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5TR6

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

PDB DOI: <https://doi.org/10.2210/pdb5TR6/pdb>

Classification: Transferase/Transferase Inhibitor

Organism(s): Homo sapiens

Expression System: Baculovirus expression vector pFastBac1-HM

Mutation(s): No

Deposited: 2016-10-25 Released: 2016-11-30

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

Experimental Data Snapshot

Method: X-RAY DIFFRACTION

Resolution: 1.93 Å

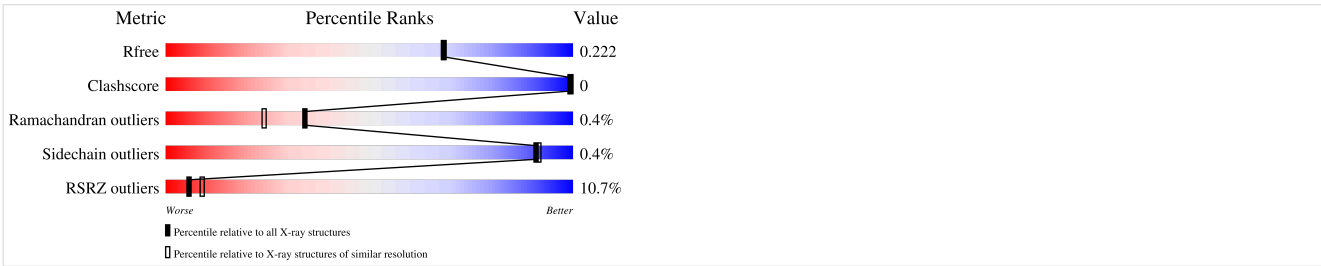
R-Value Free: 0.217

R-Value Work: 0.193

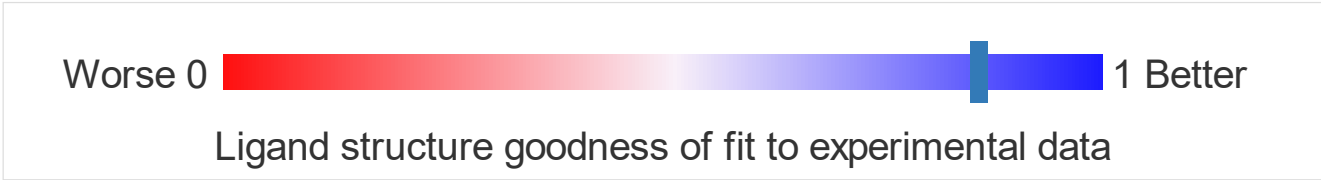
R-Value Observed: 0.195

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.](#), [Arikawa, 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.](#), [Natala, 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](#)
DOI: <https://doi.org/10.1016/j.bmcl.2016.10.087>

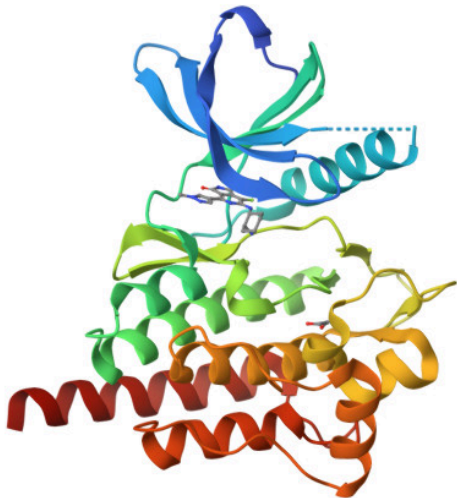
Primary Citation of Related Structures:
5TR6, 5TT7

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:
Takeda California, Inc., 10410 Science Center Drive, San Diego, CA 92121, USA. Electronic address: betty.lam@takeda.com.



