SWISS-MODEL Homology Modelling Report

Model Building Report

This document lists the results for the homology modelling project "MDHM_HUMAN P40926 Malate dehydrogenase, mitochondrial" submitted to SWISS-MODEL workspace on Aug. 27, 2024, 10:33 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:

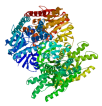
- Waterhouse A, Bertoni M, Bienert S, Studer G, Tauriello G, Gumienny R, Heer FT, de Beer TAP, Rempfer C, Bordoli L, Lepore R, Schwede T
  SWISS-MODEL: homology modelling of protein structures and complexes.
  Nucleic Acids Res 46, W296-W303. (2018) 29788355 10.1093/nar/gky427
- Bienert S, Waterhouse A, de Beer TAP, Tauriello G, Studer G, Bordoli L, Schwede T
  The SWISS-MODEL Repository - new features and functionality.
  Nucleic Acids Res 45, D313-D319. (2017) 27899672 10.1093/nar/gkw1132
- Studer G, Tauriello G, Bienert S, Biasini M, Johner N, Schwede T
  ProMod3 - A versatile homology modelling toolbox.
  PLOS Comp Biol 17(1), e1008667. (2021) 33507980 10.1371/journal.pcbi.1008667
- Studer G, Rempfer C, Waterhouse AM, Gumienny R, Haas J, Schwede T
  QMEANDisCo - distance constraints applied on model quality estimation.
  Bioinformatics 36, 1765-1771. (2020) 31697312 10.1093/bioinformatics/btz828
- 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) 28874689 10.1038/s41598-017-09654-8

Results

The user uploaded a template structure to use for the modelling process.

Models

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

Model #01	File	Built with	Oligo-State	Ligands	GMQE	QMEANDisCo Global
	PDB	ProMod3 3.4.1	homo-tetramer (matching prediction)	4 x NAI: NAI; 4 x OAA: OAA;	0.91	0.91 ± 0.05

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Range	Coverage	Description
template_upload.1.A	100.00	homo-tetramer	0.96	HHblits	Unknown	-	0.61	24 - 337	0.93	Polypeptide

