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COMMENT ON SPROUSE ET AL.

SLC30A8 Nonsynonymous Variant Is Associated With Recovery Following Exercise and Skeletal Muscle Size and Strength. Diabetes 2014;63:363–368

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In the January issue of *Diabetes*, Sprouse et al. (1) reported on the association of the *SLC30A8* nonsynonymous variant with recovery following exercise and skeletal muscle size and strength. The limitations discussed in the article need additional information.

So far, genome-wide association studies have identified 59 single nucleotide polymorphisms associated with type 2 diabetes (T2D) at the genome-wide significance level ($P < 5 \times 10^{-8}$) (2). However, it was unclear whether and in what way the currently known genetic variants can be used in practice because the combined effect of these variants (i.e., the discriminative accuracy) has not been investigated.

Two studies measured the discriminative accuracy by calculating the area under the receiver-operator characteristic curve (AUC) (3,4). Based on AUC values of approximately 0.60, the authors of both articles concluded that the genetic polymorphisms only marginally improved the prediction of T2D beyond clinical characteristics and did not provide a strong predictive value at a population level. Recently, Bao et al. (5) discussed in a systematic review of 21 articles the predictive performance of genome-wide association marker–based risk models for T2D risk and concluded that they showed a low predictive performance for the risk of T2D.

We have carried out an examination of the molecular architecture, at a resolution of 3.8 Å, of the three-dimensional structure of β-cell–specific zinc transporter, ZnT-8, predicted from the T2D-associated gene variant *SLC30A8* R325W (6). An interesting aspect of this study was that the inherited R325W abnormality may be tolerated and results in an adequate zinc transfer into the correct sites of the pancreatic islet cells. This observation may be responsible for the low predictive value of the *SLC30A8* gene variant R325W for future T2D at a population-based level.

To this day, an unresolved issue is that single nucleotide polymorphisms with strong evidence of association with T2D marginally improved the prediction of the involved pathological state.

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

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