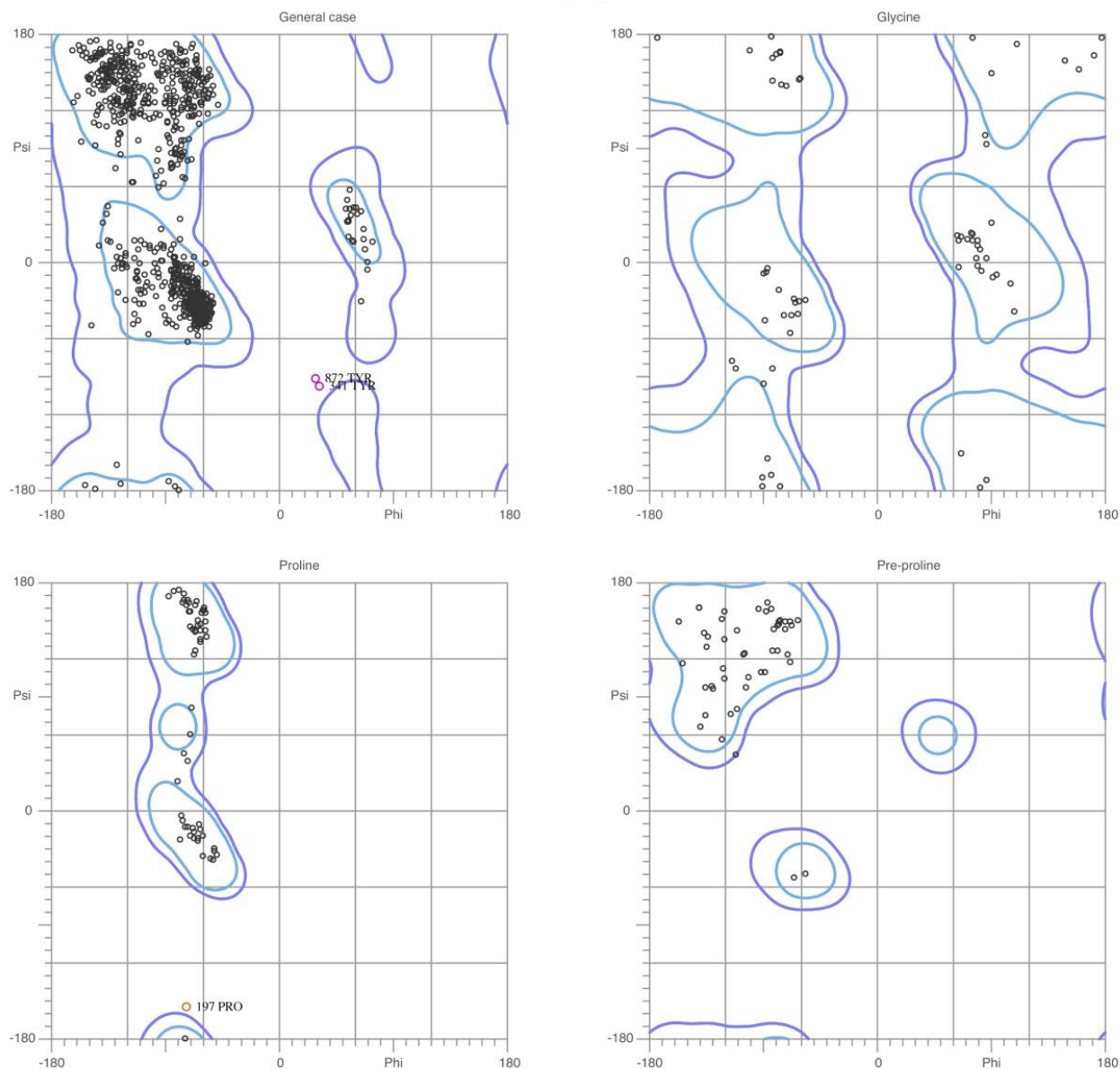


# Hybrid model of *L. braziliensis* DHFR-TS



97.3% (1010/1038) of all residues were in favored (98%) regions.  
 99.7% (1035/1038) of all residues were in allowed (>99.8%) regions.

