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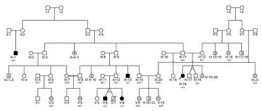
Abstracts

Articles appearing in the June 2018 issue

Chorea-acanthocytosis: Homozygous 1-kb deletion in *VPS13A* detected by whole-genome sequencing



Objective To determine a molecular diagnosis for a large multigenerational family of South Asian ancestry with seizures, hyperactivity, and episodes of tongue biting.

Methods Two affected individuals from the family were analyzed by whole-genome sequencing on the Illumina HiSeq X platform, and rare variants were prioritized for interpretation with respect to the phenotype.

Results A previously undescribed, 1-kb homozygous deletion was identified in both individuals sequenced, which spanned 2 exons of the *VPS13A* gene, and was found to segregate in other family members.

Conclusions *VPS13A* is associated with autosomal recessive chorea-acanthocytosis, a diagnosis consistent with the phenotype observed in this family. Whole-genome sequencing presents a comprehensive and agnostic approach for detecting diagnostic mutations in families with rare neurologic disorders.

NPub.org/NG/9104a

Determining the incidence of familiality in ALS: A study of temporal trends in Ireland from 1994 to 2016

Objective To assess temporal trends in familial amyotrophic lateral sclerosis (fALS) incidence rates in an Irish population and to determine factors influencing fALS ascertainment.

Methods Population-based data collected over 23 years, using the Irish amyotrophic lateral sclerosis (ALS) register and DNA biobank, were analyzed and age-standardized rates of fALS and associated familial neuropsychiatric endophenotypes were identified.

Results Between 1994 and 2016, 269 patients with a family history of ALS from 197 unique families were included on the register. Using stringent diagnostic criteria for fALS, the mean age-standardized fALS incidence rate for the study period was 11.1% (95% confidence interval [CI] 8.8–13.4). The fALS incidence rate increased steadily from 5.2% in 1994% to 19.1% in 2016, an annual increase of 0.7% (95% CI, 0.5–0.9, $p < 0.0001$). Inclusion of the presence of neuropsychiatric endophenotypes within kindreds increased the fALS incidence rate to 30%. The incidence of fALS in newly diagnosed individuals from known families increased significantly with time, accounting for 50% of all fALS diagnoses by 2016. The mean annual rate of recategorization from sporadic ALS to fALS was 3% (95% CI 2.6–3.8).

Conclusions The true population-based rate of fALS is at least 20%. Inclusion of extended endophenotypes within kindreds increases the rate of fALS to 30%. Cross-sectional analysis of clinic-based cohorts and stringent definitions of fALS underestimate the true rate of familial disease. This has implications for genetic counseling and in the recognition of presymptomatic stages of ALS.

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

***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

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

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

Complete callosal agenesis, pontocerebellar hypoplasia, and axonal neuropathy due to AMPD2 loss

A.P.L. Marsh, V. Lukic, K. Pope, et al. 2015;1:e16. doi.org/10.1212/NXG.0000000000000014