

**ROLE OF WILD TYPE PHENYLALANINE HYDROXYLASE AND THE EFFECT OF
MUTATION ON PROTEIN STRUCTURE AND FUNCTION**

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ABSTRACT

Bioinformatics is a widely used computational technique includes the sequence, structural alignment, database mining, gene finding and prediction of protein structure and function. Bioinformatics tool can be used to aid sequencing, analyse genome, observed genome mutation and also analyse and predict the structure of DNA, RNA and protein. The aims of this study were to compare and visualize the structure of wild type phenylalanine hydroxylase (PAH) with mutated PAH and to study the biological effect of mutated PAH structure to human. BLAST nucleotide was used to find the healthy human DNA sequence of PAH. We compared the mutated and healthy phenylalanine hydroxylase sequences and we found there were several point mutations. Next, open reading frame (ORF) finder was used to find the translated mutated human PAH protein sequence. RasMol visualization software was used to visualize and compare the translated protein structure of healthy and mutated PAH. Based on the visualized structure, it shows the red loop of the healthy human PAH was longer than the mutated. This mutated human PAH structure will affect the protein instability and malfunctioning of the PAH protein structure. In addition, the mutated structure of human PAH protein will cause reduce body size, altered serum urine phenylalanine levels and lead to Phenylketonuria (PKU) disease.

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CHAPTER ONE

INTRODUCTION

1.1 RESEARCH BACKGROUND

Bioinformatics is important in biological area and use the techniques and concept from informatics, statistic, computer science, physics, applied math and engineering. Bioinformatics widely used in computational technique which including the sequence, structural alignment, database mining, gene finding and prediction of protein structure and function (Luscombe, Greenbaum, & Gerstein, 2001). Bioinformatics tool can be used to aid sequencing, analyse genome and observed the genome mutation. Meanwhile, in structural biology, bioinformatics is used to analyse and predict the structure of DNA, RNA and protein. We can use bioinformatics tools such as BLAST to compare and analyse the sequences of data protein to know and comprises the biological of DNA sequences match.

PAH gene provides instruction for making an enzyme called phenylalanine hydroxylase. This PAH mainly expressed in human liver and kidneys. This wild type phenylalanine hydroxylase (PAH) enzyme will convert phenylalanine to amino acid tyrosine. Based on Figure 1.1, the PAH gene is located on the long (q) arm of chromosome 12 between the positions 22 and 24.2 and base pairs of molecular location on chromosome 12 are 102, 838, 321 to 102, 917,603.

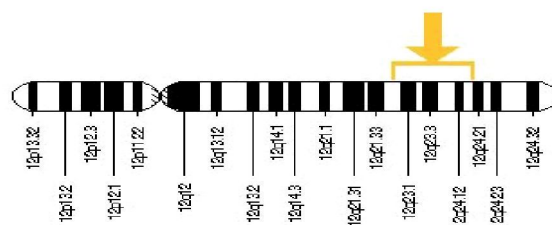


Figure 1.1: Location of PAH gene of human in chromosome 12 (Genetics Home Reference, 2008)