



The role of KIF1C in sustainable myelination in SPG58/SAX2

Amandine Duchesne, Khalid Hamid El Hachimi, Anne Vaiman, Magali Frah, Olivier Albaric, Alexis Brice, Frédéric Darios, Jean-Luc Vilotte, Giovanni Stevanin, Didier Boichard

► To cite this version:

Amandine Duchesne, Khalid Hamid El Hachimi, Anne Vaiman, Magali Frah, Olivier Albaric, et al.. The role of KIF1C in sustainable myelination in SPG58/SAX2. 19. International Congress of Neuropathology, Sep 2018, Tokyo, Japan. , 2018, ICN 2018. hal-02733860

HAL Id: hal-02733860

<https://hal.inrae.fr/hal-02733860v1>

Submitted on 2 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

P2-77

The role of KIF1C in sustainable myelination in SPG58/SAX2

Khalid El Hachimi, Anne Vaiman, Magali Frah, Olivier Albaric, Alexis Brice, Frederic Darios, Jean-Luc Vilotte, Giovanni Stevanin, Didier Boichard, Amandine Duchesne

EPHE/CNRS UMR 7225 - Inserm U 1127 - UPMC-P6 UMR S 1127 Institute of Brain and spinal cord, Paris

Hereditary spastic paraplegias (HSPs) are heterogeneous human neurodegenerative diseases. Mutations of genes encoding motor kinesins have been involved in various HSP isoforms. Mutations in KIF1C are responsible for autosomal recessive spastic paraplegia type 58 (SPG58/SAX2). Bovine progressive ataxia was first described in the Charolais breed in the early 1970s in England and further cases in this breed were subsequently reported worldwide. We can now report that progressive ataxia of Charolais cattle results from a homozygous single nucleotide polymorphism in the coding region of the KIF1C gene. In this study, we show that the mutation at the heterozygous state is associated with a better score for muscular development, explaining its balancing selection, and the resulting high frequency (13%) of the allele in the French Charolais breed. We demonstrate that the KIF1C bovine mutation leads to a functional knock-out, therefore mimicking mutations in humans affected by SPG58/SAX2. The functional consequences of KIF1C loss of function in cattle were also histologically evaluated. We showed that demyelinating plaques were due to altered oligodendrocyte membrane protrusion, and we highlight an abnormal accumulation of actin in the core of demyelinating plaques, which is normally concentrated at the leading edge of oligodendrocytes during axon wrapping. The lesions were associated with abnormal extension of paranodal sections. This model highlights the role of KIF1C protein in preserving the structural integrity and function of myelin, since the clinical signs and lesions arise in young-adult Charolais cattle. This model provides useful information for SPG58/SAX2 disease and other demyelinating lesions.