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The Need for Appropriate Genotyping Strategies for Glucocerebrosidase Mutations in Cohorts With Parkinson Disease

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The article by Tan et al¹ reporting mutations in the glucocerebrosidase gene (*GBA*) in Chinese patients with Parkinson disease (PD) is the third recent article in series of patients of Chinese ancestry.^{1–3} These studies are important because they support the previously described association of *GBA* mutations and parkinsonism in white and Ashkenazi Jewish PD cohorts^{4,5} in a population that is clearly of non-Ashkenazi Jewish ancestry.

Tan and colleagues chose to screen for only 2 *GBA* mutations, L444P and N370S. While both of these mutations are relatively common in white and Ashkenazi Jewish populations, the N370S mutation has not been reported in Asian patients with Gaucher disease.⁶ Thus, the frequency of *GBA* mutations reported in this article, 2.4%, is likely to be a vast underestimate.

In a larger cohort, Wu et al² screened 518 Taiwanese patients with PD for 2 *GBA* mutations, L444P and R120W. They identified L444P in 15 patients (2.9%) and in 4 of 339 control subjects (1.2%), with the L444P mutation being part of a recombinant allele, *RecNciI*, in 2 patients and 2 control subjects. One patient had an R120W mutation.

We have sequenced *GBA* in 184 Chinese subjects with PD from Taiwan (92 of these were described previously³) and identified 7 different mutations in a total of 10 subjects (5.4%) (Table). Four L444P alleles (2.2%) and no N370S alleles were found. Only 1 mutation, V460M, was identified among 92 Taiwanese control samples (1.1%).³ Thus, while the article by Tan and colleagues probably accurately reflects the frequency of L444P among Chinese subjects with PD, our sequencing study indicates that by merely screening for this mutation, at least half of the mutant alleles may be missed in this population. Although direct sequencing is a more labor-intensive means to identify mutant alleles, we feel that it is essential in order to identify the true mutation frequency in a non-Ashkenazi Jewish cohort.

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Table

Glucocerebrosidase Gene Mutations Identified in 184 Taiwanese Patients With Parkinson Disease

Mutation	Cases, No.
L444P	4
R131S	1
R163Q	1
L174P	1
S271G	1
D409H	1
Q497R	1