



## Immunohistochemical Method and Histopathology Judging for the Systemic Synuclein Sampling Study (S4)

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Résumé en anglais	Immunohistochemical (IHC) $\alpha$ -synuclein (Asyn) pathology in peripheral biopsies may be a biomarker of Parkinson disease (PD). The multi-center Systemic Synuclein Sampling Study (S4) is evaluating IHC Asyn pathology within skin, colon and submandibular gland biopsies from 60 PD and 20 control subjects. Asyn pathology is being evaluated by a blinded panel of specially trained neuropathologists. Preliminary work assessed 2 candidate immunoperoxidase methods using a set of PD and control autopsy-derived sections from formalin-fixed, paraffin-embedded blocks of the 3 tissues. Both methods had 100% specificity; one, utilizing the 5C12 monoclonal antibody, was more sensitive in skin (67% vs 33%), and was chosen for further use in S4. Four trainee neuropathologists were trained to perform S4 histopathology readings; in subsequent testing, their scoring was compared to that of the trainer neuropathologist on both glass slides and digital images. Specificity and sensitivity were both close to 100% with all readers in all tissue types on both glass slides and digital images except for skin, where sensitivity averaged 75% with digital images and 83.5% with glass slides. Semiquantitative (0-3) density score agreement between trainees and trainer averaged 67% for glass slides and 62% for digital images.
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