Letter to the Editor

Response to Comment on: Lin et al. (2007) *SUMO4* M55V Variant Is Associated With Diabetic Nephropathy in Type 2 Diabetes: *Diabetes* 56:1177–1180

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We thank Hamann et al. (1) for their interest in our study (2) and for demonstrating their results. They did not find the *SUMO4* M55V variant to be associated with diabetic nephropathy in Caucasian patients with type 1 (n = 237) and type 2 (n = 515) diabetes. Our study had found the *SUMO4* M55V variant to be associated with diabetic nephropathy in Taiwanese patients with type 2 diabetes (n = 430). We agree that these differences might be explained by the racial background, e.g., with Asian and Caucasian subjects.

In studies from Asian control populations, the frequencies of *SUMO4* AA, AG, and GG are reported to be 50.1, 40.0, and 9.9% in Japan (3); 47.9, 41.6, and 10.5% in Korea (4); 46.4, 45.7, and 7.9% in China (5); and 57.6, 35.6, and 6.8% in Taiwan (n = 323, our unpublished data), respectively. These frequencies were, however, different from Caucasian control populations in the studies of Smyth et al. (24.4, 49.0, and 26.6%) (6) and Wang et al. (25.5, 50.1, and 24.4%) (7). Of note is the significant association of the *SUMO4* M55V variant with the development of type 1 diabetes from Asian populations (3–5) in contrast to the lack of association with type 1 diabetes in European Caucasian patients (6). More recently, Noso et al. (8) reported the frequencies of *SUMO4* AA, AG, and GG to be 41, 47, and 12% in Japanese patients with type 2 diabetes; in our study of a Taiwanese population, the frequencies of these variants were 48, 44, and 8%, respectively (2). However, Hamann et al. did not report the frequency of *SUMO4* AA, AG, or GG in their patients with diabetes.

Humans do not always share the same causes and prevalences of diseases. In some cases, these differences are due to genetic or environmental constitution. Some studies have demonstrated that the prevalence of diabetic nephropathy is higher in Asian patients with diabetes than it is among Caucasian patients with diabetes (9,10). In the study by Hamann et al., diabetic nephropathy was defined as microalbuminuria of more than 20 mg/l in two or three samples of morning urine obtained within 12 months (11). However, we determined the severity of diabetic nephropathy by measuring urinary albumin-to-creatinine ratio for three consecutive urine collections and subdividing the results into: *1*) normoalbuminuria, *2*) microalbuminuria, and *3*) macroalbuminuria. The most important finding in our study was a significant linear trend for the *SUMO4* genotype between the macroalbuminuric group and normoalbuminuric group. The mean urinary albumin-to-creatinine ratio was significantly higher in the GG group than it was in the AA and AG groups. However, Hamann et al. (1) showed no difference in the prevalence of diabetic nephropathy in patients with AA in comparison to patients with AG and GG.

In conclusion, these two studies indicate significant genetic heterogeneity in the association of the *SUMO4* M55V variant with diabetic nephropathy in type 2 diabetic patients between Asian and Caucasian populations.

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Received for publication 20 April 2007 and accepted 22 April 2007.

DOI: 10.2337/db07-0547

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