Distribution of the founder mutation in ATP13A2 gene causing Kufor-Rakeb syndrome (PARK9) in Greenland

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Kufor-Rakeb syndrome (KRS) is a rare autosomal recessive inherited juvenile parkinsonian syndrome caused by a frameshift mutation in exon 22 in ATP13A2 (c.2473C>AA, p.Leu825AsnfsX32) (1). Disease onset varied from 10 to 29 years of age, the latest reported for KRS, and were found in a family from Atammik (six persons) and a person from Upernavik/Illulisat. Symptoms at onset were asymmetric in three patients, and the clinical features were highly variable within a wide spectrum of an extrapyramidal-pyramidal syndrome with cognitive/psychiatric features in all patients. Ataxia was seen in two patients and electrophysiologically verified axonal neuropathy in one, features not previously related to KRS. Dopamine transporter scans showed symmetrical, severely reduced uptake in striatum in two patients. MRI was without atrophy in one patient despite disease duration of 17 years, and cerebral and cerebellar atrophy was seen in another patient after disease duration of four years. None of the eight heterozygous carriers from the family in Atammik have KRS symptoms, suggest that the mutant protein does not interfere and destroy the function of the wild-type ATP13A2 protein. In the present work we want to type about 1000 samples from 11 cities in Greenland to calculate the allel frequencies of this founder mutation. Primary studies show that the founder mutation is widely spread in Greenland. At the moment we have the following results of carriers: Aasiaat 0/102, Nuuk 3/60, Sisimiut 0/17, Tasiilaq 2/44, Maniitsoq 1/3, Upernavik 0/58. All the samples are anonymous tested and originating from filter paper from the screening of pregnant women for cholestasis familiaris groenlandica (CFG) and propionic acidemia (PCCB).

References