BIOZENTRUM
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The Center for Molecular Life Sciences

SWISS-MODEL Homology Modelling Report

Model Building Report

This document lists the results for the homology modelling project "Untitled Project" submitted to SWISS-MODEL workspace on July 7, 2018, 12:18 p.m..The submitted primary amino acid sequence is given in Table T1.

If you use any results in your research, please cite the relevant publications:

- Waterhouse, A., Bertoni, M., Bienert, S., Studer, G., Tauriello, G., Gumienny, R., Heer, F.T., de Beer, T.A.P., Rempfer, C., Bordoli, L., Lepore, R., Schwede, T. SWISS-MODEL: homology modelling of protein structures and complexes. Nucleic Acids Res. gky427 (2018). doi>
- Guex, N., Peitsch, M.C., Schwede, T. Automated comparative protein structure modeling with SWISS-MODEL and Swiss-PdbViewer: A historical perspective. Electrophoresis 30, S162-S173 (2009). doi>
- Bienert, S., Waterhouse, A., de Beer, T.A.P., Tauriello, G., Studer, G., Bordoli, L., Schwede, T. The SWISS-MODEL Repository - new features and functionality. Nucleic Acids Res. 45, D313-D319 (2017). doi>
- Benkert, P., Biasini, M., Schwede, T. Toward the estimation of the absolute quality of individual protein structure models. Bioinformatics 27, 343-350 (2011). doi>
- Bertoni, M., Kiefer, F., Biasini, M., Bordoli, L., Schwede, T. Modeling protein quaternary structure of homo- and hetero-oligomers beyond binary interactions by homology. Scientific Reports 7 (2017). doi>

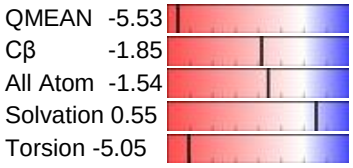
Results

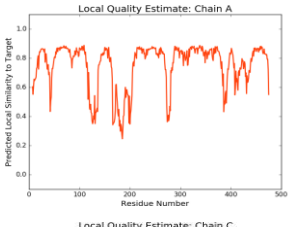
The SWISS-MODEL template library (SMTL version 2018-06-29, PDB release 2018-06-22) was searched with BLAST (Camacho et al.) and HHBlits (Remmert et al.) for evolutionary related structures matching the target sequence in Table T1. For details on the template search, see Materials and Methods. Overall 84 templates were found (Table T2).

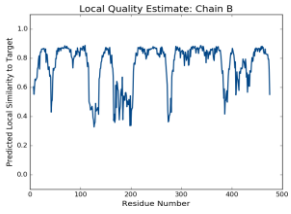
Models

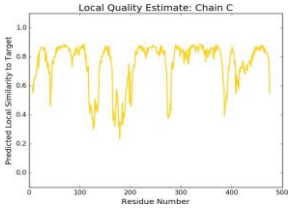
The following model was built (see Materials and Methods "Model Building"):

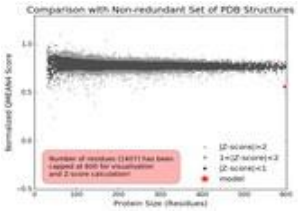
Model #01	File	Built with	Oligo-State	Ligands	GMQE	QMEAN
	PDB	ProMod3 Version 1.1.0.	homo-trimer (matching prediction)	None	0.66	-5.53











Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Range	Coverage	Description
5mju.1.A	63.13	homo-trimer	0.65	HHblits	X-ray	3.71Å	0.47	7 - 475	0.86	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1

Ligand	Added to Model	Description
6Z6	✕ - Binding site not conserved.	2-Amino-5,6,7,8-tetrahydro-4-(4-methoxyphenyl)-7-(naphthalen-1-yl)-5-oxo-4H-chromene-3-carbonitrile

