NEXT GENERATION SEQUENCING OF CHROMOSOME 9 LOCUS IN FTD-ALS PEDIGREE FROM THE NETHERLANDS

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Introduction: Frontotemporal lobar degeneration (FTLD) is the second most common form of presenile dementia after Alzheimer’s disease (AD), representing ~5% of all dementia cases and as much as 10-20% of presenile dementia. It is a heterogeneous disorder that can co-occur with amyotrophic lateral sclerosis (ALS), giving place FTD-ALS. Although this disease is highly heritable a genetic cause is yet to be identified in the majority of cases. A large number of linkage studies have linked this disorder to chromosome 9.

Aim: To identify the genetic lesion causing FTD-ALS in 6 families from the Netherlands.

Methods: Parametric linkage analysis was conducted using MERLIN considering an autosomal dominant mode of inheritance. The prevalence of the disease in the general population was set to 0.00001 and the penetrance ranged from 0.1 to 0.9 depending on the age.

After linkage analysis, all exons and exon-intron boundaries (50bp), 5´ UTRs (+ 650 bp upstream), 3´UTRs, sno/miRNA and conserved regions in the linked region in chromosome 9 were sequenced using Agilent’s SureSelect Target Enrichment Kit for Illumina Paired-End Multiplex Sequencing.

Results: Parametric linkage analysis linked FTD-ALS to a 61Mb region in chromosome 9 in one of the tested pedigrees (highest LOD score = 3.53). Next generation sequencing of the regions of interest in chromosome 9 is undergoing.