Biological Assembly 1



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

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

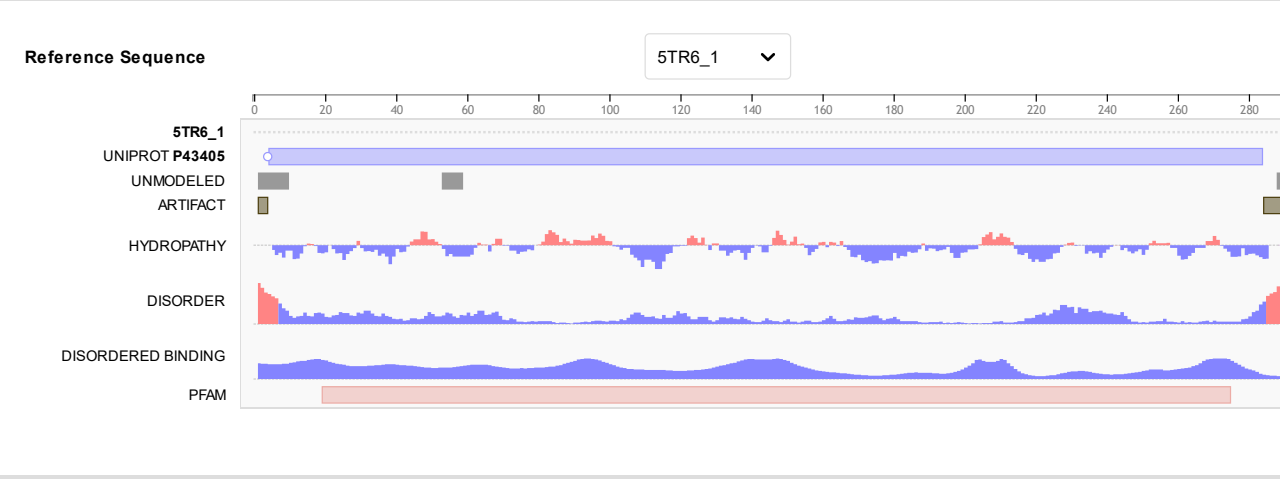
30% Identity50% Identity70% Identity90% Identity95% Identity100% Identity

UniProt Group

P43405

Sequence Annotations

Expa



Small Molecules

Ligands 2 Unique				
ID	Chains	Name / Formula / InChI Key	2D Diagram	3D Interactions
7K G	B [auth A]	6-[[[(1R,2S)-2-aminocyclohexyl]amino]-7-fluoro-4-(1-methyl-1H-pyrazol-4-yl)-1,2-dihydro-3H-pyrrolo[3,4-c]pyridin-3-one C ₁₇ H ₂₁ F N ₆ O MJHOMTRKVMKCNE-NWDGAFQWSA-N		Interactions Interactions & Density
Download Instance Coordinates				
ED O	C [auth A]	1,2-ETHANEDIOL C ₂ H ₆ O ₂ LYCAIKOWRPUZTN-UHFFFAOYSA-N		Interactions Interactions & Density
Download Instance Coordinates				

Binding Affinity Annotations		
ID	Source	Binding Affinity
7KG	BindingDB: 5TR6	IC50: min: 2, max: 4620 (nM) from 6 assay(s) EC50: 9.8 (nM) from 1 assay(s)

Experimental Data & Validation

Experimental Data

Method: X-RAY DIFFRACTION

Resolution: 1.93 Å

R-Value Free: 0.217

R-Value Work: 0.193

R-Value Observed: 0.195
Space Group: **P**₂**1**₂**1**

Unit Cell:

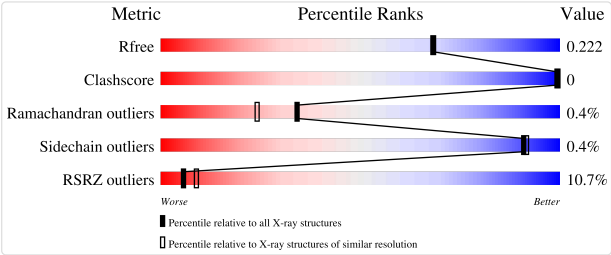
Length (Å)	Angle (°)
a = 39.941	α = 90
b = 85.283	β = 90
c = 90.283	γ = 90

Software Package:

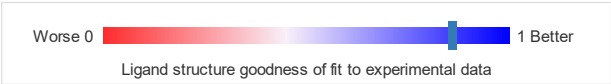
Software Name	Purpose
HKL-2000	data collection
REFMAC	refinement
PDB_EXTRACT	data extraction
HKL-2000	data reduction
HKL-2000	data scaling
MOLREP	phasing
DENZO	data reduction
SCALEPACK	data scaling

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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