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DNA-microarray as an alternative diagnostic tool for targeted genetic carrier screening in population of Yakut ethnic group

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Motivation and Aim: There are populations that have kept apart for many centuries, show less genetic variability and they differ in their genetic structure from representatives of other groups – genetic isolates. One of its representative is the population of Yakut ethnic group that demonstrate a high prevalence of rare autosomal recessive disorders due to the founder effect [1]. We evaluated the heterozygous carrier frequencies of five monogenic disorders enriched in the population among healthy individuals using own developed low density DNA-microarray. The results were verified by genotyping using real-time PCR and PCR-RLFP assays. Testing using DNA-microarray showed 99 % sensitivity and 100 % specificity. *Methods and Algorithms*: Oligonucleotide probes addressing point mutations 4582_4583insT in CUL7, c.5741G > A in NBAS, c.806C > T in DIA1 c.1090G > C in FAH., c.-23+1G > A in GJB2 causing 3-M syndrome, SOPH-syndrome, Methaemoglobinaemia type 1, Tyrosinemia type 1, Nonsyndromic hearing loss and deafness (DFNB1) type 1A respectively and wild type probes were printed unto epoxy coated glass slide by non-contact manner using A Perkin Elmer Piezzorray (Perkin Elmer) microarrayer. The assay using developed microarray chip based on reverse hybridization which include two step multiplex PCR with production of one-stranded Cy5 labeled-PCR products following its hybridization with oligonucleotide probes [2]. *Results*: We developed population specific low-density microarray and performed genotyping of 120 healthy individuals for major mutations causing 3-M syndrome, SOPH-syndrome, Methaemoglobinaemia type 1, Nonsyndromic hearing loss and deafness (DFNB1) type 1A, Tyrosinemia type 1. The results of genotyping demonstrate a high frequency of all five genetic disorders tested and were: 3-M syndrome – 1:25, SOPH-syndrome – 1:50, Methaemoglobinaemia type 1 – 1:25, DFNB1 – 1:11, Tyrosinemia type 1 – 1:100.
Conclusion: Obtained results of high level of carrier frequencies of above genetic diseases indicates a high need of its prevention through implementation of carrier screening programs in population. The developed population specific low density oligonucleotide microarray can be considered as an alternative highly specific low-cost tool for heterozygous carrier screening and genetic diagnostics in Republic of Sakha (Yakutia). In addition, it can easily be modified to accommodate additional mutations.
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