Electronic letter

Homoplasmic 3316G→A in the *ND1* gene of the mitochondrial genome: a pathogenic mutation or a neutral polymorphism?

EDITOR—We read with interest the article by Odawara *et al.*¹ in which the authors reported that a homoplasmic mutation, 3316G→A, in the *ND1* gene of the mitochondrial genome was associated with type 2 diabetes in the Japanese population. Recently, we have performed the same study in the Chinese population and, interestingly, we obtained a different result.

A total of 277 subjects with type 2 diabetes aged 29–85 years (mean 58.9 (SD 12.0) years) who attended the Diabetes Clinic of United Christian Hospital, Hong Kong, were recruited into this study after informed consent was obtained. The diagnosis was based on the independent criteria of the World Health Organization: (1) a 75 g oral glucose tolerance test with a two hour value of 11.0 mmol/l or more, (2) a random plasma glucose of 11.0 mmol/l or more with typical symptoms of diabetes, or (3) a fasting plasma glucose of 7.8 mmol/l or more on more than one occasion. Healthy non-diabetic control subjects were recruited from the community health screening programme of United Christian Hospital and they all had normal fasting plasma glucose levels. All the subjects were unrelated and were ethnic Chinese.

Genomic DNA was extracted from peripheral venous blood samples using a QIAamp blood kit for DNA isolation (Qiagen, Hilden, Germany). PCR was performed to amplify the mtDNA nucleotide 3116–3353 fragment, which spans 16S rRNA, tRNA^{leu(UUR)}, and the *ND1* gene region. The primers used for mutation screening were as previously described.² PCR products were purified as templates for sequencing by DNA purification kits (Micro-

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spinTM S-300HR columns, Amersham Pharmacia Biotech, Bucks, UK). Automated DNA sequencing was performed with fluorescence labelled primers using the Cy5TM AutocycleTM Sequencing kit (Amersham Pharmacia Biotech, Bucks, UK) and according to the manufacturer's instructions on an ALFexpress DNA sequencer (Amersham Pharmacia Biotech, Bucks, UK). Automated DNA sequencing was performed to screen all patients.

In our study, we found the mutation 3316G→A in nine out of 277 patients with type 2 diabetes and 10 out of 241 non-diabetic controls. All were homoplasmic mutations. The frequency in control subjects (4.15%) is higher than in patients (3.25%), and there is no statistical difference between these groups (Fisher's exact test, $p=0.64$). In contrast to the Japanese studies, our results suggest that the 3316G→A mutation does not relate to type 2 diabetes in the Chinese population. We agree with Chinnery *et al.*^{3,4} that it is difficult to confirm the pathogenicity of homoplasmic mitochondrial mutation, and different nuclear genetic backgrounds may influence the nature and severity of the disease.

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