Mutation Spectrum of *CFTR* Gene in Cystic Fibrosis Patients with Meconium Ileuss

Gita Taurina [1], ***Linda Piekuse*** [1], ***Inga Kempa*** [1], ***Zita Krumina*** [2], ***Liene Kornejeva*** [2], ***Ieva Micule*** [2], ***Vija Svabe*** [3], ***Astrida Krumina*** [4]

[1] *Rīga Stradiņš University, Scientific Laboratory of Molecular Genetics, Latvia*
[2] *Children's Clinical University Hospital, Medical Genetics Clinic, Latvia*
[3] *Children's Clinical University Hospital, Department of Pulmonology and Allergology, Latvia*
[4] *Latvian Biomedical Research and Study Center*

Introduction. Cystic fibrosis (CF) is one of the most common severe autosomal recessive diseases in Latvia. Liver disease, meconium ileus (MI) and distal intestinal obstruction syndrome (DIOS) occur almost exclusively in patients carrying severe *CFTR* gene class I–II mutations on both alleles. These two classes are characterized by truncated CFTR protein or result in protein trafficking defects in the cell. However, there is no evidence of a phenotype relationship with specific gene mutations. From all cystic fibrosis patients, in 10–15% the first presentation is meconium ileus, therefore in 50–80% MI patients cystic fibrosis diagnose is confirmed.

Aim. The aim of the study is to determine the allelic frequencies of the *CFTR* gene mutation in cystic fibrosis patients with MI.

Material and methods. Between 1998–2013, 445 individuals with suspicion about cystic fibrosis were sent for *CFTR* gene mutation testing to RSU Scientific Laboratory of Molecular Genetics. 61 patients of these had clinically diagnosed cystic fibrosis. During the study 32 MI patients were analyzed for the 50 most frequent mutations in European descent cystic fibrosis patients. For 9 out of 32 MI patients cystic fibrosis were clinically diagnosed, among which 8 were confirmed by molecular testing.

Results. Of all patients with MI sent to laboratory, in 28.1% cystic fibrosis were molecularly diagnosed. From all clinically confirmed cystic fibrosis patients 14.8% had meconium ileus. In all cystic fibrosis patients with MI, except one, at least one *CFTR* gene chromosome had class I or class II mutation (CM). One patient had a compound heterozygous of class I and class IV mutations. In 38.9% of cystic fibrosis chromosomes were dF508 mutation (II CM), 22.2% had dele2.3 mutation (I CM), each of P67L (IV CM), W1282X (I CM), R553X (I CM) and 621+1G>T (I CM) mutations were in 5.6%. Three chromosomes were unidentified forming 16.7% of all *CFTR* chromosomes in MI patients.

Conclusions. Patients presenting meconium ileus should be tested for *CFTR* gene mutations. In Latvia, the most common mutations in CF patients are dF508 and dele2.3 mutations.

IV