

# Consensus Enolase of *Trypanosoma Cruzi*: Evaluation of Their Immunogenic Properties Using a Bioinformatics Approach

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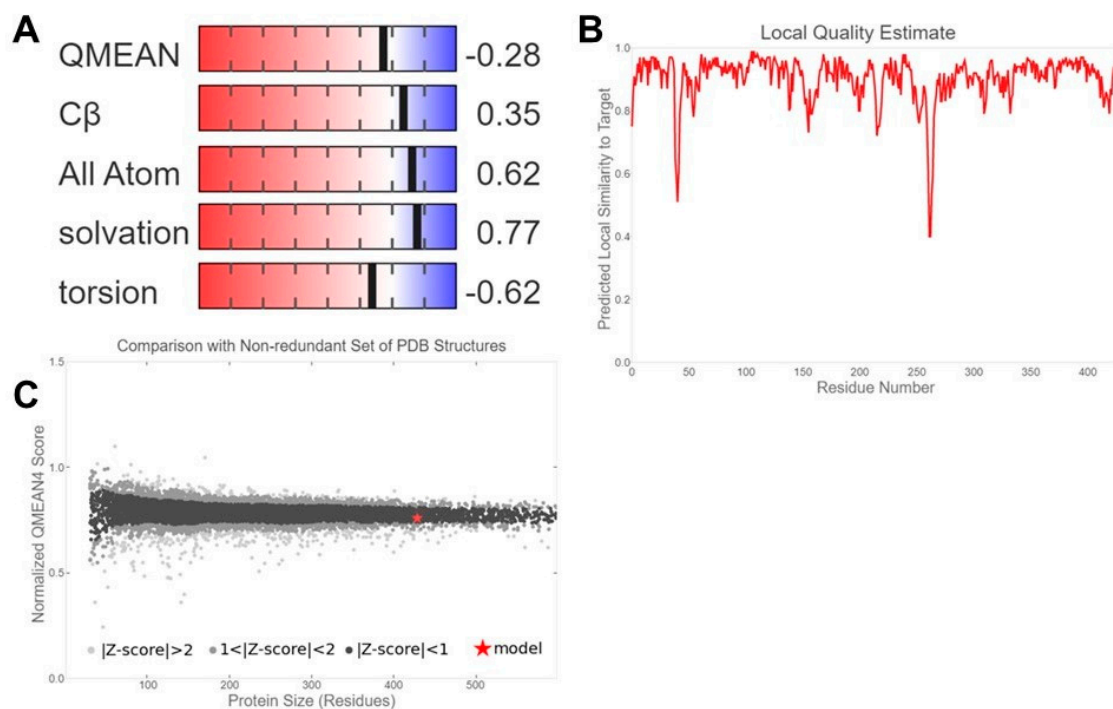
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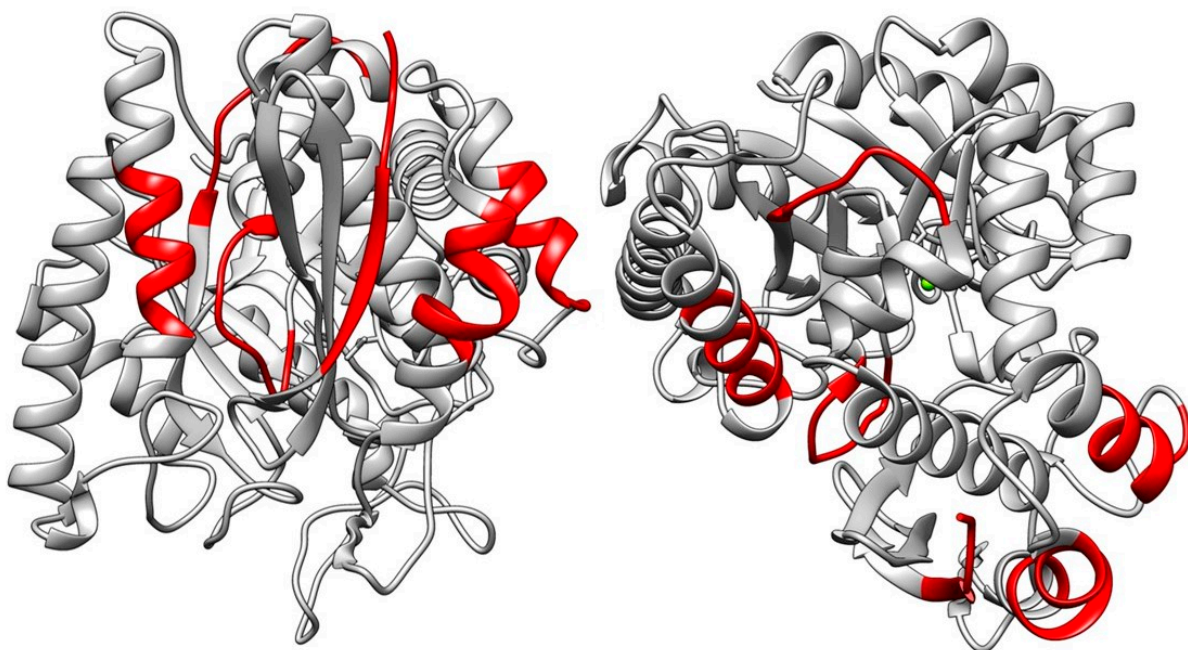