Ligand	Added to Model	Description
6Z6	✕ - Binding site not conserved.	2-Amino-5,6,7,8-tetrahydro-4-(4-methoxyphenyl)-7-(naphthalen-1-yl)-5-oxo-4H-chromene-3-carbonitrile
6Z6	✕ - Binding site not conserved.	2-Amino-5,6,7,8-tetrahydro-4-(4-methoxyphenyl)-7-(naphthalen-1-yl)-5-oxo-4H-chromene-3-carbonitrile
7O9	✕ - Binding site not conserved.	(2~{S},3~{S})-2-azanyl-3-[[3-[[4-(trifluoromethyl)phenyl]carbonylamino]phenyl]methoxy]butanedioic acid
7O9	✕ - Binding site not conserved.	(2~{S},3~{S})-2-azanyl-3-[[3-[[4-(trifluoromethyl)phenyl]carbonylamino]phenyl]methoxy]butanedioic acid
7O9	✕ - Binding site not conserved.	(2~{S},3~{S})-2-azanyl-3-[[3-[[4-(trifluoromethyl)phenyl]carbonylamino]phenyl]methoxy]butanedioic acid

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Target    MGKPARKGCEWKRFLKNNWVLLSTVAAVVLG▮TTGVLVREHSNLSTLEKFYFAFPGE▮LMRMLKL▮▮LPL▮▮SSM▮TGVA
5mju.1.A  ---QN▮TKEDVKSFLRRNALLLLTVLAV▮LGVVLGFLLRPY-PLSPREVKYFAFPGELLMRMLKML▮LPL▮VSSL▮TGLA

Target    ALDSNVSGK▮GLRAVVYYFCTTL▮AV▮LG▮VLVVS▮KPGVTQKVGE▮ART------GSTPEVSTVDAMLDL▮RNMFPENL
5mju.1.A  SLDAKASGRLGMRAVVYYMSTT▮▮AVVLG▮▮LVL▮▮HPGAASAA▮-TASVGAAGSAENAPSKEVLDCFLDLARN▮FPSNL

Target    VQACFQQYKTKREEVKPPSDPEMNMTEESFTAVMTTA▮SKNKTKEYK▮VGMYSDG▮NVLGL▮VFCLVFGLV▮GKMGEKGQ
5mju.1.A  VSAAFRSYSTTYEERT▮TGT----------------------RVKVPVGQEVEGMN▮LGLVVFSMVFGFALGKMGEQGQ

Target    ▮LVDFFNALSDATMK▮VQ▮▮MCYMPLG▮LFL▮AGK▮▮EVEDWE▮FR-KLGLYMATVLTGLA▮HS▮V▮LPL▮YF▮VVRKNP
5mju.1.A  LLVDFFNSLNEATMKLVA▮▮MWYAPLG▮LFL▮AGK▮VEMEDLEVLGGQLGMYMVTV▮VGLV▮HGL▮VLPL▮YFL▮TRKNP

Target    FRFAMGMAQALLTALM▮SSSSATLPVTFRCAEENNQVDKR▮TRFVLPVGAT▮NMDGTALYEAVAAVF▮AQLNDLDLG▮GQ
5mju.1.A  FVF▮AG▮LQAL▮TALGTSSSSATLP▮TFKCLEENNGVDKR▮TRFVLPVGAT▮NMDGTALYEAVAA▮F▮AQVNNYELDFGQ

Target    ▮▮T▮S▮TATSAS▮GAAGVPQAGLVTMV▮VLSAVGLPAEDVTL▮▮AVDWLLDRFRTMVNVLGDAFGTG▮VEKLSKKELEQM
5mju.1.A  ▮▮T▮S▮TATAAS▮GAAG▮PQAGLVTMV▮VLTAVGLPTDD▮TL▮▮AVDWLLDRFRTMVNVLGDALGAG▮VEHLSRKELEKQ

