Phase 1. DECEMBER 2019

Malformations of cerebral cortical development (MCD) are one of the main etiology for epilepsy and developmental delay disorders. Among MCD, heterotopias are a group of genetic heterogeneous entities. The wide range of reported defects, from microdeletions and microduplications to point mutations, requires a panel of genetic technologies capable of detecting both genomic imbalances and sequence variations.

Phase 1 objectives

- Heterotopia patients study group and biological samples collection set up
- Experimental protocol optimization for mutational screening by direct sequencing
- Chromosomal microarray investigation protocol set up

Methods and results

This phase included activities of collection of data and biological samples from heterotopia patients as well as set up and optimization of molecular testing based on chromosomal microarray and sequencing. The samples of probands and their parents (peripheral blood) were processed and used for DNA isolation. Sanger sequencing protocol for *FLNA* and *DCX* genes analysis was optimized and set up using the Applied Biosystems ABI 3500 Genetic Analyzer system. The genomic screening for DNA copy number variations was started using array-based comparative genomic hybridization technique (array-CGH, Agilent SureScan platform). The first genomic profiles were generated on high density oligonucleotide microarray slides OGT 4x180K, and evaluated for copy number imbalances.

Conclusions

The objectives of this phase were completely achieved.

- A database of heterotopia patients was set up and data recorded.
- Uniform procedures for sample processing and DNA extraction were established and the collection of nucleic acids samples was set up.
- Sanger sequencing technique for *FLNA* and *DCX* genes was optimized and the experimental protocol was established for the project next phases.

- The experimental protocol was set up and the genomic screening activity started using array-CGH technique.
- The results were communicated in different scientific meetings in the field of genetics and neuropsychiatry (Medical Genetics Conference, Timisoara and National Conference of Romanian Association of Fight Against Epilepsy, Bucuresti).