**Figure S1. Consensus enolase of *T. cruzi* modelling results:** **A.** General values obtained; **B.** Local quality plot between the model and the crystallized structure; **C.** Comparison of the QMEAN of the modeled protein with other experimentally obtained structures.

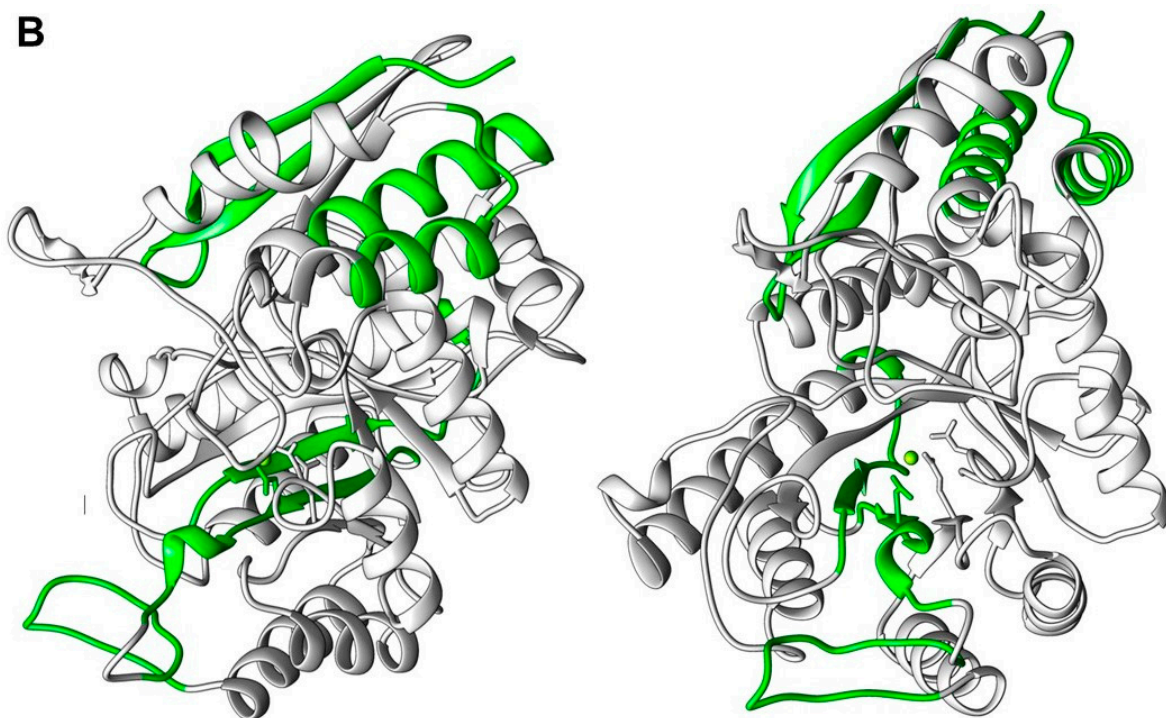


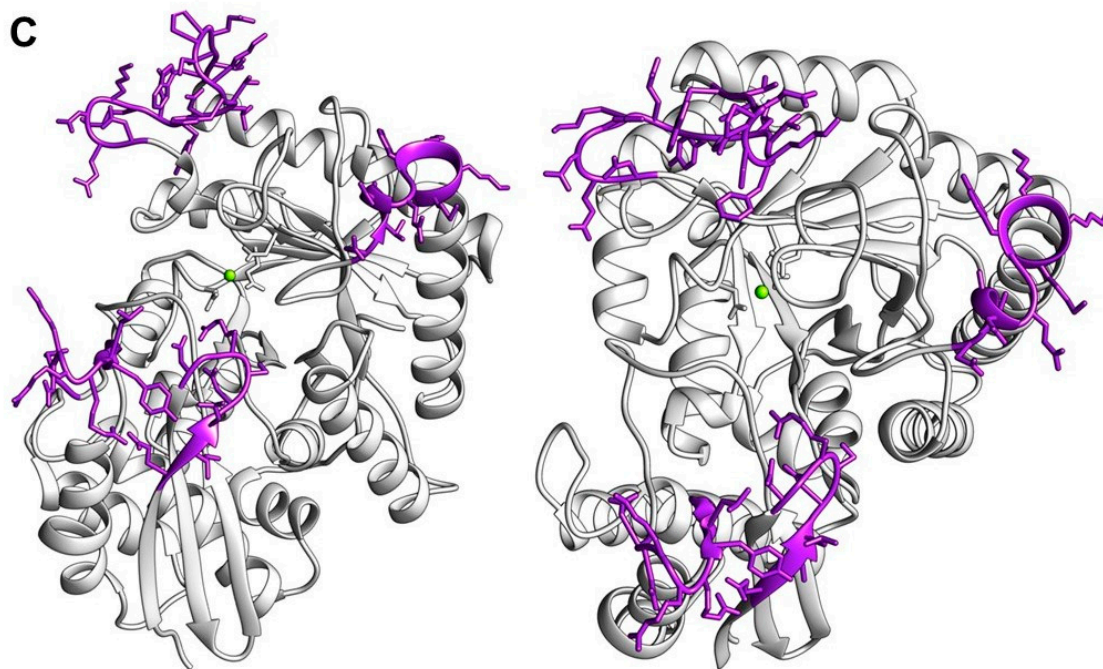
**Figure S2. Ramachandran's graphs corresponding to consensus enolase:** A. General graph (without proline and glycine); B. Exclusive glycine graphic; C. Exclusive proline graphic; D. Graph of amino acids immediately preceding proline in the sequence

