

 PARKINSON DISEASE

# Antibodies reveal age of Lewy pathology in PD

Monoclonal antibodies (mAbs) raised against different conformations of  $\alpha$ -synuclein can provide insights into the maturity of Lewy pathology in the brains of patients with Parkinson disease (PD), according to new research reported in *Neuropathology and Applied Neurobiology*.

Lewy neurites and Lewy bodies, consisting of misfolded  $\alpha$ -synuclein, are important neuropathological hallmarks of PD. Maturation of Lewy pathology is signified by various morphological changes, as well as post-translational modifications such as phosphorylation and ubiquitylation.

For the new study, Virginia Lee and colleagues generated

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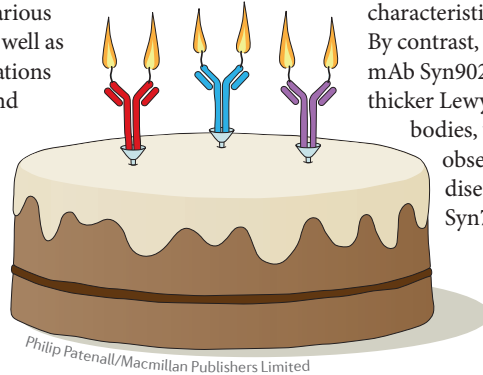
mAbs against two different conformations of  $\alpha$ -synuclein, termed strain A and strain B. “We used strain-selective mAbs as tools to interrogate the heterogeneity of  $\alpha$ -synuclein pathology in a large cohort of well-characterized post-mortem brains from patients with PD,” explains Lee.

The researchers observed that strain A-selective mAb Syn7015 bound predominantly to small Lewy neurites and Lewy dots, which are characteristic of early-stage PD. By contrast, the strain B-selective mAb Syn9029 tended to target thicker Lewy neurites and Lewy bodies, which are generally observed at more-advanced disease stages. In addition, Syn7015 colocalized with

phospho-Ser129- $\alpha$ -synuclein, a marker of early  $\alpha$ -synuclein pathology, whereas Syn9029 colocalized with the later markers ubiquitin and P62.

“We want to conduct additional studies to characterize  $\alpha$ -synuclein strains isolated from the brains of patients with PD or other neurodegenerative diseases to gain better insights into the pathogenesis of diseases with  $\alpha$ -synuclein pathology,” comments Lee. “Antibodies such as Syn7015 and Syn9029 will help to expand our understanding of the processes underlying PD progression, as well as to provide novel targets for the development of biomarker assays and disease-modifying therapies.”

Heather Wood



**ORIGINAL ARTICLE** Covell, D. J. *et al.* Novel conformation-selective alpha-synuclein antibodies raised against different *in vitro* fibril forms show distinct patterns of Lewy pathology in Parkinson's disease. *Neuropathol. Appl. Neurobiol.* <http://dx.doi.org/10.1111/nan.12402> (2017)

**FURTHER READING** Guo, J. L. *et al.* Distinct  $\alpha$ -synuclein strains differentially promote tau inclusions in neurons. *Cell* **154**, 103–117 (2013)