There were 3 outliers (phi, psi):

197 PRO (-74.1, -154.7)

341 TYR (31.8, -97.6)

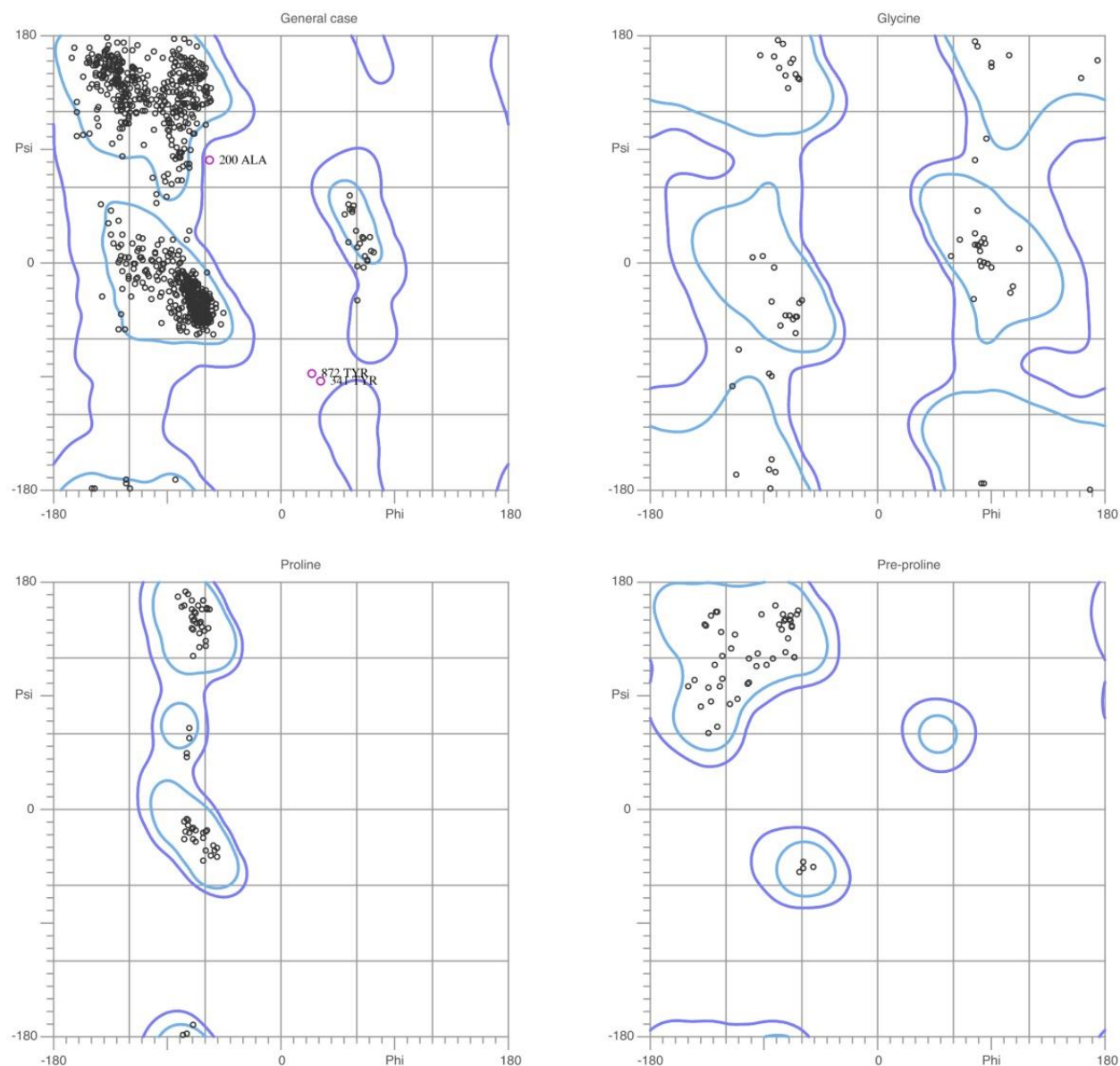
872 TYR (28.8, -91.4)

<http://kinemage.biochem.duke.edu>

Lovell, Davis, et al. Proteins 50:437 (2003)

**Figure S1.** Ramachandran plot for hybrid model of *L. braziliensis*

# Hybrid model of *L. panamensis* DHFR-TS



97.2% (1009/1038) of all residues were in favored (98%) regions.

99.7% (1035/1038) of all residues were in allowed (>99.8%) regions.