**A**



**B**

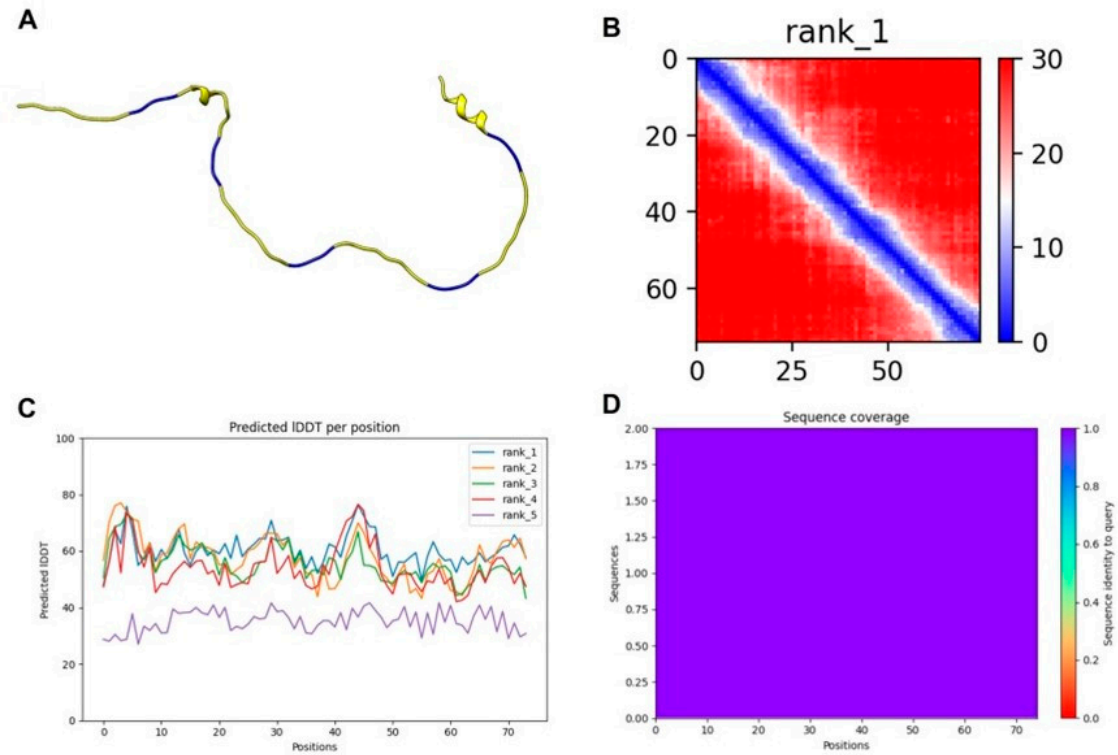




**Figure S3. Visualization of predicted epitopes in the consensus enolase structure:** **A.** Predicted MHC-I epitopes highlighted in red, showing six epitopes detailed in Table 4. **B.** Predicted MHC-II epitopes highlighted in green, showing seven epitopes as detailed in Table 4. **C.** Predicted epitopes for B cells highlighted in purple, showing five epitopes, detailed in Table 5.