Included Ligands

Ligand	Description
4 x NAI	NAI
4 x OAA	OAA

```
Target                  MLSALARPASAALRRSFSTSAQNNAKVAVLGASGGIGQPLSLLLKNSPLVSRLTL
template_upload.1.A     ----------------------NAKVAVLGASGGIGQPLSLLLKNSPLVSRLTL

Target                  YDIAHTPGVAADLSHIETKAAVKGYLGPEQLPDCLKGCDVVVIPAGVPRKPGMTR
template_upload.1.A     YDIAHTPGVAADLSHIETKAAVKGYLGPEQLPDCLKGCDVVVIPAGVPRKPGMTR
```

```
Target                  DDLFNTNATIVATLTAACAQHCPEAMICVIANPVNSTIPITAEVFKKHGVYNPNK
template_upload.1.A     DDLFNTNATIVATLTAACAQHCPEAMICVIANPVNSTIPITAEVFKKHGVYNPNK

Target                  IFGVTTLDIVRANTFVAELKGLDPARVNVPVIGGHAGKTIIPLISQCTPKVDFPQ
template_upload.1.A     IFGVTTLDIVRANTFVAELKGLDPARVNVPVIGGHAGKTIIPLISQCTPKVDFPQ

Target                  DQLTALTGRIQEAGTEVVKAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVEC
template_upload.1.A     DQLTALTGRIQEAGTEVVKAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVEC

Target                  SFVKSQETECTYFSTPLLLGKKGIEKNLGIGKVSSFEEKMISDAIPELKASIKKG
template_upload.1.A     SFVKSQETECTYFSTPLLLGKKGIEKNLGIGKVSSFEEKMISDAIPELKASIKKG

Target                  EDFVKTLK
template_upload.1.A     EDFVKTL-


Target                  MLSALARPASAALRRSFSTSAQNNAKVAVL
template_upload.1.B     ----------------------NAKVAVL

Target                  GASGGIGQPLSLLLKNSPLVSRLTLYDIAH
template_upload.1.B     GASGGIGQPLSLLLKNSPLVSRLTLYDIAH

Target                  TPGVAADLSHIETKAAVKGYLGPEQLPDCL
template_upload.1.B     TPGVAADLSHIETKAAVKGYLGPEQLPDCL

Target                  KGCDVVVIPAGVPRKPGMTRDDLFNTNATI
template_upload.1.B     KGCDVVVIPAGVPRKPGMTRDDLFNTNATI

Target                  VATLTAACAQHCPEAMICVIANPVNSTIPI
template_upload.1.B     VATLTAACAQHCPEAMICVIANPVNSTIPI

Target                  TAEVFKKHGVYNPNKIFGVTTLDIVRANTF
template_upload.1.B     TAEVFKKHGVYNPNKIFGVTTLDIVRANTF

Target                  VAELKGLDPARVNVPVIGGHAGKTIIPLIS
template_upload.1.B     VAELKGLDPARVNVPVIGGHAGKTIIPLIS

Target                  QCTPKVDFPQDQLTALTGRIQEAGTEVVKA
template_upload.1.B     QCTPKVDFPQDQLTALTGRIQEAGTEVVKA

Target                  KAGAGSATLSMAYAGARFVFSLVDAMNGKE
template_upload.1.B     KAGAGSATLSMAYAGARFVFSLVDAMNGKE

Target                  GVVECSFVKSQETECTYFSTPLLLGKKGIE
template_upload.1.B     GVVECSFVKSQETECTYFSTPLLLGKKGIE

Target                  KNLGIGKVSSFEEKMISDAIPELKASIKKG
template_upload.1.B     KNLGIGKVSSFEEKMISDAIPELKASIKKG

Target                  EDFVKTLK
template_upload.1.B     EDFVKTL-


Target                  MLSAL
template_upload.1.C     -----

Target                  ARPAS
template_upload.1.C     -----

Target                  AALRR
template_upload.1.C     -----
```

```
Target                  SFSTS
template_upload.1.C     -----

Target                  AQNNA
template_upload.1.C     ---NA

Target                  KVAVL
template_upload.1.C     KVAVL

Target                  GASGG
template_upload.1.C     GASGG

Target                  IGQPL
template_upload.1.C     IGQPL

Target                  SLLLK
template_upload.1.C     SLLLK

Target                  NSPLV
template_upload.1.C     NSPLV

Target                  SRLTL
template_upload.1.C     SRLTL

Target                  YDIAH
template_upload.1.C     YDIAH

Target                  TPGVA
template_upload.1.C     TPGVA

Target                  ADLSH
template_upload.1.C     ADLSH

Target                  IETKA
template_upload.1.C     IETKA

Target                  AVKGY
template_upload.1.C     AVKGY

Target                  LGPEQ
template_upload.1.C     LGPEQ

Target                  LPDCL
template_upload.1.C     LPDCL

Target                  KGCDV
template_upload.1.C     KGCDV

Target                  VVIPA
template_upload.1.C     VVIPA

Target                  GVPRK
template_upload.1.C     GVPRK

Target                  PGMTR
template_upload.1.C     PGMTR

Target                  DDLFN
template_upload.1.C     DDLFN

Target                  TNATI
template_upload.1.C     TNATI
```

```
Target                  VATLT
template_upload.1.C     VATLT

Target                  AACAQ
template_upload.1.C     AACAQ

Target                  HCPEA
template_upload.1.C     HCPEA

Target                  MICVI
template_upload.1.C     MICVI

Target                  ANPVN
template_upload.1.C     ANPVN

Target                  STIPI
template_upload.1.C     STIPI

Target                  TAEVF
template_upload.1.C     TAEVF

Target                  KKHGV
template_upload.1.C     KKHGV

Target                  YNPNK
template_upload.1.C     YNPNK

Target                  IFGVT
template_upload.1.C     IFGVT

Target                  TLDIV
template_upload.1.C     TLDIV

Target                  RANTF
template_upload.1.C     RANTF

Target                  VAELK
template_upload.1.C     VAELK

Target                  GLDPA
template_upload.1.C     GLDPA

Target                  RVNVP
template_upload.1.C     RVNVP

Target                  VIGGH
template_upload.1.C     VIGGH

Target                  AGKTI
template_upload.1.C     AGKTI

Target                  IPLIS
template_upload.1.C     IPLIS

Target                  QCTPK
template_upload.1.C     QCTPK

Target                  VDFPQ
template_upload.1.C     VDFPQ

Target                  DQLTA
template_upload.1.C     DQLTA
```

```
Target                  LTGRI
template_upload.1.C     LTGRI

Target                  QEAGT
template_upload.1.C     QEAGT

Target                  EVVKA
template_upload.1.C     EVVKA

Target                  KAGAG
template_upload.1.C     KAGAG

Target                  SATLS
template_upload.1.C     SATLS

Target                  MAYAG
template_upload.1.C     MAYAG

Target                  ARFVF
template_upload.1.C     ARFVF

Target                  SLVDA
template_upload.1.C     SLVDA

Target                  MNGKE
template_upload.1.C     MNGKE

Target                  GVVEC
template_upload.1.C     GVVEC

Target                  SFVKS
template_upload.1.C     SFVKS

Target                  QETEC
template_upload.1.C     QETEC

Target                  TYFST
template_upload.1.C     TYFST

Target                  PLLLG
template_upload.1.C     PLLLG

Target                  KKGIE
template_upload.1.C     KKGIE

Target                  KNLGI
template_upload.1.C     KNLGI

Target                  GKVSS
template_upload.1.C     GKVSS

Target                  FEEKM
template_upload.1.C     FEEKM

Target                  ISDAI
template_upload.1.C     ISDAI

Target                  PELKA
template_upload.1.C     PELKA

Target                  SIKKG
template_upload.1.C     SIKKG
```

```
Target                  EDFVK
template_upload.1.C     EDFVK

Target                  TLK
template_upload.1.C     TL-
```

