COMPUTATIONAL STUDY OF TARGETS IN LUNG ADENOCARCINOMA

Avanti Moghe

Advisor: Dr. Kevin Crowthers

Introduction

Lung Adenocarcinoma (LUAD):

- a malignant tumor which originates in the peripheral regions of the lungs (Lu et al., 2025).
- a subtype of non-small cell lung cancer

Computation modeling:

- a type of technological tool used to study genomes, proteins, and other biological processes.
- Homology methods, in-silico methods, and MD simulations are different methods for the analysis of biological processes (Khan et al. 2016)

Research Question

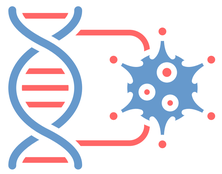
How do the KRAS G12C and EGFR L858R mutations alter the protein's structural and regulatory regions in lung adenocarcinoma, and what implications do these changes have for its oncogenic activity and mutation-specific drug targeting?

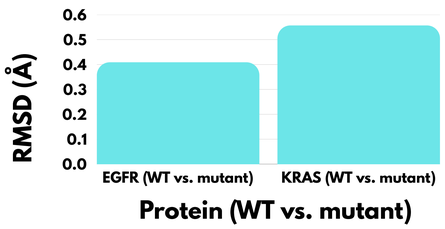
Hypothesis

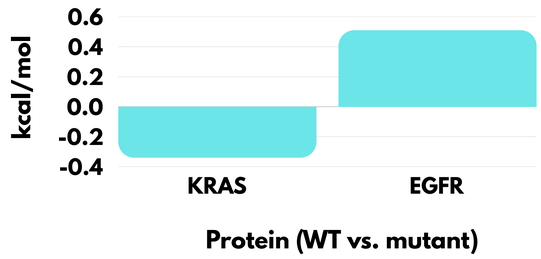
The G12C and L858R cause local structural changes within the protein which affects the drug binding affinity and capabilities of the given mutated protein.

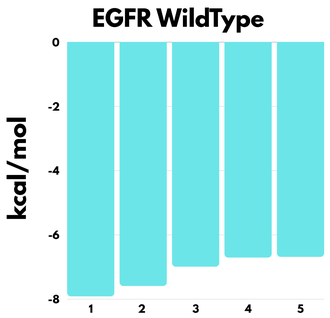
Methodology

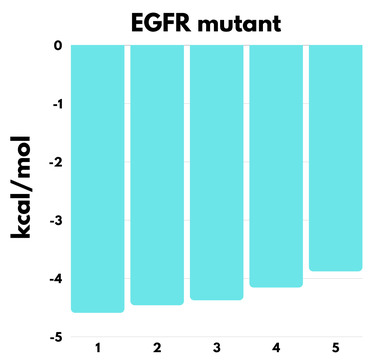
1. Use cBioPortal and COSMIC database to identify most common mutations within the protein which contributes to LUAD.
2. Observing and Analyzing Wildtype vs Mutant Proteins. How do mutatins change the protein and its functions.
3. Analyze drug binding affinities of both mutated proteins and how do they compare to each other.

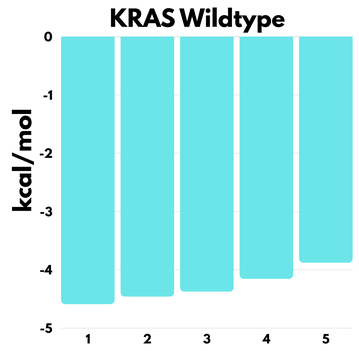


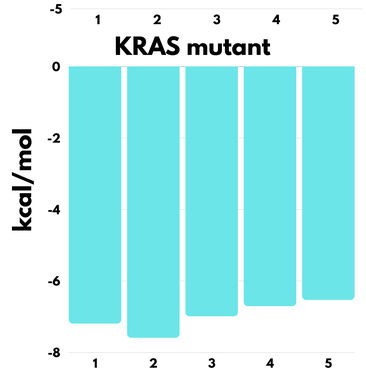












Results

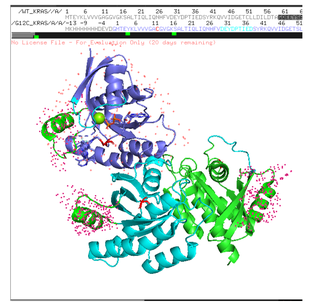
- Chosen common mutations of G12C for the KRAS protein and L858R for the EGFR protein.
- Comparison of wildtype vs mutated proteins gave changes caused by the protein, as well as structural show low RMSD score
- Drug binding scores for wildtype vs mutant.

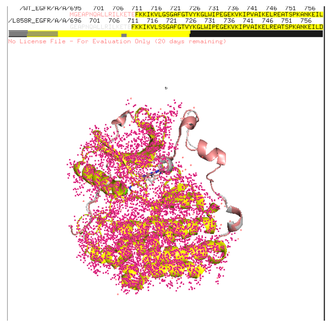
Analysis

- Common hotspot mutations such as G12C and L858R induce local structural changes which affect the function o the protein.
- Low RMSD values indicated limited structual changes and that the mutated protein is similar in form to the original protein
- Drug beinding scores indicate the way the protein reacts to the drug and whether the drug is therapeutically effective.

Future Implications and Direction

- Mutations can significantly alter drug binding, highlighting the need for precision medicine.
- Computational docking provides a rapid, cost-effective way to predict mutation-specific drug effectiveness.
- Supports further experimental validation or molecular dynamics simulations.





Key Sources & Acknowledgements