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Abstracts

Articles appearing in the March 2018 issue

Defining standard enzymatic dissociation methods for individual brains and spinal cords in EAE

Objective To determine the capacity, effectiveness, efficiency, and reliability of select tissue dissociation methods to isolate mononuclear cells from the CNS of mice with experimental autoimmune encephalomyelitis (EAE).

Methods As part of an assay qualification, we tested the isolation method Percoll PLUS vs a commercially available enzymatic Neural Tissue Dissociation Kit (Kit), and the enzymes accutase and papain in C57BL/6 mice with active EAE. In a stepwise approach, we applied the following 4 criteria to each dissociation method: (1) mononuclear cell viability postprocessing was required to be ≥80% per brain or spinal cord sample, (2) absolute live mononuclear cell numbers was required to be $\geq 5 \times 10^5$ per brain or spinal cord sample of mice with clinical EAE, (3) test-retest reliability had to be verified, and (4) the absolute mononuclear cell numbers in brain and spinal cord had to correlate with the EAE disease course.

Results Enzymatic dissociations allowed for greatly increased cell yield and specifically allowed for downstream assays from individual brains and spinal cords in C57BL/6 mice with EAE. All enzymatic dissociations provided a more efficient and effective method for isolating mononuclear cells from brains and spinal cord. Only the Kit assay provided a significant correlation between absolute mononuclear cell numbers in the spinal cord and EAE disease severity.

Conclusions Enzymatic dissociation of CNS tissue of C57BL/6 mice with active EAE with the Kit should be the standard method. The identification of optimized CNS dissociation methods in EAE has the potential to identify cellular events that are pertinent to MS pathogenesis.

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Glycine receptor modulating antibody predicting treatable stiff-person spectrum disorders

Background Glycine receptor α-1 subunit (GlyRα1)–immunoglobulin G (IgG) is diagnostic of stiff-person syndrome (SPS) spectrum but has been reported detectable in other neurologic diseases for which significance is less certain.

Methods To assess GlyRα1-IgGs as biomarkers of SPS spectrum among patients and controls, specimens were tested using cell-based assays (binding [4°C] and modulating [antigen endocytosing, 37°C]). Medical records of seropositive patients were reviewed.

Results GlyRα1-IgG (binding antibody) was detected in 21 of 247 patients with suspected SPS spectrum (8.5%) and in 8 of 190 healthy subject sera (4%) but not CSF. Among 21 seropositive patients, 20 had confirmed SPS spectrum clinically, but 1 was later determined to have a functional neurologic disorder. Sera from 9 patients with SPS spectrum, but not 7 controls, nor the functional patient, caused GlyRα1 modulation (100% specificity). SPS spectrum phenotypes included progressive encephalomyelitis with rigidity and myoclonus (PERM) (8), classic SPS (5), stiff limb (5), stiff trunk (1), and isolated exaggerated startle (hyperekplexia, 1). Neuropsychiatric symptoms present in 12 patients (60%) were anxiety (11), depression (6), and delirium (3). Anxiety was particularly severe in 3 patients with PERM. Objective improvements in SPS neurologic symptoms were recorded in 16 of 18 patients who received first-line immunotherapy (89%, 9/10 treated with corticosteroids, 8/10 treated with IV immunoglobulin, 3/4 treated with plasma exchange, and 1 treated with rituximab). Treatment-sparing maintenance strategies were successful in 4 of 7 patients (rituximab [2/3], azathioprine [1/1], and mycophenolate [1/3]).

Conclusions GlyRα1-modulating antibody improves diagnostic specificity for immunologically treatable SPS spectrum disorders.

Classification of evidence This study provides Class IV evidence that GlyRα1-modulating antibody accurately identifies patients with treatable SPS spectrum disorders.

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