RESPONSE TO COMMENT ON LIU ET AL.

Latent Autoimmune Diabetes in Adults With Low-Titer GAD Antibodies: Similar Disease Progression With Type 2 Diabetes: A Nationwide, Multicenter Prospective Study (LADA China Study 3). Diabetes Care 2015;38:16–21

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We thank Shah and Yu (1) for their comments on our study (2) and for the opportunity to discuss some key points on the GAD antibody (GADA) pattern and its relation with progression of type 1 diabetes, especially for latent autoimmune diabetes in adults (LADA). They suggest that low-titer GADA subjects in our study might have low-affinity GADA representing biologically "false positivity" and GADA affinity could be analyzed with an electrochemiluminescence (ECL)-based assay to determine if this was the case. Indeed, the important role of different GADA patterns has been studied extensively and the number, titer, and affinity of GADA are decisive biomarkers in discriminating and predicting type 1 diabetes (3).

Subjects with single or low-titer GADA have a low risk of disease progression, potentially because they represent a technically false-positive group or a biologically distinct group. These two options are mutually exclusive and the former may be relevant to some studies of LADA. Against the former, we have duplicated the assay by our Diabetes Autoantibody Standardization Program–standardized radioimmunoassay method, so false positivity rates are very low and the quantile-quantile plot indicates that the positive signal represents a distinct group of subjects (4). In support of the latter, compared with patients with type 2 diabetes, low-titer GADA patients had more total HLA-DQA1 susceptibility haplotypes and more were on insulin therapy at entry into the study (2,4).

We agree with Shah and Yu (1) that studies of GADA affinity would be of value, as 10% of these low-titer GADA patients developed β-cell failure and none converted to high-titer GADA. The comprehensive measurement of GADA, including affinity, titer, different epitope recognition, isotypes, and concurrent status of other islet autoantibodies, should be of value as GADA affinity and titer are not always correlated (5). Considering most studies of GADA affinity were done in classic juvenile-onset type 1 diabetes (3,5), it will be valuable to know whether GADA affinity can better discriminate the heterogeneity of LADA, perhaps by using the ECL-based GADA assay, which is a promising alternative to complicated competitive binding experiments.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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