There were 3 outliers (phi, psi):

200 ALA (-57.2, 82.2)

341 TYR (31.2, -93.7)

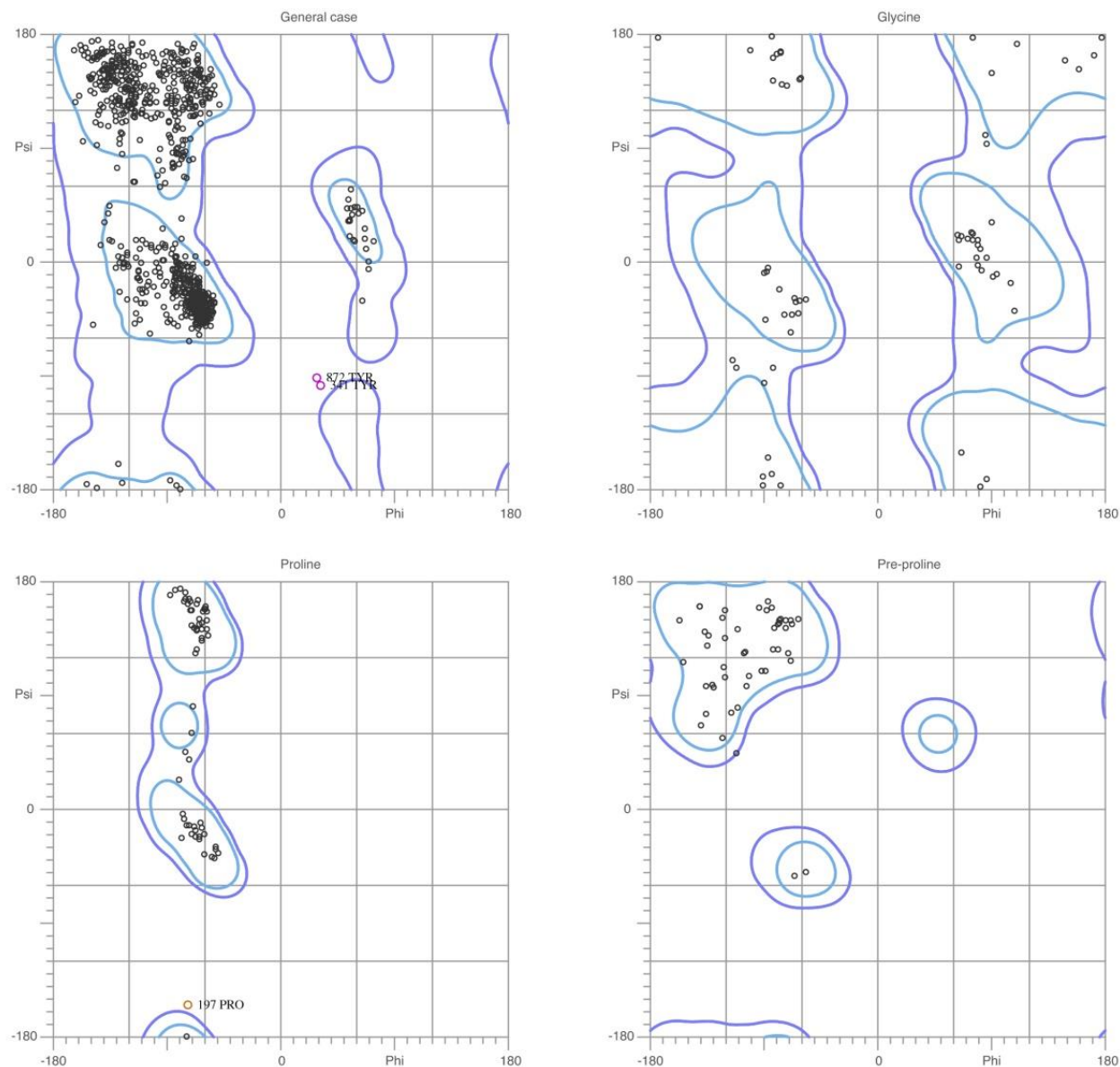
872 TYR (24.8, -87.2)

<http://kinemage.biochem.duke.edu>

Lovell, Davis, et al. Proteins 50:437 (2003)

**Figure S2.** Ramachandran plot for hybrid model of *L. panamensis*

# Hybrid model of *L. amazonensis* DHFR-TS



97.3% (1010/1038) of all residues were in favored (98%) regions.  
 99.7% (1035/1038) of all residues were in allowed (>99.8%) regions.

