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CLIA ID # 05D2209417

Patient Report:

FINAL

| <u>Amprion Accession #</u> | <u>Collection Date</u> | <u>Received Date</u> | <u>Report Date</u> |
|----------------------------|------------------------|----------------------|--------------------|
| 20-50298 | 11/11/2020 | 11/15/2020 | 11/18/2020 |

Patient: Patient, Troy
DOB: 1/29/1957
Sex: M
MRN: 99999988
Specimen Type: Cerebrospinal Fluid
Specimen ID: S999516

Ordering Physician: Dr. Registered Physician
Client Account: 111111
Client Name: Main Hospital
Client Address: 12345 1st Street Anytown,
US, 00001

Client Telephone #: 999-258-6523

SAAmplify™-αSYN (CSF)

Result

Not Detected

Interpretation:

Misfolded α-Synuclein protein aggregates not detected.

Comments:
N/A

Report Reviewed By: Technical Signature

Date: 11/18/2020

This test was developed and its performance characteristics determined by Amprion, Inc. This test is used for clinical purposes. It should not be regarded as investigational or for research. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing.

Intended Use:

SAAmplify- α SYN (CSF) is an in vitro diagnostic test for qualitative detection of aggregates of misfolded α -synuclein (α Syn) in cerebrospinal fluid (CSF) intended for use in adult patients with clinically uncertain cognitive decline or clinically uncertain Parkinsonian syndromes. Results are used to aid diagnosis of synucleinopathies such as Parkinson's disease (PD), dementia with Lewy bodies (DLB), Alzheimer's disease with Lewy body pathology (AD-LB), and multiple system atrophy (MSA). The results must be interpreted in conjunction with other patient clinical information. The test is for professional use only.

Test and Methodology:

SAAmplify- α SYN (CSF) is a seed amplification assay (SAA). The novel SAA strategy essentially mimics the biological process in which in vivo protein misfolding and aggregation follow a seeding/nucleation mechanism. Briefly, CSF samples are incubated with an excess of monomeric human recombinant (rec) α Syn and subjected to intermittent shaking/incubation cycles. If soluble misfolded α Syn aggregates are present in the sample, these aggregates are amplified using rec- α Syn as substrate. α Syn aggregates formed in the reaction are detected as an increase in fluorescence due to the presence of the amyloid-specific binding dye, Thioflavin T (ThT). In the absence of α Syn seeds, fluorescence remains below the validated assay cutoff.

Limitations:

SAAmplify- α SYN (CSF) utilizes fluorescence to detect increases in α Syn aggregate formation. Validation studies have determined that certain substances such as blood, hemoglobin, and conjugated bilirubin may affect results at concentrations where visible discoloration is evident. The laboratory will evaluate all specimens submitted for suitability for testing. Sensitivity for detection of α Syn aggregates with a Detected-2 profile is low; therefore results should be interpreted with caution for the purposes of rule in/rule out MSA.

References:

1. Rizzo, G., et al. (2016). "Accuracy of clinical diagnosis of Parkinson disease: A systematic review and meta-analysis." *Neurology* 86(6): 566-576.
2. Rizzo, G., et al. (2018). "Accuracy of clinical diagnosis of dementia with Lewy bodies: a systematic review and meta-analysis." *J Neurol Neurosurg Psychiatry* 89(4): 358-366.
3. Wenning G.K., et al. (2022). "The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy." *Movement Disorders* 37(6): 1131-1148.