Copy number aberrations in hereditary spastic paraplegia

C. Beetz[1], P. Byrne[2], C. Depienne[3], E. Reid[4], L. Schöls[5], A. Nygren[6], J. Schickel[1], T. Deufel[1]

[1]Uniklinikum Jena, Germany; [2]University of Dublin, Ireland; [3]INSERM Paris, France; [4]Adenbrooke's Hospital Cambridge, UK; [5]Uniklinikum Tübingen, Germany (for GeNeMove); [6]MRC-Holland, The Netherlands

Despite *SPG4* (*SPAST* gene, spastin protein) being the major hereditary spastic paraplegia (HSP) locus, there is large heterogeneity underlying the remaining ~60% of cases. We have previously shown for *SPG4* that, besides the long recognised "small" mutations, large genomic deletions represent an additional and surprisingly frequent class of disease-causing alterations. We subsequently widened pertinent analyses to (i) investigate the very extend of *SPAST* deletions and (ii) screen for copy number aberrations in other HSP genes. In all cases investigated so far, deletion of *SPAST* exon 1 is accompanied by deletion of the promotor. Furthermore, we found evidence for this class of deletions to be associated with earlier disease onset than observed for other *SPAST* mutations. We also identified copy number aberrations in *SPG3A*, *SPG6*, *SPG7*, and *SPG31* amongst a large cohort of HSP patients. The implications of our findings will be discussed.