Syn-One Test®
PATHOLOGY REPORT

Case#:	XXXXXXX
Patient:	Test, Patient
Lab Receipt Date:	XX/XX/XXXX
Lab Report Date:	XX/XX/XXXX

Patient Information

Patient:	Test, Patient
Case #:	XXXXXXX
DOB:	1/13/1952
Gender:	Male
Indications:	G90.9 Autonomic Dysfunction

Provider Information

Clinician:	John Doe, MD
Biopsy Date:	10/31/2022
Account:	CND Life Sciences
Address:	9165 E Del Camino Dr. Ste 101 Scottsdale, AZ 85258
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Conclusions

Synucleinopathy:	There is pathologic evidence of phosphorylated alpha-synuclein deposition within cutaneous nerves. This finding is consistent with a diagnosis of an alpha-synucleinopathy. Clinical correlation is required to distinguish the type of synucleinopathy.
Small Fiber Neuropathy:	There was reduced intraepidermal nerve fiber density. This can be seen in a small fiber neuropathy, polyneuropathies and in peripheral and central neurodegenerative disorders.
Amyloidosis:	There is no pathologic evidence of amyloid deposition in cutaneous nerves. A normal Congo red stain does not exclude a diagnosis of amyloidosis.

Macroscopic Description and Processing

Three (3) skin biopsies in Zamboni fixative were received. The vials were labeled as left posterior cervical, left distal thigh and left distal leg and biopsies were measured to be 3 mm. The biopsies were in adequate condition. They were washed, cryoprotected and sectioned. The following stains were performed:

1. Standard dual immunostaining with protein gene product (PGP 9.5) and phosphorylated alpha-synuclein
2. Standard Congo red staining
3. Standard hematoxylin and eosin staining

Microscopic Description

Phosphorylated Alpha-Synuclein

Abnormal

Phosphorylated alpha-synuclein deposition was observed in all biopsies.

Intraepidermal Nerve Fibers

Abnormal

Intraepidermal nerve fiber density was abnormal in the distal thigh and distal leg biopsy.

Amyloid Deposition (Congo Red)

Normal

Modified Congo red staining shows no evidence of apple-green birefringence under polarized light in any of the biopsies.

Skin Histology (Hematoxylin and Eosin)

Abnormal - See comments*

Routine hematoxylin and eosin staining histopathologic abnormalities in the posterior cervical biopsy (see page 2).

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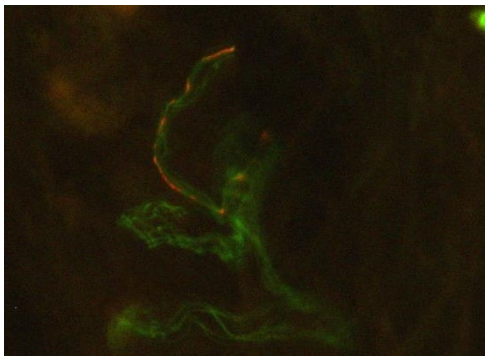
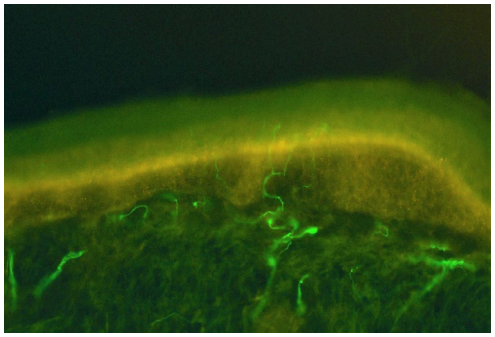
Pathology Results



Phosphorylated Alpha-Synuclein (P-SYN)

Bx Site	P-SYN Deposition	Description
Posterior Cervical (Left)	**Abnormal**	**One colocalized fiber seen across all stained sections.**
Distal Thigh (Left)	**Abnormal**	**One colocalized fiber seen across all stained sections.**
Distal Leg (Left)	**Abnormal**	**One colocalized fiber seen across all stained sections.**

The green regions indicate PGP 9.5 immunostained nerve fibers. The regions in red/orange are immunostained regions of phosphorylated alpha-synuclein within nerve fibers. This region displays evidence of phosphorylated alpha-synuclein deposition.