Target    DVSSEVN▮VNPFALEST▮LDNEDSDTKKSYVNGGFAVDKSDT▮SFTQTSQF
5mju.1.A  DAELGNSV------------------------------------------
```

Materials and Methods

Template Search

Template search with BLAST and HHBlits has been performed against the SWISS-MODEL template library (SMTL, last update: 2018-06-29, last included PDB release: 2018-06-22).

The target sequence was searched with BLAST against the primary amino acid sequence contained in the SMTL. A total of 28 templates were found.

An initial HHblits profile has been built using the procedure outlined in (Remmert et al.), followed by 1 iteration of HHblits against NR20. The obtained profile has then be searched against all profiles of the SMTL. A total of 56 templates were found.

Template Selection

For each identified template, the template's quality has been predicted from features of the target-template alignment. The templates with the highest quality have then been selected for model building.

Model Building

Models are built based on the target-template alignment using ProMod3. Coordinates which are conserved between the target and the template are copied from the template to the model. Insertions and deletions are remodelled using a fragment library. Side chains are then rebuilt. Finally, the geometry of the resulting model is regularized by using a force field. In case loop modelling with ProMod3 fails, an alternative model is built with PROMOD-II (Guex et al.).

Model Quality Estimation

The global and per-residue model quality has been assessed using the QMEAN scoring function (Benkert et al.) . For improved performance, weights of the individual QMEAN terms have been trained specifically for SWISS-MODEL.

Ligand Modelling

Ligands present in the template structure are transferred by homology to the model when the following criteria are met: (a) The ligands are annotated as biologically relevant in the template library, (b) the ligand is in contact with the model, (c) the ligand is not clashing with the protein, (d) the residues in contact with the ligand are conserved between the target and the template. If any of these four criteria is not satisfied, a certain ligand will not be included in the model. The model summary includes information on why and which ligand has not been included.

Oligomeric State Conservation

The quaternary structure annotation of the template is used to model the target sequence in its oligomeric form. The method (Bertoni et al.) is based on a supervised machine learning algorithm, Support Vector Machines (SVM), which combines interface conservation, structural clustering, and other template features to provide a quaternary structure quality estimate (QSQE). The QSQE score is a number between 0 and 1, reflecting the expected accuracy of the interchain contacts for a model built based a given alignment and template. Higher numbers indicate higher reliability. This complements the GMQE score which estimates the accuracy of the tertiary structure of the resulting model.

References

- **BLAST**
  Camacho, C., Coulouris, G., Avagyan, V., Ma, N., Papadopoulos, J., Bealer, K., Madden, T.L. BLAST+: architecture and applications. BMC Bioinformatics 10, 421-430 (2009). doi>
- **HHblits**
  Remmert, M., Biegert, A., Hauser, A., Söding, J. HHblits: lightning-fast iterative protein sequence searching by HMM-HMM alignment. Nat Methods 9, 173-175 (2012). doi>

Table T1:

Primary amino acid sequence for which templates were searched and models were built.

