WHAT'S HAPPENING IN

Neurology® Genetics

Neurology.org/NG

Abstracts

Articles appearing in the June 2019 issue

Novel pathogenic *XK* mutations in McLeod syndrome and interaction between XK protein and chorein

Objective To identify *XK* pathologic mutations in 6 patients with suspected McLeod syndrome (MLS) and a possible interaction between the chorea-acanthocytosis (ChAc)- and MLS-responsible proteins: chorein and XK protein.

Methods Erythrocyte membrane proteins from patients with suspected MLS and patients with ChAc, ChAc mutant carriers, and normal controls were analyzed by XK and chorein immunoblotting. We performed mutation analysis and XK immunoblotting to molecularly diagnose the patients with suspected MLS. Lysates of cultured cells were coimmunoprecipitated with anti-XK and anti-chorein antibodies.

Results All suspected MLS cases were molecularly diagnosed with MLS, and novel mutations were identified. The average onset age was 46.8 ± 8 years, which was older than that of the patients with ChAc. The immunoblot analysis revealed remarkably reduced chorein immunoreactivity in all patients with MLS. The immunoprecipitation analysis indicated a direct or indirect chorein-XK interaction.

Conclusions In this study, *XK* pathogenic mutations were identified in all 6 MLS cases, including novel mutations. Chorein immunoreactions were significantly reduced in MLS erythrocyte membranes. In addition, we demonstrated a possible interaction between the chorein and XK protein via molecular analysis. The reduction in chorein expression is similar to that between Kell antigens and XK protein, although the chorein-XK interaction is a possibly noncovalent binding unlike the covalent Kell-XK complex. Our results suggest that reduced chorein levels following lack of XK protein are possibly associated with molecular pathogenesis in MLS.

NPub.org/NG/9303a

HTT haplogroups in Finnish patients with Huntington disease

Objective To study genetic causes of the low frequency of Huntington disease (HD) in the Finnish population, we determined *HTT* haplogroups in the population and patients with HD and analyzed intergenerational cytosine-adenosine-guanosine (CAG) stability.

Methods A national cohort of patients with HD was used to identify families with mutant *HTT* (*mHTT*). *HTT* haplogroups were determined in 225 archival samples from patients and from 292 population samples. CAG repeats were phased with *HTT* haplotypes using data from parent-offspring pairs and other *mHTT* carriers in the family.

Results The allele frequencies of *HTT* haplotypes in the Finnish population differed from those in 411 non-Finnish European subjects ($p < 0.00001$). The frequency of haplogroup A was lower than that in Europeans and haplogroup C was higher. Haplogroup A alleles were significantly more common in patients than in controls. Among patients with HD, haplotypes A1 and A2 were more frequent than among the controls ($p = 0.003$). The mean size of the CAG repeat change was +1.38 units in paternal transmissions being larger than that (−0.17) in maternal transmissions ($p = 0.008$). CAG repeats on haplogroup A increased by 3.18 CAG units in paternal transmissions, but only by 0.11 units in maternal transmissions ($p = 0.008$), whereas haplogroup C repeat lengths decreased in both paternal and maternal transmissions.

Conclusions The low frequency of HD in Finland is partly explained by the low frequency of the HD-associated haplogroup A in the Finnish population. There were remarkable differences in intergenerational CAG repeat dynamics that depended on *HTT* haplotype and parent sex.

NPub.org/NG/9303b

Most-Read Articles

As of April 30, 2019

***KCNQ2* encephalopathy: Features, mutational hot spots, and ezogabine treatment of 11 patients**

J.J. Millichap, K.L. Park, T. Tsuchida, et al. 2016;2:e96. doi.org/10.1212/NXG.0000000000000096

***CHCHD10* variant p.(Gly66Val) causes axonal Charcot-Marie-Tooth disease**

M. Auranen, E. Ylikallio, M. Shcherbii, et al. 2015;1:e1. doi.org/10.1212/NXG.0000000000000003

The Clinical Outcome Study for dysferlinopathy: An international multicenter study

E. Harris, C.L. Bladen, A. Mayhew, et al. 2016;2:e89. doi.org/10.1212/NXG.0000000000000089

Mendelian randomization shows a causal effect of low vitamin D on multiple sclerosis risk

B. Rhead, M. Bäärnhielm, M. Gianfrancesco, et al. 2016;2:e97. doi.org/10.1212/NXG.0000000000000097

A novel *DYNC1H1* mutation causing spinal muscular atrophy with lower extremity predominance

Q. Niu, X. Wang, M. Shi, Q. Jin. 2015;1:e20. doi.org/10.1212/NXG.0000000000000017

