

**Editors' Note:** Wu et al. argue that, in certain races, the *SMPD1* p.L302P mutation does not play an important role in Parkinson disease risk. Orr-Urtreger et al. are not surprised, since this is a founder Ashkenazi mutation. They suggest sequencing of the entire *SMPD1* gene, in a much larger cohort of patients and controls, to examine the possible effects of rare *SMPD1* mutations in non-Ashkenazi populations. Silvestri et al. and St. Louis et al. compare their findings in studies of sleep disorders in patients with myotonic dystrophy type 2 (DM2) and try to explain differences in their results, especially regarding obstructive sleep apnea. They agree on the necessity of prospective large-scale studies in patients with DM2 looking objectively at sleep abnormalities.

—Chafic Karam, MD, and Robert C. Griggs, MD

#### THE p.L302P MUTATION IN THE LYSOSOMAL ENZYME GENE *SMPD1* IS A RISK FACTOR FOR PARKINSON DISEASE

**Ruey-Meei Wu, Chin-Hsien Lin, Han-I Lin, Taipei, Taiwan:** Gan-Or et al.<sup>1</sup> replicated data on a large number of patients with Parkinson disease (PD) in 2 Ashkenazi Jewish cohorts. We would suggest that the authors obtain data from other populations to support the pathogenic role of *SMPD1* in the risk of PD. We have genotyped *SMPD1* p.L302P using TaqMan Genotyping Assays on the StepOnePlus Real-Time PCR machine (Applied Biosystems, Foster City, CA) in 1,139 participants. This group comprised 579 patients with PD and 560 control subjects in a Taiwanese population. Among the PD group, 199 patients were young onset (<50 years). We did not identify any p.L302P mutation in patients or control subjects. The *SMPD1* p.L302P mutation is unlikely to play a major role in PD risk in our ethnicity.<sup>2-4</sup> Different demographics and region-specific genetic and environmental interactions may contribute to the differences in results.<sup>5</sup>

**Author Response: Avi Orr-Urtreger, Ziv Gan-Or, Tel-Aviv, Israel:** Wu et al. analyzed their PD cohort and controls from Taiwanese origin for the *SMPD1* p.L302P mutation and no carriers of this mutation were identified. The *SMPD1* p.L302P is a founder mutation

causing Niemann-Pick type A disease among Ashkenazi Jews and a risk factor for PD in this population.<sup>1</sup> In contrast, this specific mutation was never described in the Taiwanese population. Until 2009, no Niemann-Pick patients with *SMPD1* mutations were identified in Taiwan, and then only one patient with compound heterozygous genotype (p.P330R/p.A451D) was described.<sup>6</sup> To reach statistical significance, we analyzed 938 patients with PD and compared them to more than 10,000 controls. Lin et al. analyzed only 579 patients with PD and 560 controls. It is not reasonable to expect the replication of the effect of a founder Ashkenazi mutation in a small population in which the *SMPD1* p.L302P was never described and in which other *SMPD1* mutations are very rare. To examine the possible effects of rare *SMPD1* mutations on this population, sequencing of the entire *SMPD1* gene is required in a much larger cohort of patients and controls.

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1. Gan-Or Z, Ozelius LJ, Bar-Shira A, et al. The p.L302P mutation in the lysosomal enzyme gene *SMPD1* is a risk factor for Parkinson disease. *Neurology* 2013;80:1606–1610.
2. Farrer MJ, Stone JT, Lin CH, et al. Lrrk2 G2385R is an ancestral risk factor for Parkinson's disease in Asia. *Parkinsonism Relat Disord* 2007;13:89–92.
3. Lin CH, Chen ML, Chen GS, Tai CH, Wu RM. Novel variant Pro143Ala in HTRA2 contributes to Parkinson's disease by inducing hyperphosphorylation of HTRA2 protein in mitochondria. *Hum Genet* 2011;130:817–827.
4. Lin CH, Tan EK, Chen ML, et al. Novel ATP13A2 variant associated with Parkinson disease in Taiwan and Singapore. *Neurology* 2008;71:1727–1732.
5. Ross CA, Smith WW. Gene-environment interactions in Parkinson's disease. *Parkinsonism Relat Disord* 2007;13 (suppl 3):S309–S315.
6. Lan MY, Lin SJ, Chen YF, et al. A novel missense mutation of the *SMPD1* gene in a Taiwanese patient with type B Niemann-Pick disease. *Ann Hematol* 2009;88:695–697.

#### RESTLESS LEGS SYNDROME AND DAYTIME SLEEPINESS ARE PROMINENT IN MYOTONIC DYSTROPHY TYPE 2

**Gabriella Silvestri, Maria Laura Ester Bianchi, Anna Losurdo, Giacomo Della Marca, Rome:** Lam et al.<sup>1</sup> studied the frequency of restless legs syndrome, excessive daytime sleepiness (EDS), and fatigue in 30 patients with myotonic dystrophy type

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## The p.L302P mutation in the lysosomal enzyme gene *SMPD1* is a risk factor for Parkinson disease

Ruey-Meei Wu, Avi Orr-Urtreger, Chin-Hsien Lin, et al.

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