Molecular analysis of phenylalanine hydroxylase (PAH) gene from dried blood spots from Libyan phenylketonuria patients

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Phenylketonuria (PKU) is an autosomal recessive inborn error of metabolism due to deficiency in the phenylalanine hydroxylase gene (PAH). This study describes the distribution of PAH mutations in nine probands from Libya with the diagnosis of phenylketonuria and hyperphenylalaninemia. Molecular genetics screening was done at the Shafallah Medical Genetics Center laboratory by resequencing and analysis of the entire coding sequences, exon flanking regions and splice sites of PAH. Genomic DNA was isolated from dry blood spots (n=9) by organic extraction technique and purified using centrifugal column filter device. The 13 exons, exon-intron boundaries and splice sites of the PAH were amplified by polymerase chain reaction using in-house designed primers and optimized conditions. The DNA sequencing reactions were carried out by automated sequencer using BigDye Terminator chemistry.

Two homologous PAH mutations were found in 7/9 probands and were c.838G>A/p. E280K (missense) and c.1055delG (frame shift). The frame shift mutation produces a truncated protein of 399 amino acid length. Two Probands were homozygous for the missense mutation, three were homozygous for the frame shift mutation and two were compound heterozygous for both mutations. This initial study should be followed by an analysis of phenotype – genotype correlation pattern to better understand the disease process.