There were 3 outliers (phi, psi):

197 PRO (-74.1, -154.7)

341 TYR (31.8, -97.6)

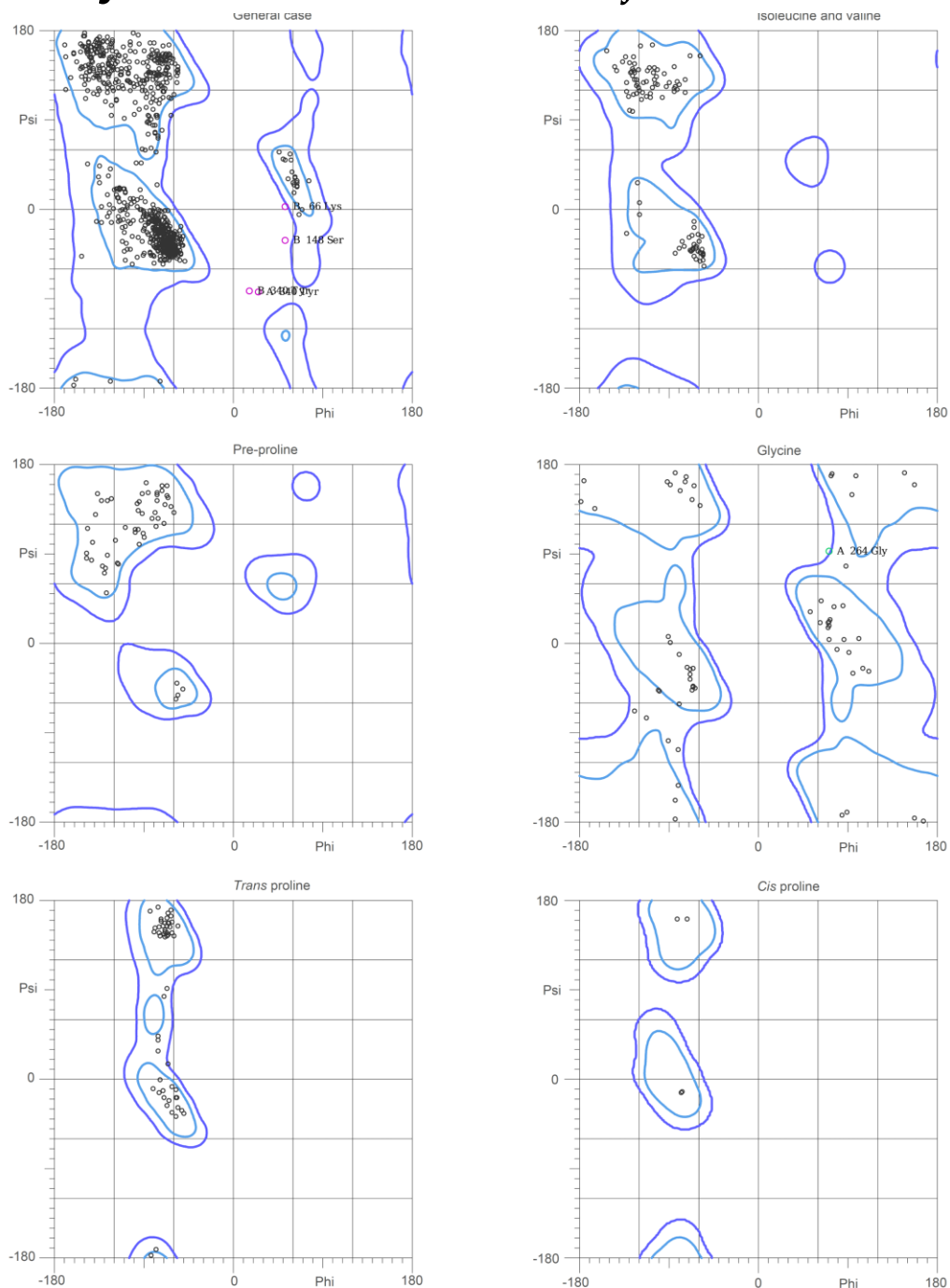
872 TYR (28.8, -91.4)

<http://kinemage.biochem.duke.edu>

Lovell, Davis, et al. Proteins 50:437 (2003)

**Figure S3.** Ramachandran plot for hybrid model of *L. amazonensis*

# Hybrid model of *L. major* DHFR-TS



96.9% (1004/1036) of all residues were in favored (98%) regions.  
99.5% (1031/1036) of all residues were in allowed (>99.8%) regions.