Materials and Methods

User Template Alignment

The user entered their own target sequence together with an uploaded a template structure file in PDB format.

Model Building

Models are built based on the target-template alignment using ProMod3 (Studer et al.). 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.

Model Quality Estimation

The global and per-residue model quality has been assessed using the QMEAN scoring function (Studer et al.).

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

- Camacho C, Coulouris G, Avagyan V, Ma N, Papadopoulos J, Bealer K, Madden TL
  BLAST+: architecture and applications.
  BMC Bioinformatics, 10, 421-430. (2009) 20003500 10.1186/1471-2105-10-421
- Steinegger M, Meier M, Mirdita M, Vöhringer H, Haunsberger SJ, Söding J
  HH-suite3 for fast remote homology detection and deep protein annotation.
  BMC Bioinformatics 20, 473. (2019) 31521110 10.1186/s12859-019-3019-7

Table T1:

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

```
MLSALARPASAALRRSFSTSAQNNAKVAVLGASGGIGQPLSLLLKNSPLVSRLTLYDIAHTPGVAADLSHIETKAAVKGYLGPEQLPDCLKGCDVVVIPA
GVPRKPGMTRDDLFNTNATIVATLTAACAQHCPEAMICVIANPVNSTIPITAEVFKKHGVYNPNKIFGVTTLDIVRANTFVAELKGLDPARVNVPVIGGH
AGKTIIPLISQCTPKVDFPQDQLTALTGRIQEAGTEVVKAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKGIE
KNLGIGKVSSFEEKMISDAIPELKASIKKGEDFVKTLK
```

Table T2:

Template	Seq Identity	Oligo-state	QSQE	Found by	Method	Resolution	Seq Similarity	Coverage	Description
template_upload.1.A	100.00	homo-tetramer	0.96	HHblits	Unknown	NA	0.61	0.93	Polypeptide

The table above shows the top 1 filtered templates. A further 1 template was found which was considered to be less suitable for modelling than the filtered list.
template_upload.1.A