

THE SPECTRUM OF MUTATION IN PAH GENE AMONG KAZAKHS WITH PHENYLKETONURIA

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Introduction: Phenylketonuria (PKU) is inborn amino acid error etiologic factor is mutation in phenylalanine hydroxylase gene (PAH gene). It described over 500 mutations in PAH gene. The frequency and spectrum of mutations have ethnic characteristics.

Methods: We studied DNA of 34 Kazakh patients with PKU from unrelated families. DNA was isolated with salt standard method. At first we make molecular genetic study of most frequent mutations in PAH gene (R158Q, R252W, R261Q, R408W, P281L, IVS14+5G>T, IVS10-11G>A and IVS12+1G>A) by PCR. If mutations were unidentified, we searched more rare mutations in PAH gene by direct automated sequencing.

Results: The informative value of kit for 8 common mutations in PAH gene for Kazakhs was 35.2%. After automatic direct sequencing, we obtained following range of mutations in Kazakhs: R243Q (0.265), R408W (0.147), P281L (0.088), IVS4+5G>T (0.044), IVS10-11G>A (0.029), V230I (0.029), IVS12+1G>A (0.029), A300S, W187X, I65N, R243L, R158Q, IVS2+5G>A, Y387H, IVS10-14C>G, V399=, c.326e>G by 0.015. The frequency of unidentified mutations after automatic direct sequencing decreased from 0,648 to 0.221. Most common mutations in PAH gene by type were missense (60.3%), then splice (11.8%) and nonsense (1.5%). Most mutations in PAH gene were located in E7 region (36.8%), than E12 (14.7%), I10 and I4 (4.4%), E3, E6 and I12 (2.9%), E5, E8 and E11 by 1.5%.

Conclusion: We established a preliminary range of mutations in PAH gene in Kazakhs patients with PKU in Kazakhstan. Using the kit for 8 common mutations in PAH gene for Kazakhs is not informative, because these mutations are more common in European populations that depends on with ethnic characteristics of the spectrum of mutations. We analyzed the types and locations of mutations in PAH gene in Kazakhs. Ethnic features must consider for choosing a panel of mutations, for sequencing of the most significant regions of PAH gene and molecular genetic diagnosis of PKU patients and their families, including direct and indirect prenatal diagnosis of PKU.