Response to Comment on: Chang et al. (2007) Association Study of the Genetic Polymorphisms of the Transcription Factor 7-like 2 (*TCF7L2*) Gene and Type 2 Diabetes in the Chinese Population: *Diabetes* 56:2631–2637

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We appreciate the comments from Ku et al. (1). Although previously genome-wide linkage studies were and, currently, genome-wide association studies are the preferred approaches for the search of genetic causes of complex diseases, such as type 2 diabetes, the candidate gene approach remains a very useful tool as a supplement to the whole-genome search. In some published genome-wide association studies of type 2 diabetes, this locus would fall off the screen when a stringent criterion for the positive association was applied (2). When we noticed that the frequencies of rs7903146 (intron 3) and rs12255372 (intron 4), previously reported to be associated with type 2 diabetes, were rare in the Chinese population, we extended our single nucleotide polymorphism (SNP) study to cover the whole gene (3). We then identified a novel SNP (rs290487 in intron 7) associated with type 2 diabetes, implying a population-attributable risk fraction of 18.7% in the Chinese population residing in Taiwan. Our study clearly demonstrated the role of the candidate gene approach in type 2 diabetes.

Furthermore, the association with the same SNPs or haplotype in different populations indicated a founder effect. Identification of a novel SNP association in the Chinese population residing in Taiwan suggested a different founder from that in the previously reported populations. Interestingly, Ng et al. (4) reported the association of rs11196218 (intron 4) with type 2 diabetes in a Chinese (mainly Cantonese) population residing in Hong Kong. Two different SNPs are associated with type 2 diabetes in two different Chinese populations, suggesting different ancestral origins of these two Chinese populations.

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Received and accepted for publication 12 September 2007.

DOI: 10.2337/db07-1302

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