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

By Deepak Reyon and Ben Lewis
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”
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)

Lee, Hamilton, Gleeson, unpublished
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Caragea, Lee, Hamilton, Gleeson, unpublished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