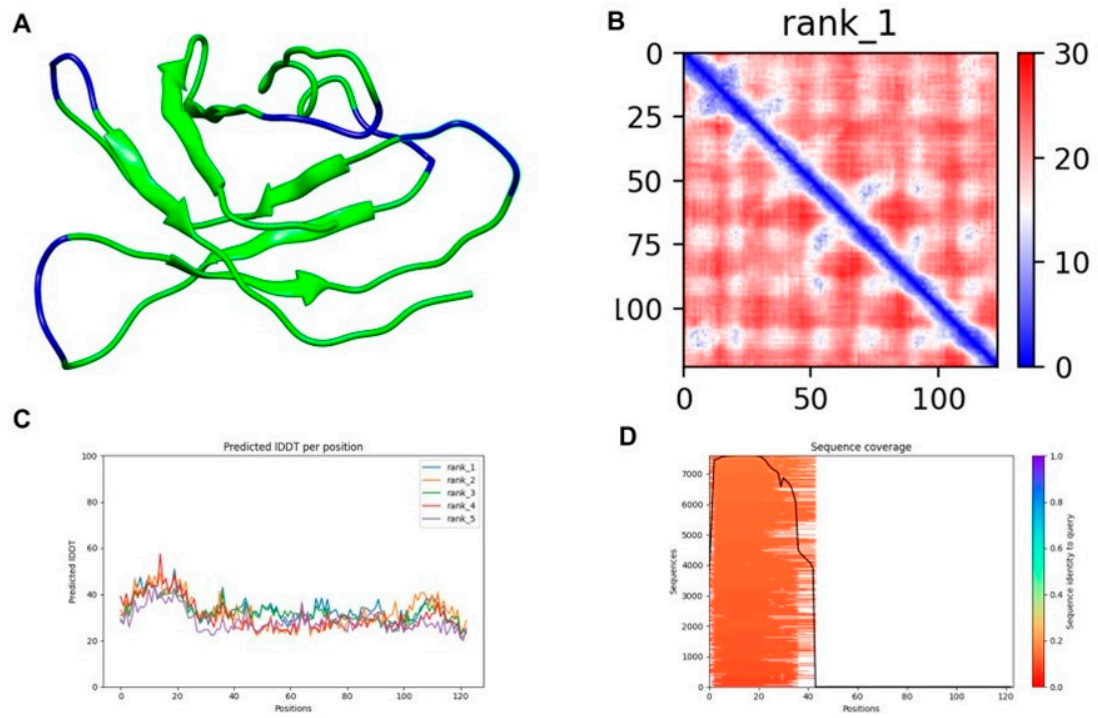


Figure S4



**Figure S4. MHC I protein chimeric construct modelling with AlphaFold.** **A.** Structure obtained corresponding to the MHC I type chimera, yellow for epitopes and blue for linker type proteins); **B.** Distogram with the number of sequences per position between pairs of residues (it indicates the spatial relationship, bluer is more reliable); **C.** LDDT Score of the 5 models created (values above 90 are ideal); **D.** Number of sequences per position (This graph shows us sequences found that in parts follow the same order as the Problem sequence).

Figure S5



**Figure S5. MHC II protein chimeric construct modelling with AlphaFold.** **A.** Structure obtained corresponding to the MHC II type chimera, green for epitopes and blue for linker type proteins); **B.** Distogram with the number of sequences per position between pairs of residues (it indicates the spatial relationship, bluer is more reliable); **C.** LDDT Score of the 5 models created (values above 90 are ideal); **D.** Number of sequences per position (This graph shows us sequences found that in parts follow the same order as the Problem sequence).

**Table S1. DTUs analyzed to obtain a consensus enolase sequence.**

DTU 1	Link	Reference
Dm 28c	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_59b1d9cd42">tritrypdb.org/tritrypdb/app/record/dataset/DS_59b1d9cd42</a>	[1]
Jrc1 4	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_72f799a558">tritrypdb.org/tritrypdb/app/record/dataset/DS_72f799a558</a>	N/R
Sylvio X10/1	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_45e8b704c2">tritrypdb.org/tritrypdb/app/record/dataset/DS_45e8b704c2</a>	[2]
