A novel StripAssay for the detection of cystic fibrosis mutations in the Turkish population

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Cystic fibrosis (CF) is among the most common life-threatening autosomal recessive disorders, with an estimated incidence of approximately 1 in 3500–4000 live births in Caucasians. The disease is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Worldwide, the most frequent mutation F508del accounts for 18–87% of CF chromosomes depending upon ethnicity. This mutation decreases along a northwest to southeast gradient, and shows a frequency of only around 25% in the Turkish population. In general, a very high heterogeneity in pathogenic CFTR mutations has been reported in Turkish patients.

We have developed a reverse-hybridization assay for the rapid and simultaneous analysis of 24 CFTR mutations, as well as the IVS8 polyT (5T/7T/9T) variants. The CF StripAssay TUR shows a coverage of around 60% of mutations found in the Turkish population, which is more than any other commercial CF test currently available. The assay is based on multiplex DNA amplification and hybridization to teststrips consisting of allele-specific oligonucleotide probes for each mutant and wild-type allele. The procedure is rapid, simple and convenient, accessible to automation and requires very small amounts of samples, which is of particular importance for prenatal diagnosis and newborn screening.

Detection of the mutation D1152H in the CFTR gene in University Hospital Brno, Czech Republic

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For the DNA analysis of CFTR gene we use since autumn 2009 (the beginning of newborn screening of cystic fibrosis (CF) in CR) the kit Elucigene, which allows the detection of 32 or 50 mutations of CFTR gene including the mutation D1152H. Newborns numbered 84 485 were born and looked through for CF in the Moravian part of the Czech Republic in two years period (1.12.2009 to 31.12.2011). The mutation D1152H in CFTR gene was the second most frequent CF mutation we detected in newborns.

The DNA analysis of CFTR gene was performed in 953 newborns and we found 7 alleles with the mutation D1152H in CFTR gene – 6 healthy heterozygotes and one compound heterozygote with CFTR genotype: [N1303K] + [D1152H] without clinical manifestations of cystic fibrosis and with the normal value of chloride in sweat in newborn age.

The phenotype associated with mutation D1152H with another CFTR mutation in the trans position, there are only a very limited knowledge (phenotypic characteristics: chronic sinopulmonary disease, bronchiectasis – about 70%, Pseudomonas colonisation – less than 30%, the majority are pancreatic sufficient, the disease is diagnosed on average at the age of 30 years.

Our adult patients with CFTR genotype: [F508del] + [D1152H] corresponds to these phenotype, the diagnosis of CF was established in 2011.

In male carriers of the CFTR mutation D1152H we confirmed an origin by determining the Y-chromosome haplogroup, a group of Y-chromosomes related by descent from a set of STR markers PowerPlex® Y. We analysed 7 male individuals and identified two Y-chromosome haplogroups both descendent from West Europe in D1152H carriers and an individual with Jewish descent.