COMMENT ON SO ET AL.

Autoantibody Reversion: Changing Risk Categories in Multiple-Autoantibody–Positive Individuals. Diabetes Care 2020;43:913–917

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Diabetes Care 2020;43:e102 | https://doi.org/10.2337/dc20-0409

So et al. (1) have recently published an article in *Diabetes Care* stating that there is a small percentage of previously multiple-autoantibody–positive type 1 diabetes (T1D) at-risk individuals who reverted to 0 or 1 autoantibody positivity during follow-up visits. Although the proportion of "reverters" to "maintainers" was vastly different, they stated that the risk of progressing to T1D was decreased in these individuals according to the staging of preclinical T1D currently accepted. They went on to say that the 5-year cumulative risk of these "reverters" to develop T1D was 11%; this is significantly lower than the 42% risk held by the maintainers (1).

However, there are individuals who are multiple-autoantibody positive who do not progress to T1D; consequently, there were "reverters" who developed T1D (1). These conflicting findings raise the following question: is the current "gold standard" of autoantibody detection good enough? The detection of autoantibodies within the sera of at-risk individuals is currently being utilized to recruit subjects for clinical trials to prevent the onset of diabetes (2). Based on the latest findings, these autoantibodies do not appear to meet the level of specificity and sensitivity required to characterize preclinical T1D. Thus, exposing relatively healthy individuals to drugs that may cause adverse effects may not be the appropriate approach to manage the onset of T1D.

There is a need to focus on more specific biomarkers to accurately identify at-risk individuals as well as precisely diagnose patients with prediabetes. For example, current studies have shown that posttranslationally modified antigens can elicit an immune response in autoimmune conditions. This has been seen in rheumatoid arthritis (3), where autoantibodies toward citrullinated antigens have been identified and play an important role in the immunogenicity seen (4). T1D appears to show a similar trend; autoantibodies to oxidative posttranslational modifications in β-cell antigens have been found and may prove to be a promising set of more specific and sensitive biomarkers for T1D (5). Based on these findings, as well as the work of So et al., we suggest that the current staging of T1D needs to be reevaluated and more specific biomarkers are required in order to begin to recruit at-risk individuals for clinical trials.

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

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