Brazil A4	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_610b8f99b0">tritrypdb.org/tritrypdb/app/record/dataset/DS_610b8f99b0</a>	[3]
H8	<a href="http://www.ncbi.nlm.nih.gov/nuccore/KC862322.1">www.ncbi.nlm.nih.gov/nuccore/KC862322.1</a>	[4]
<b>DTU 2</b>		
Esmeraldo	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_467358987e">tritrypdb.org/tritrypdb/app/record/dataset/DS_467358987e</a>	N/R
Y	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_9ddef8c95e">tritrypdb.org/tritrypdb/app/record/dataset/DS_9ddef8c95e</a>	[5]
YC6	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_9540582c52">tritrypdb.org/tritrypdb/app/record/dataset/DS_9540582c52</a>	[3]
<b>DTU 3</b>		
231	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_4405580551">tritrypdb.org/tritrypdb/app/record/dataset/DS_4405580551</a>	[6]
<b>DTU 5</b>		
Bug2148	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_6a49629990">tritrypdb.org/tritrypdb/app/record/dataset/DS_6a49629990</a>	[7]
<b>DTU 6</b>		
TCC	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_f35827c3d2">tritrypdb.org/tritrypdb/app/record/dataset/DS_f35827c3d2</a>	[1]
Marinkellei B7	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_b0489ab98b">tritrypdb.org/tritrypdb/app/record/dataset/DS_b0489ab98b</a>	[2]
TulaCI2	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_4900730c76">tritrypdb.org/tritrypdb/app/record/dataset/DS_4900730c76</a>	[8]
CL Brener non-esmeraldo -like	<a href="http://tritrypdb.org/tritrypdb/app/record/dataset/DS_f8bddf3a97">tritrypdb.org/tritrypdb/app/record/dataset/DS_f8bddf3a97</a>	[9]
Cl Brener	<a href="http://www.ncbi.nlm.nih.gov/nuccore/XM_814607.1/">www.ncbi.nlm.nih.gov/nuccore/XM_814607.1/</a>	[10]

