

***Combining Structural Modeling,
Evolutionary Information,
and Machine Learning
to Improve Prediction of
Nucleic Acid Binding Sites
in Telomerase***

By
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Importance Of Telomerase

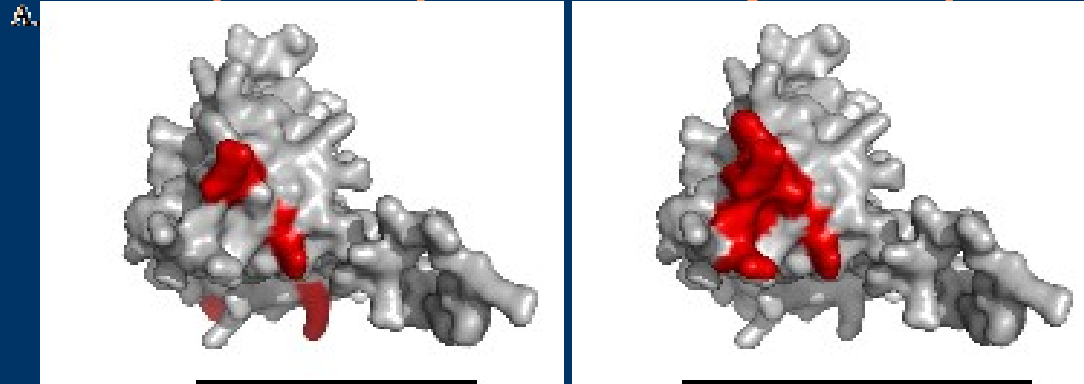
- “Telomerase is a ribonucleoprotein enzyme that adds telomeric DNA repeat sequences to the ends of linear chromosomes.”
 - “The enzyme plays pivotal roles in cellular senescence and aging”
 - “It provides a telomere maintenance mechanism for ~90% of human cancers, so it is a promising target for cancer therapy”
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Procedure

- Interface residue prediction
 - RNABindr and DNABindr were used
 - Both are Naïve Bayes classifiers
 - Sequence based
- Structure prediction
 - N terminal from human telomerase predicted by threading, using the FUGUE server.

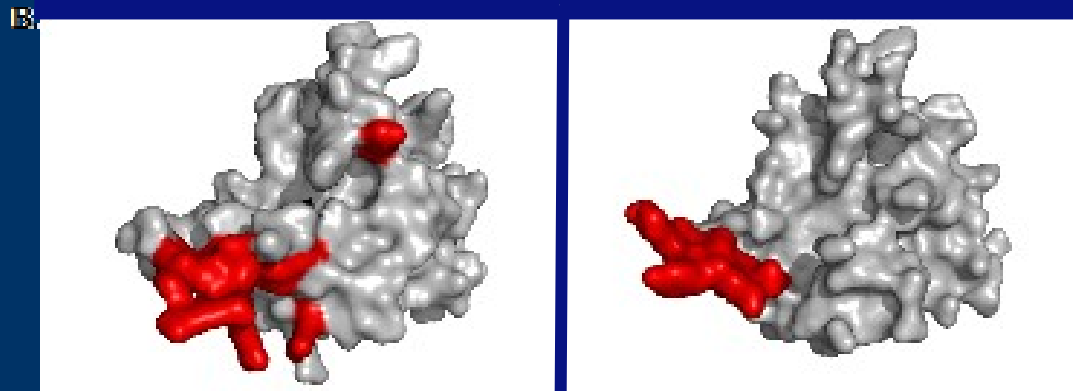
Results:

*RNA binding residues in TEN domains:
Human(Model) vs Tetrahymena(PDB)*



human TEN
predicted

human TEN
verified

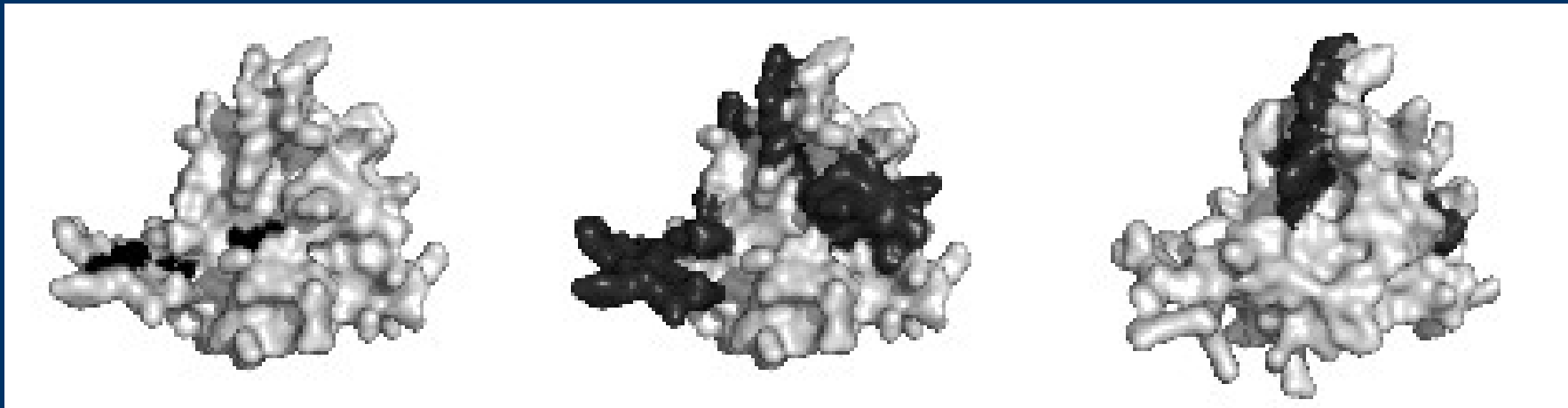


human TEN
predicted

Tetrahymena TEN
verified

Results:

*DNA binding residues in TEN domains:
Human(Model) vs Tetrahymena(PDB)*



Tetrahymena
verified

Tetrahymena
predicted

human
verified

Caragea, Lee, Hamilton, Gleeson, unpublished

Future Research:

- Use the information that we have from the predicted structure to improve the interface residue predictions
 - Predict using PSSMs based on structure and an SVM
 - Use structure of the RNA binding domain that was recently published.
 - Structure of the RNA-Binding Domain of Telomerase: Implications for RNA Recognition and Binding – Susan Rouda and Emmanuel Skordalakes
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