CALIFORNIA STATE SCIENCE FAIR
2015 PROJECT SUMMARY

Name(s)

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Project Number

35287

Project Title

Effective Targeted Therapy for Non-Small Cell Lung Cancer using EGFR Tyrosine Kinase Inhibitors Based on the Mutation ty

Abstract

Objectives/Goals

To enhance the treatment of patients with Non-small cell lung cancer (NSCLC) by finding out how and why individuals respond differently to varying inhibitors based on their mutation type and location in the EGFR tyrosine kinase domain, and generate a more effective way to prescribe medications to patients in order to present them with the best treatment plan possible. To study the differences between each mutation, and each tyrosine kinase inhibitor (TKI). Find the molecular formula and other information about each inhibitor. Find amino acid, nucleotide, and property changes for each mutation.

Methods/Materials

Data was collected and analyzed from many data warehouses, and studies. BioMart, and I-TASSER were used to sort the mutations by type and location, and to study the baseline EGFR domains/exons in depth. A program was written in R to compute the mean values of response for various TKIs.

Results

The two most common mutations, L858R and exon 19-deletions account for 90% of EGFR mutated NSCLC. Based on the analysis, it was concluded that for patients with an exon 19-deletion or L858R mutations the best treatment option is erlotinib with 73% average response rate. Another important mutation is T790M-mutation, which is also known as an acquired mutation because it appears in more than 50% of patients after they get treated with certain TKIs. The T790M-mutation behaves differently from most mutations, the amino acid threonine is replaced by methionine, which affects the binding capability of many TKIs. However, AZD9291 and CO-1686 have irreversible binding capabilities, and hence prove to be the best treatment options for T790M-mutations, with average response rates of 64% and 58% respectively.

Conclusions/Discussion

It was concluded that if cancer patients with EGFR tyrosine kinase mutations were treated with EGFR TKIs based on the mutation pattern then EGFR TKIs will be more effective. This is because each mutation is caused by an amino acid change, changing one or more properties of the protein being made. Each property change results in a different chemical structure change of some part of the protein. Each drug has a specific chemical structure, and because of this, they will bind differently to the EGFR protein, either successfully inhibiting the EGFR or not. This means that patients with a NSCLC EGFR tyrosine kinase mutation will have a clear plan on how to continue their treatment.

Summary Statement

Finding optimal treatment for non-small cell lung cancer patients based on their mutation type and location.

Help Received

Professor Gazdar and Wakelee answered a few questions I had on this topic.