Scripta Scientifica Medica, vol. 34 (2002), pp 77-78

MOLECULAR GENETIC TESTS – A BASIC APPROACH FOR INVESTIGATING THE GENOME OF THE POPULATION

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ABSTRACT

Fundamental importance of molecular genetic tests in solving clinical problems is outlined. Relations between genetic counseling and laboratory for molecular pathology in putting molecular genetic tests into practice are focused. Authors look at the possibilities for immediate application of DNA analysis according to the degree of exploration of different genes, determining monogenic diseases. Attention is paid to the methods for direct and indirect DNA analysis used postnatally and prenatally both for diagnosis and prevention. Definition of 'informative' risk family is given, being an object for indirect methods of DNA analysis. Molecular genetic tests are shown as basis for research, genetic investigations of the populations and the diseases spread in them and for creating and applying mass and selective diagnostic and preventing screening programs that aim at ameliorating the human genome and decreasing the number of patients with socially significant hereditary diseases.

Key words: molecular genetic tests, DNA analysis, human genome, medical genetic counseling, Varna

Molecular genetic tests have fundamental importance for investigating human genome and are widely applied in solving problems in clinical practice (1,2,5). Their popularization is worth and perspective and this is the aim of the present paper. Nowadays, in Bulgaria molecular genetic tests are performed in the Laboratory for Molecular Pathology in Sofia. Patients who need molecular genetic testing are counseled and evaluated by the geneticists working in the genetic counseling and referred to the Laboratory.

At presence, scientific knowledge gives the chance DNA analysis to be done in the patients with some monogenic diseases presenting with typical clinical symptoms. These are the cases when the pathologic gene is charted, cloned and its heterogeneity is well investigated, for instance the CF gene (5). In other entities, like xxxxx DNA testing is possible only in families with more relatives presenting with the disease. When the pathologic gene is charted, but not well studied or gene coping exists, genetic material could be preserved in DNA bank (1,6) for the time when DNA testing becomes possible, as it happens with patients with Strumpel spastic paraparesis.

In the patients with a certain monogenic disease DNA analysis could be performed and gene status easily determined in cases where the allelic variants in the population are few or one or couple are most common. When there is a variety of the pathologic alleles and the frequency of each of them is very low, as it is with the haemophilic gene (5), finding the mutation/s/ in every concrete patient is a difficult task and sometimes it takes years to determine it. In the groups of entities with mutual coping of the phenotype caused by mutations in different gene loci, as, e. g., the sensory motor polyneuropathies (1,3,4,6,7), DNA testing is very complicated. In these cases the alleles of the best known gene are specified and this is usually the gene causing the most common disease in the group. Genotype-phenotype correlation in the rest of the clinical forms often remains important scientific and practical problem.

There are two approaches in performing DNA analysis. The first one is direct - mutation detection with the help of known DNA probes, and the second one is indirect - by following-up polymorphic DNA markers (1,5). The indirect analysis can be applied only to some families called 'informative'. In the informative families each of the parents' chromosomes could be exactly identified for its DNA structure in certain regions. These are the polymorphic markers, which are neutral mutations, i. e. not expressed in the phenotype. In the families that are not informative it is not possible to identify the chromosomes with the disease-causing mutation. The indirect DNA analysis is quite valuable for practical cases, but possible wrong interpretations must be minded being a result of crossing over, which has not changed markers' characteristics used for the analysis. This risk is very actual for the huge genes like that of Duchene muscular dystrophy, but also exists when poly-

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morphic parts in a group of small neighbouring genes are used as markers, e. g., in β-thalassemia.

Molecular genetic tests are used for postnatal and prenatal analysis (1) that increases their significance for diagnostics and prevention and sometimes for the treatment of the hereditary diseases. Molecular genetic research data give view to the allelic variety of genes and the frequency of the different alleles in the population. They make their correlation with specific clinical phenotype evident. Thus, specifying the genotype of the patients, it could be possible to predict the degree of the clinical manifestation and prevent some of the complications. Prevention could be done even earlier through applying mass and selective screening programmes (1), aiming at decreasing the number of cases of socially significant hereditary diseases.

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