Intraepidermal Nerve Fiber Density

Bx Site	Observed Measurement (fibers/mm)	Normal Range (fibers/mm)
Posterior Cervical (Left)	**15**	≥17.5
Distal Thigh (Left)	**5.5**	≥8.4
Distal Leg (Left)	**0.6**	≥5.1

The image on the left is not of the patient's own specimen but is included as an example only. The linear green structures indicate PGP 9.5 immunostained nerve fibers. This region displays reduced intraepidermal nerve fiber density. Patient-specific images are available upon request.

Additional Comments (if applicable)

***Posterior cervical: clinically significant histologic abnormalities: Edge of squamous cell carcinoma in situ. Follow- up with dermatology is warranted.**
Distal thigh: no significant histologic abnormalities
Distal leg: no significant histologic abnormalities

Signed: Todd Levine, MD
Medical Director, CMO

Guidance for Use
The Syn-One Test® is a skin biopsy-based test intended to identify specific pathological markers located in cutaneous tissue to aid in the diagnosis of neurological disorders. The central diagnostic feature of Syn-One is the application of immunofluorescent techniques to identify and visualize phosphorylated alpha-synuclein co-located in cutaneous nerves to aid in the diagnosis of a synucleinopathy, a group of neurodegenerative disorders that includes Parkinson's disease (PD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA), pure autonomic failure (PAF), and REM sleep behavior disorder (RBD)*. An abnormal result that identifies phosphorylated alpha-synuclein is indicative of a synuclein pathology but cannot distinguish between the synucleinopathies. Clinicians should use the results from the synuclein assay of the Syn-One Test along with other clinical features to help make a more specific diagnosis.

Syn-One includes the application of an immunofluorescent protein gene product (PGP 9.5) stain that enables quantitative measurement of intraepidermal nerve fiber density (IENFD). A reduced IENFD is indicative of nerve degeneration as seen in some neurodegenerative diseases and peripheral neuropathies.

Syn-One includes a Congo red stain for amyloid as a part of the neuropathologic assessment. The finding of amyloid deposits could indicate a potential cause for epidermal and autonomic nerve pathology, generalized peripheral neuropathy, autonomic dysfunction, and other multi-organ disorders and should prompt an evaluation for primary and secondary causes of amyloidosis.

Syn-One includes a hematoxylin and eosin (H&E) stain, which allows for the evaluation of dermatologic conditions that could mimic neuropathies and identify other benign and malignant skin abnormalities that may be present. The H&E results pertain only to the tissue biopsies taken for this test. Any clinically apparent lesions warrant separate analysis by a dermatologist.

Stability data is not available for tissue specimens kept in fixative for more than 120 hours. The stability of phosphorylated alpha-synuclein deposition has not been established for prolonged fixative times. Prolonged fixative time could result in an artificial decrease in the intraepidermal nerve fiber density.

REM sleep behavior disorder (RBD) is considered a prodromal synucleinopathy. The sensitivity and specificity data of the Syn-One Test for the detection of phosphorylated alpha-synuclein in patients with RBD has not been established. Ongoing research is being conducted in patients with RBD.

References
For additional information on the skin biopsy technique and detection of phosphorylated alpha-synuclein see:

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Immunohistochemistry and immunofluorescence tests were developed, and their performance characteristics were determined, by CND Life Sciences, Scottsdale, AZ. They have not been cleared or approved by the U.S. Food and Drug Administration. CND Life Sciences, Inc. is accredited by the College of American Pathologists (CAP) and holds a Clinical Laboratory Improvement Amendments (CLIA) Certificate of Accreditation to perform high-complexity testing.

P-SYN and PGP 9.5: Technical component performed at CLIA # 03D2151444: 9165 E Del Camino Dr. Ste 101, Scottsdale, AZ 85258. Professional component performed at CLIA # XXX

H&E and Congo red: Technical component performed at CLIA # 03D2151444: 9165 E Del Camino Dr. Ste 101, Scottsdale, AZ 85258. Professional component performed at CLIA # XXX

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