Abstracts

Articles appearing in the June 2018 issue

Neurodegeneration as the presenting symptom in 2 adults with xeroderma pigmentosum complementation group F

Objective To describe the features of 2 unrelated adults with xeroderma pigmentosum complementation group F (XP-F) ascertained in a neurology care setting.

Methods We report the clinical, imaging, molecular, and nucleotide excision repair (NER) capacity of 2 middle-aged women with progressive neurodegeneration ultimately diagnosed with XP-F.

Results Both patients presented with adult-onset progressive neurologic deterioration involving chorea, ataxia, hearing loss, cognitive deficits, profound brain atrophy, and a history of skin photosensitivity, skin freckling, or skin neoplasms. We identified compound heterozygous pathogenic mutations in *ERCC4* and confirmed deficient NER capacity in skin fibroblasts from both patients.

Conclusions These cases illustrate the role of NER dysfunction in neurodegeneration and how adult-onset neurodegeneration could be the major symptom bringing XP-F patients to clinical attention. XP-F should be considered by neurologists in the differential diagnosis of patients with adult-onset progressive neurodegeneration accompanied by global brain atrophy and a history of heightened sun sensitivity, excessive freckling, and skin malignancies.

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Rare variants and de novo variants in mesial temporal lobe epilepsy with hippocampal sclerosis

Objective We investigated the role of rare genetic variants and of de novo variants in the pathogenesis of mesial temporal lobe epilepsy related to hippocampal sclerosis (MTLE-HS).

Methods Whole-exome sequencing (WES) was performed in patients with MTLE-HS and their unaffected parents (trios). Genes or gene sets that were enriched with predicted damaging rare variants in the patients as compared to population controls were identified. Patients and their parents were compared to identify whether the variants were de novo or inherited.

Results After quality control, WES data from 47 patients (26 female), including 23 complete trios, were available for analysis. Compared with population controls, significant enrichment of rare variants was observed in *SEC24B*. Integration of gene set data describing neuronal functions and psychiatric disorders showed enrichment signal on fragile X mental retardation protein (FMRP) targets. Twenty-one de novo variants were identified, with many known to cause neuropsychiatric disorders. The FMRP-targeted genes also carried more de novo variants. Inherited compound heterozygous and homozygous variants were identified.

Conclusions The genetic architecture underlying MTLE-HS is complex. Multiple genes carrying de novo variants and rare variants among FMRP targets were identified, suggesting a pathogenic role. MTLE-HS and other neuropsychiatric disorders may have shared biology.

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M. Auranen, E. Ylikallio, M. Shcherbii, et al. 2015;1:e1. doi.org/10.1212/NXG.000000000000003

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Q. Niu, X. Wang, M. Shi, Q. Jin. 2015;1:e20. doi.org/10.1212/NXG.000000000000017

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.000000000000089

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A.P.L. Marsh, V. Lukic, K. Pope, et al. 2015;1:e16. doi.org/10.1212/NXG.000000000000014

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