Abstract

Niemann-Pick disease type C (NPC) is a rare, severe disease with autosomal recessive inheritance. Disease is caused by pathogenic mutations located in genes *NPC1/NPC2*. These genes encode lysosomal non enzymatic NPC1/NPC2 proteins that are part of lipid transport. As a result of malfunction of these proteins intracellular accumulation of lipids occurs, in particular free cholesterol and glycolipids.

Causal therapy is currently still unsatisfactory therefore new therapies are evolved. However these therapies depend on whether the patient cells contain at least residual amount of transcript *NPC1* gene.

In a group of patiens, for which a fibroblast culture was available, I analyzed the effect of pathogenic mutations on the expression level of the transcript. Results showed that for all pathogenic mutations transcript level is low, but detectable.

Moreover, I characterized the structure of the *NPC1* gene promoter. By sequence analysis I found polymorphisms rs8099071, rs28403610, rs2981422, rs1652354, rs1788774, rs1788772 in promoter. On the basis of the composition of polymorphisms in individual patiens, I estimate six different haplotypes.

I performed mutation analysis in DNA of recently diagnosed patient. I found only one pathogenic mutation p.I1061T (c.3182T> C) in the NPC1 gene. Therefore I tested genes *NPC1/NPC2* for the presence of extensive deletions/duplications using the MLPA method. However, even using this method, the second mutation was not detected.