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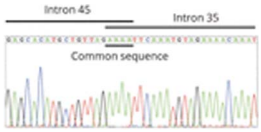
Abstracts

Articles appearing in the June 2019 issue

Novel pathogenic *VPS13A* gene mutations in Japanese patients with chorea-acanthocytosis



Objective To identify mutations in *vacuolar protein sorting 13A* (*VPS13A*) for Japanese patients with suspected chorea-acanthocytosis (ChAc).

Methods We performed a comprehensive mutation screen, including sequencing and copy number variation (CNV) analysis of the *VPS13A* gene, and chorein Western blotting of erythrocyte ghosts. As the results of the analysis, 17 patients were molecularly diagnosed with ChAc. In addition, we investigated the distribution of *VPS13A* gene mutations and clinical symptoms in a total of 39 molecularly diagnosed Japanese patients with ChAc, including 22 previously reported cases.

Results We identified 11 novel pathogenic mutations, including 1 novel CNV. Excluding 5 patients with the unknown symptoms, 97.1% of patients displayed various neuropsychiatric symptoms or forms of cognitive dysfunction during the course of disease. The patients carrying the 2 major mutations representing over half of the mutations, exon 60–61 deletion and exon 37 c.4411C > T (R1471X), were localized in western Japan.

Conclusions We identified 13 different mutations in *VPS13A*, including 11 novel mutations, and verified the clinical manifestations in 39 Japanese patients with ChAc.

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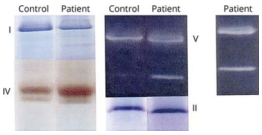
Hybrid gel electrophoresis using skin fibroblasts to aid in diagnosing mitochondrial disease



Objective We developed a novel, hybrid method combining both blue-native (BN-PAGE) and clear-native (CN-PAGE) polyacrylamide gel electrophoresis, termed BCN-PAGE, to perform in-gel activity stains on the mitochondrial electron transport chain (ETC) complexes in skin fibroblasts.

Methods Four patients aged 46–65 years were seen in the Metabolic Clinic at Alberta Children's Hospital and investigated for mitochondrial disease and had BN-PAGE or CN-PAGE on skeletal muscle that showed incomplete assembly of complex V (CV) in each patient. Long-range PCR performed on muscle-extracted DNA identified 4 unique mitochondrial DNA (mtDNA) deletions spanning the *ATP6* gene of CV. We developed a BCN-PAGE method in skin fibroblasts taken from the patients at the same time and compared the findings with those in skeletal muscle.

Results In all 4 cases, BCN-PAGE in skin fibroblasts confirmed the abnormal CV activity found from muscle biopsy, suggesting that the mtDNA deletions involving *ATP6* were most likely germline mutations that are associated with a clinical phenotype of mitochondrial disease.

Conclusions The BCN-PAGE method in skin fibroblasts has a potential to be a less-invasive tool compared with muscle biopsy to screen patients for abnormalities in CV and other mitochondrial ETC complexes.

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

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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