N/R= No Reference

## References

- Berna, L.; Rodriguez, M.; Chiribao, M.L.; Parodi-Talice, A.; Pita, S.; Rijo, G.; Alvarez-Valin, F.; Robello, C. Expanding an expanded genome: long-read sequencing of *Trypanosoma cruzi*. *Microb. Genom.* **2018**, *4*, doi:10.1099/mgen.0.000177.
- Franzen, O.; Talavera-Lopez, C.; Ochaya, S.; Butler, C.E.; Messenger, L.A.; Lewis, M.D.; Llewellyn, M.S.; Marinkelle, C.J.; Tyler, K.M.; Miles, M.A.; et al. Comparative genomic analysis of human infective *Trypanosoma cruzi* lineages with the bat-restricted subspecies *T. cruzi marinkellei*. *BMC Genomics* **2012**, *13*, 531, doi:10.1186/1471-2164-13-531.
- Wang, W.; Peng, D.; Baptista, R.P.; Li, Y.; Kissinger, J.C.; Tarleton, R.L. Strain-specific genome evolution in *Trypanosoma cruzi*, the agent of Chagas disease. *PLoS. Pathog.* **2021**, *17*, e1009254, doi:10.1371/journal.ppat.1009254.
- Carabarin-Lima, A.; Rodriguez-Morales, O.; Gonzalez-Vazquez, M.C.; Baylon-Pacheco, L.; Reyes, P.A.; Arce-Fonseca, M.; Rosales-Encina, J.L. In silico approach for the identification of immunological properties of enolase from *Trypanosoma cruzi* and its possible usefulness as vaccine in Chagas disease. *Parasitol. Res.* **2014**, *113*, 1029–1039, doi:10.1007/s00436-013-3737-0.
- Callejas-Hernandez, F.; Rastrojo, A.; Poveda, C.; Girones, N.; Fresno, M. Genomic assemblies of newly sequenced *Trypanosoma cruzi* strains reveal new genomic expansion and greater complexity. *Sci. Rep.* **2018**, *8*, 14631, doi:10.1038/s41598-018-32877-2.
- Baptista, R.P.; Reis-Cunha, J.L.; DeBarry, J.D.; Chiari, E.; Kissinger, J.C.; Bartholomeu, D.C.; Macedo, A.M. Assembly of highly repetitive genomes using short reads: the genome of discrete typing unit III *Trypanosoma cruzi* strain 231. *Microb. Genom.* **2018**, *4*, doi:10.1099/mgen.0.000156.
- Callejas-Hernandez, F.; Girones, N.; Fresno, M. Genome Sequence of *Trypanosoma cruzi* Strain Bug2148. *Genome. Announc.* **2018**, *6*, doi:10.1128/genomeA.01497–17.
- Hamilton, P.B.; Lewis, M.D.; Cruickshank, C.; Gaunt, M.W.; Yeo, M.; Llewellyn, M.S.; Valente, S.A.; Maia da Silva, F.; Stevens, J.R.; Miles, M.A.; et al. Identification and lineage genotyping of South American trypanosomes using fluorescent fragment length barcoding. *Infect. Genet. Evol.* **2011**, *11*, 44–51, doi:10.1016/j.meegid.2010.10.012.



9. Weatherly, D.B.; Boehlke, C.; Tarleton, R.L. Chromosome level assembly of the hybrid *Trypanosoma cruzi* genome. *BMC. Genomics*. **2009**, *10*, 255, doi:10.1186/1471-2164-10-255.
10. El-Sayed, N.M.; Myler, P.J.; Bartholomeu, D.C.; Nilsson, D.; Aggarwal, G.; Tran, A.N.; Ghedin, E.; Worthey, E.A.; Delcher, A.L.; Blandin, G.; et al. The genome sequence of *Trypanosoma cruzi*, etiologic agent of Chagas disease. *Science* **2005**, *309*, 409–415, doi:10.1126/science.1112631.