```
MGKPARKGCEWKRFLKNNWVLLSTVAAVVLGITTGVLVREHSNLSTLEKFYFAFPGEILMRMLKLIILPLIISSMITGVAALDSNVSGKIGLRAVVYYFC
TTLIAVILGIVLVVSIKPGVTQKVGEIARTGSTPEVSTVDAMLDLIRNMFPENLVQACFQQYKTKREEVKPPSDPEMNMTEESFTAVMTTAISKNKTKEY
KIVGMYSDGINVLGLIVFCLVFGLVIGKMGEKGQILVDFFNALSDATMKIVQIIMCYMPLGILFLIAGKIIEVEDWEIFRKLGLYMATVLTGLAIHSIVI
LPLIYFIVVRKNPFRFAMGMAQALLTALMISSSSATLPVTFRCAEENNQVDKRITRFVLPVGATINMDGTALYEAVAAVFIAQLNDLDLGIGQIITISIT
ATSASIGAAGVPQAGLVTMVIVLSAVGLPAEDVTLIIAVDWLLDRFRTMVNVLGDAFGTGIVEKLSKKELEQMDVSSEVNIVNPFALESTILDNEDSDTK
KSYVNGGFAVDKSDTISFTQTSQF
```

Table T2:

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Coverage	Description
5llu.1.A	60.08	homo-trimer	0.66	HHblits	X-ray	3.32Å	0.46	0.91	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1
5llu.1.A	65.01	homo-trimer	0.64	BLAST	X-ray	3.32Å	0.48	0.88	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1
5mju.1.A	63.13	homo-trimer	0.65	HHblits	X-ray	3.71Å	0.47	0.86	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1
5mju.1.A	65.01	homo-trimer	0.63	BLAST	X-ray	3.71Å	0.48	0.88	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1
6gct.1.A	42.95	homo-trimer	0.62	HHblits	EM	NA	0.41	0.92	Neutral amino acid transporter B(0)
6gct.1.A	48.89	homo-trimer	0.56	BLAST	EM	NA	0.44	0.78	Neutral amino acid transporter B(0)
5llm.1.A	65.01	monomer		BLAST	X-ray	3.25Å	0.48	0.88	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1
5llm.1.A	63.13	monomer		HHblits	X-ray	3.25Å	0.47	0.86	Excitatory amino acid transporter 1,Neutral amino acid transporter B(0),Excitatory amino acid transporter 1
5e9s.1.A	33.42	homo-trimer	0.58	HHblits	X-ray	2.80Å	0.36	0.77	Proton/glutamate symporter, SDF family
5e9s.1.B	33.42	homo-trimer	0.58	HHblits	X-ray	2.80Å	0.36	0.77	Proton/glutamate symporter, SDF family

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Coverage	Description
5dwy.1.A	33.42	homo-trimer	0.58	HHblits	X-ray	2.70Å	0.36	0.77	Proton/glutamate symporter, SDF family
5dwy.1.C	33.42	homo-trimer	0.58	HHblits	X-ray	2.70Å	0.36	0.77	Proton/glutamate symporter, SDF family
6bat.1.A	34.25	homo-trimer	0.58	HHblits	X-ray	3.40Å	0.37	0.76	Glutamate transporter homolog
4ky0.1.C	33.42	homo-trimer	0.56	HHblits	X-ray	3.00Å	0.36	0.76	Proton/glutamate symporter, SDF family
4ky0.1.A	33.42	homo-trimer	0.56	HHblits	X-ray	3.00Å	0.36	0.76	Proton/glutamate symporter, SDF family
2nwl.1.A	34.25	homo-trimer	0.55	HHblits	X-ray	2.96Å	0.37	0.76	glutamate symport protein
4p3j.1.A	34.25	homo-trimer	0.54	HHblits	X-ray	3.50Å	0.37	0.76	GltPh
2nwx.1.A	34.25	homo-trimer	0.54	HHblits	X-ray	3.29Å	0.37	0.76	425aa long hypothetical proton glutamate symport protein
4x2s.1.B	35.00	homo-trimer	0.52	HHblits	X-ray	4.21Å	0.37	0.76	425aa long hypothetical proton glutamate symport protein
4x2s.1.A	35.00	homo-trimer	0.52	HHblits	X-ray	4.21Å	0.37	0.76	425aa long hypothetical proton glutamate symport protein
2nww.1.A	34.25	homo-trimer	0.45	HHblits	X-ray	3.20Å	0.37	0.76	425aa long hypothetical proton glutamate symport protein
4oyf.1.C	34.25	homo-hexamer	0.25	HHblits	X-ray	3.41Å	0.37	0.76	GLUTAMATE SYMPORT PROTEIN
6bat.1.A	43.70	homo-trimer	0.43	BLAST	X-ray	3.40Å	0.40	0.48	Glutamate transporter homolog
