Genome studies in Hereditary Spastic Paraplegia

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The various forms of Hereditary Spastic Paraplegia (HSP) comprise a genetically heterogeneous set of neurological disorders. Currently ~20 different HSP genes have been identified yet these explain only 50-60% of the genetic effect, at best. Traditional methods of gene identification require linkage analysis of large families, but face increasing difficulties to identify such extended pedigrees for rare HSP forms. Significantly, new technology and innovative strategies promise to revolutionize gene identification in Mendelian disease and take advantage of relatively small pedigrees. We are presenting data that support the applicability of so-called exome sequencing as an effective tool in gene identification in highly penetrant phenotypes such as HSP. We further introduce a new study that aims to identify HSP genes in small autosomal dominant families with HSP. A collaborative effort within the HSP scientific community should allow building a comprehensive genome variation database that will improve the genetic understanding of the disease and help ultimately to define specific pathways.