There were 5 outliers (phi, psi):

- A 264 Gly (72.0, 93.5)
- A 340 Tyr (25.3, -83.2)
- B 66 Lys (52.4, 3.5)
- B 148 Ser (52.5, -31.5)
- B 340 Tyr (16.3, -83.0)

<http://kinemage.biochem.duke.edu>

Lovell, Davis, et al. Proteins 50:437 (2003)

**Figure S4.** Ramachandran plot for hybrid model of *L. major*

# DHFR Multiple Sequence Alignment

Sequence type explicitly set to Protein  
Sequence format is Pearson

Sequence 1: DHFR\_L.amazonensis 203 aa  
Sequence 2: DHFR\_L.braziliensis 205 aa  
Sequence 3: DHFR\_L.panamensis 205 aa  
Sequence 4: DHFR\_L.major 204 aa  
Sequence 5: DHFR\_Homo\_sapiens 187 aa  
Start of Pairwise alignments

Sequences (1:2) Aligned. Score: 78.8177  
Sequences (1:3) Aligned. Score: 79.8030  
Sequences (1:4) Aligned. Score: 89.1626  
Sequences (1:5) Aligned. Score: 20.8556  
Sequences (2:3) Aligned. Score: 99.0244  
Sequences (2:4) Aligned. Score: 79.9020  
Sequences (2:5) Aligned. Score: 24.0642  
Sequences (3:4) Aligned. Score: 80.8824  
Sequences (3:5) Aligned. Score: 24.0642  
Sequences (4:5) Aligned. Score: 23.5294

CLUSTAL 2.1 multiple sequence alignment

```
DHFR_Lb      ---CFSIIIVAVDEQHGIGDGKTIIPWQVPEDMAFFKQDTLLRNKKPPTTEKKRNAVVMGRQ
DHFR_Lp      ---CFSIIIVAVDEQHGIGDGKTIIPWQVPEDMAFFKQDTLLRNKKPPTTEKKRNAVVMGRQ
DHFR_La      ---AFSIVVALDKQHIGIGDGESIPWQVPEDMAFFKQDTLLRNKKPPTDKKRNAVVMGRK
DHFR_Lm      ---AFSIVVALDMQHIGIGDGESIPWRVPEDMTFFKNQDTLLRNKKPPTTEKKRNAVVMGRK
DHFR_Hs      MVGSLNCIVAVSQNMGIGKNGDLPWPELRNEFRYFQRMTTSS----VEGQNLVIMGKK
              .. :***. : ***.. :**  . : : : * . . : *:* *::*:

DHFR_Lb      TWESVPLKVRPLKGRNLNVVLSSKATVDELLAALPEGKRTAAQDLVVVNGGLAEALHLLA
DHFR_Lp      TWESVPLKVRPLKGRNLNVVLSSKATVDELLAPLPEGKRAAAQDLVVVNGGLAEALHLLA
DHFR_La      TWESVPLKVRPLKGRNLNVVLSSKATVEELLAPLPEEKRAAAQDIVVVNGGLAAAVRLLA
DHFR_Lm      TWESVPLKVRPLKGRNLNVVLSSKATVEELLAPLPEGQRAAAQDVVVVNGGLAEALRLLA
DHFR_Hs      TWFSIPEKVRPLKGRINLVLS-----RELKEPPQGAHFLSRSLDDALKLTE
              ** :*:* * *****:*:*  : . .*. . . . * *::*:

DHFR_Lb      RPPHCSSIETAYCVGGAQVYS DAPCVEKLQEVYLTIRIYATAPECTRFYFPFPTNAAA
DHFR_Lp      RPPHCSSIETAYCVGGAQVYS DAPCVEKLQEVYLTIRIYATAPECTRFYFPFPTNAAA
DHFR_La      RPPYCSSIETAYCVGGAQVYADAMLSPCVEKLQEVYLTIRIHTTAPACTRFFFPFPPE-NAA
DHFR_Lm      RPLYCSSIETAYCVGGAQVYADAMLSPCIEKLQEVYLTIRIYATAPECTRFFFPFPPE-NAA
DHFR_Hs      QPELANKVDMMWIVGSSVYKEAMNHP---GHLKLFVTRIMQDFESDTFFPEIDLEKYKL
              :*  ....: . : ***:*:* :**  * :::***  * * :

DHFR_Lb      AAWDLAWTQGRQRSETGGVEYEIRKYVP
DHFR_Lp      AAWDLAWTQGRQRSETGGVEYEIRKYVP
DHFR_La      TAWDLASSQGRRKSAVDGLEFEICKYVP
DHFR_Lm      TAWDLASSQGRRKSEAEGLEFEICKYVP
DHFR_Hs      LPEYPGVLSDVQEKGIKYKFEVYEKND
              . . . . . :::: :
```

**Figure S5:** Results of a multiple sequence alignment using ClustalW software, comparing the sequences of *Leishmania* and *Homo sapiens*. Conserved residues are highlighted in yellow, semiconserved residues in gray, and non-conserved residues in red.