Abstracts

Articles appearing in the June 2018 issue

Somatic GNAQ mutation in the *forme fruste* of Sturge-Weber syndrome

Objective To determine whether the GNAQ R183Q mutation is present in the *forme fruste* cases of Sturge-Weber syndrome (SWS) to establish a definitive molecular diagnosis.

Methods We used sensitive droplet digital PCR (ddPCR) to detect and quantify the GNAQ mutation in tissues from epilepsy surgery in 4 patients with leptomeningeal angiomas; none had ocular or cutaneous manifestations.

Results Low levels of the GNAQ mutation were detected in the brain tissue of all 4 cases—ranging from 0.42% to 7.1% frequency—but not in blood-derived DNA. Molecular evaluation confirmed the diagnosis in 1 case in which the radiologic and pathologic data were equivocal.

Conclusions We detected the mutation at low levels, consistent with mosaicism in the brain or skin (1.0%–18.1%) of classic cases. Our data confirm that the *forme fruste* is part of the spectrum of SWS, with the same molecular mechanism as the classic disease, and that ddPCR is helpful where conventional diagnosis is uncertain.

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ANXA11 mutations prevail in Chinese ALS patients with and without cognitive dementia

Objective To investigate the genetic contribution of ANXA11, a gene associated with amyotrophic lateral sclerosis (ALS), in Chinese patients with ALS with and without cognitive dementia.

Methods Sequencing all the coding exons of ANXA11 and intron–exon boundaries in 18 patients with familial amyotrophic lateral sclerosis (FALS), 353 unrelated patients with sporadic amyotrophic lateral sclerosis (SALS), and 12 Chinese patients with ALS–frontotemporal lobar dementia (ALS-FTD). The transcripts in peripheral blood generated from a splicing mutation were examined by reverse transcriptase PCR.

Results We identified 6 nonsynonymous heterozygous mutations (5 novel and 1 recurrent), 1 splice site mutation, and 1 deletion of 10 amino acids (not accounted in the mutant frequency) in 11 unrelated patients, accounting for a mutant frequency of 5.6% (1/18) in FALS, 2.3% (8/353) in SALS, and 8.3% (1/12) in ALS-FTD. The deletion of 10 amino acids was detected in 1 clinically undetermined man with an ALS family history who had atrophy in hand muscles and myotonic discharges revealed by EMG. The novel p. P36R mutation was identified in 1 FALS index patient, 1 patient with SALS, and 1 patient with ALS-FTD. The splicing mutation (c.174-2A>G) caused in-frame skipping of the entire exon 6. The other missense mutations including p.D40G, p.V128M, p.S229R, p.R302C, and p.G491R were found in 6 unrelated patients with SALS.

Conclusions The ANXA11 gene is one of the most frequently mutated genes in Chinese patients with SALS. A canonical splice site mutation leading to skipping of the entire exon 6 further supports the loss-of-function mechanism. In addition, the study findings further expand the ANXA11 phenotype, first highlighting its pathogenic role in ALS-FTD.

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