



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 angiomatosis; 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 We sequenced all the coding exons of *ANXA11* and intron–exon boundaries in 18 patients of Chinese origin with familial ALS (FALS), 353 with unrelated sporadic ALS (SALS), and 12 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, 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 one clinically undetermined man with 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, 1 SALS, and 1 ALS-FTD case. The splicing mutation (c.174-2A>G) caused in-frame skipping of the entire exon 6. Missense mutations including p.D40G, p.V128M, p.S229R, p.R302C, and p.G491R were found in 6 unrelated patients with SALS.

Conclusions *ANXA11* is the most frequently mutated gene 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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