Investigating the Effects of Mutations of Crucial Amino Acids on the Protein Expression and Folding of CDK2 Cancer Gene

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Each year, twenty million people are diagnosed with cancer. Its prevalence is increasing at a faster pace than any other disease. Cyclin-Dependent Kinase 2 (CDK2) plays a key role in regulating the cell cycle. Overexpression of CDK2 causes dysregulation of the cell cycle, resulting in uncontrolled cell growth. There are two approaches to address CDK2 overexpression: one option entails creating mutations in the CDK2 gene that immobilizes its functionality, essentially trapping the cell in a G0 phase. The alternative option is to use CDK2 inhibitors that neutralize its activity. The objective of this study was to create mutations in CDK2 gene's crucial amino acids and measure their effects on protein production. Seven strategic mutations were selected in two essential regions: Glycine-Rich Loop and Activation Loop. Mutations were created using gradient PCR, a method that optimizes yield by adjusting annealing temperatures. These products were sent for Sanger Sequencing. The protein content was measured for each mutant at 280 nm. Mutation E12R inhibited CDK2 gene expression by 80% compared to wild type, while mutation T160E-E162T showed 95% inhibition. Mutation T160L exhibited protein expression levels similar to wild type, whereas mutation T160E resulted in a four-fold increase in CDK2 protein content. The results show that mutations E12R and T160E-E162T were most effective at suppressing CDK2 activity, potentially inhibiting cancer. However, mutation T160E would likely increase CDK2 activity, leading to an increased risk of cancer. These findings highlight the importance of crucial amino acids in CDK2 expression and its impact on disease progression.

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