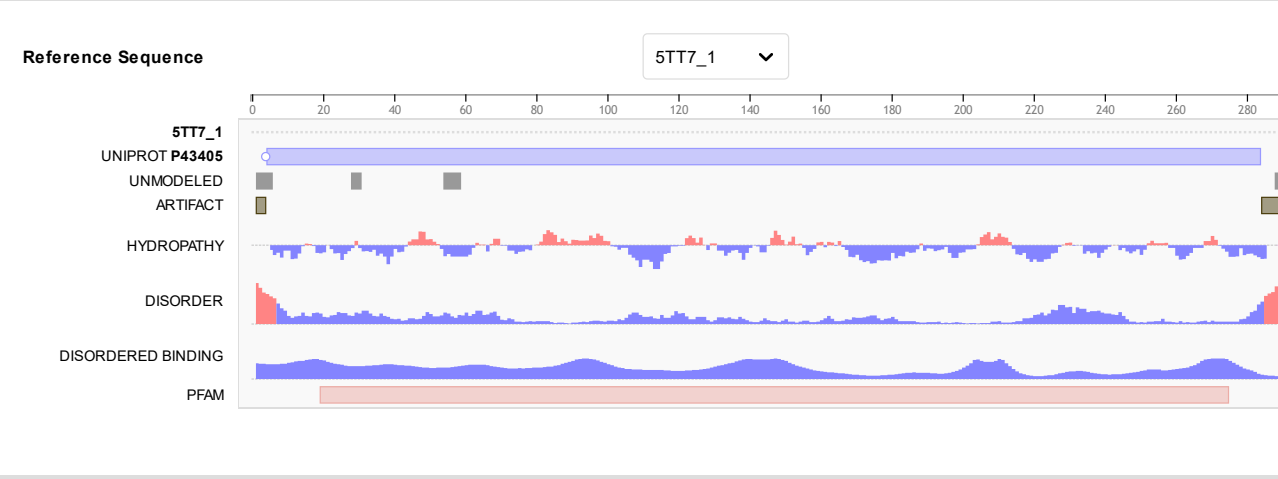
30% Identity50% Identity70% Identity90% Identity95% Identity100% Identity

UniProt Group

P43405

Sequence Annotations

Expa



Small Molecules

Ligands 1 Unique

ID	Chains	Name / Formula / InChI Key	2D Diagram	3D Interactions
7KF	B [auth A]	2-[[[(1R,2S)-2-aminocyclohexyl]amino]-4-[(3-methylphenyl)amino]-6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidin-5-one C ₁₉ H ₂₄ N ₆ O VPNLOOYVNORYBV-UONOGXRCSA-N		<div>Interactions<div></div></div> <div>Interactions & Density<div></div></div>

Download Instance Coordinates

Binding Affinity Annotations		
ID	Source	Binding Affinity
7KF	BindingDB: <div>5TT7</div>	IC ₅₀ : min: 7.94, max: 13 (nM) from 2 assay(s)
		EC ₅₀ : 35 (nM) from 1 assay(s)

Experimental Data & Validation

Experimental Data

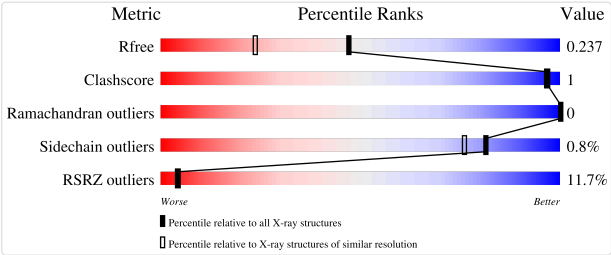
Method: X-RAY DIFFRACTION
Resolution: 1.77 Å
R-Value Free: 0.234
R-Value Work: 0.206
R-Value Observed: 0.208
Space Group: P2₁2₁

Unit Cell:	
Length (Å)	Angle (°)
a = 39.815	α = 90

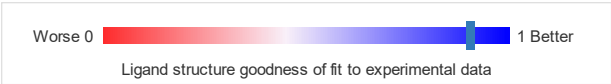
Length (Å)	Angle (°)
b = 85.204	β = 90
c = 88.912	γ = 90
Software Package:	
Software Name	Purpose
HKL-2000	data scaling
REFMAC	refinement
PDB_EXTRACT	data extraction
HKL-2000	data reduction
MOLREP	phasing
DENZO	data reduction
SCALEPACK	data scaling

Structure Validation

View Full Validation Report



Ligand Structure Quality Assessment ⓘ



Entry History

Deposition Data

Released Date: 2016-11-30
Deposition Author(s): Yano, J., Jennings, A., Lam, B., Hoffman, I.D.

Revision History (Full details and data files)

- Version 1.0: 2016-11-30**
Type: Initial release
- Version 1.1: 2016-12-14**
Changes: Database references
- Version 1.2: 2017-11-22**
Changes: Refinement description
- Version 1.3: 2024-03-06**
Changes: Data collection, Database references

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