5e9s.1.B	42.97	homo-trimer	0.42	BLAST	X-ray	2.80Å	0.40	0.49	Proton/glutamate symporter, SDF family
5e9s.1.A	42.97	homo-trimer	0.42	BLAST	X-ray	2.80Å	0.40	0.49	Proton/glutamate symporter, SDF family
4izm.1.A	44.09	homo-trimer	0.42	BLAST	X-ray	4.50Å	0.40	0.48	425aa long hypothetical proton glutamate symport protein
5dwy.1.A	42.97	homo-trimer	0.41	BLAST	X-ray	2.70Å	0.40	0.49	Proton/glutamate symporter, SDF family
5dwy.1.C	42.97	homo-trimer	0.41	BLAST	X-ray	2.70Å	0.40	0.49	Proton/glutamate symporter, SDF family
4ky0.1.C	43.24	homo-trimer	0.40	BLAST	X-ray	3.00Å	0.39	0.49	Proton/glutamate symporter, SDF family
4ky0.1.A	43.24	homo-trimer	0.40	BLAST	X-ray	3.00Å	0.39	0.49	Proton/glutamate symporter, SDF family
4p6h.1.A	44.09	homo-trimer	0.39	BLAST	X-ray	4.08Å	0.40	0.48	GltPh
4p3j.1.A	44.09	homo-trimer	0.39	BLAST	X-ray	3.50Å	0.40	0.48	GltPh
2nwl.1.A	43.70	homo-trimer	0.37	BLAST	X-ray	2.96Å	0.40	0.48	glutamate symport protein
2nwx.1.A	43.70	homo-trimer	0.37	BLAST	X-ray	3.29Å	0.40	0.48	425aa long hypothetical proton glutamate symport protein
3kbc.1.A	44.06	homo-trimer	0.36	BLAST	X-ray	3.51Å	0.40	0.50	425aa long hypothetical proton glutamate symport protein
5cfy.1.A	43.30	homo-hexamer	0.11	BLAST	X-ray	3.50Å	0.40	0.50	425aa long hypothetical proton glutamate symport protein
4izm.1.A	20.00	homo-trimer	0.08	HHblits	X-ray	4.50Å	0.30	0.15	425aa long hypothetical proton glutamate symport protein
4p3j.1.A	21.25	homo-trimer	0.06	HHblits	X-ray	3.50Å	0.30	0.15	GltPh
4p6h.1.A	21.25	homo-trimer	0.06	HHblits	X-ray	4.08Å	0.30	0.15	GltPh

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Coverage	Description
3kbc.1.A	22.89	homo-trimer	0.01	HHblits	X-ray	3.51Å	0.31	0.16	425aa long hypothetical proton glutamate symport protein
4x2s.1.A	16.46	monomer		HHblits	X-ray	4.21Å	0.31	0.15	425aa long hypothetical proton glutamate symport protein
4x2s.1.B	16.46	monomer		HHblits	X-ray	4.21Å	0.31	0.15	425aa long hypothetical proton glutamate symport protein
5cfy.1.A	20.99	homo-trimer	0.08	HHblits	X-ray	3.50Å	0.30	0.15	425aa long hypothetical proton glutamate symport protein
4oye.1.A	20.99	homo-trimer	0.07	HHblits	X-ray	4.00Å	0.30	0.15	425aa long hypothetical proton glutamate symport protein
2nww.1.A	16.92	monomer		HHblits	X-ray	3.20Å	0.31	0.12	425aa long hypothetical proton glutamate symport protein
4oyf.1.C	16.92	monomer		HHblits	X-ray	3.41Å	0.31	0.12	GLUTAMATE SYMPORT PROTEIN
5dwy.1.A	20.00	monomer		HHblits	X-ray	2.70Å	0.31	0.12	Proton/glutamate symporter, SDF family
5dwy.1.C	20.00	monomer		HHblits	X-ray	2.70Å	0.31	0.12	Proton/glutamate symporter, SDF family
5e9s.1.A	20.00	monomer		HHblits	X-ray	2.80Å	0.31	0.12	Proton/glutamate symporter, SDF family
2nwx.1.A	16.92	monomer		HHblits	X-ray	3.29Å	0.31	0.12	425aa long hypothetical proton glutamate symport protein

The table above shows the top 50 filtered templates. A further 23 templates were found which were considered to be less suitable for modelling than the filtered list.
4oye.1.A, 4x2s.1.A, 4x2s.1.B, 5llu.1.A, 4izm.1.A, 4ky0.1.A, 4ky0.1.C, 3v8f.1.A, 5e9s.1.B, 2nwl.1.A, 2nww.1.A, 4p6h.1.A, 6bau.1.A, 5cfy.1.A, 3v8g.1.A, 3v8g.1.C, 6gct.1.A, 5llm.1.A, 4oyf.1.C, 3kbc.1.A, 5mju.1.A, 6bav.1.A, 6bat.1.A