

## **Application of genomic testing for patient diagnosis regarding Duchenne/Becker muscular dystrophy**

On 17/10/2012 a case was referred to our center with a family history of a male patient (32 years) possibly affected with Duchenne/Becker muscular dystrophy and where the patient's sister was pregnant in her first pregnancy, already in the 13<sup>th</sup> week. The purpose of genetic testing was to confirm the diagnosis of the type of muscular dystrophy in the affected brother through the detection of the pathogenic mutation, in order to then perform carrier testing in the pregnant sister (50% risk) and potential prenatal diagnosis in the embryo.

To the extent that: (a) the reported clinical symptoms of the patient were unable to exclude with certainty the diagnosis other types of muscular dystrophy, (b) initial genetic testing for deletions/duplications of the DMD gene (75-80% of mutations) was negative, and (c) because of the pregnancy, there was limited time for further genetic tests if the diagnosis of Duchenne/Becker muscular dystrophy was not confirmed through targeted testing of the DMD gene only, following genetic counseling it was decided to perform genomic analysis of ~370 genes associated with all known muscular dystrophies and neuromuscular disorders in the affected brother.

Genomic testing was completed in 8 weeks and revealed the presence of the novel c.531-24T> G mutation in intron 6 of the DMD gene, which had not been reported previously in the literature. Evaluation of this new mutation in the patient led to the finding that the mutation disrupted the proper expression of the gene, leading to relatively mild clinical symptoms of the disease. The inheritance of the mutation in the family quickly confirmed that the patient's mother was a carrier of the pathogenic mutation (as expected), the mutation was not present in the other healthy brother, but was however present in the pregnant sister (carrier).

Prenatal genetic testing at 22 weeks of pregnancy, which immediately followed on 17/12/2012 through amniotic fluid sampling, revealed that the male fetus had inherited the pathogenic mutation and was expected to be affected with the disease.

This case highlights the particular value of genomic analysis for neuromuscular diseases, since in this specific case, within eight weeks and during pregnancy, this type of analysis provided full coverage for almost all known types of muscular dystrophy, and revealed the genetic cause of the disease, preventing the birth of an affected child. It is worth mentioning that a few months later the mother was in her second pregnancy, again with a male fetus, and this time it was found that it did not harbor the pathogenic mutation, leading to the birth of an apparently healthy child.