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Genome-Wide Association Study Identifies Two Novel Loci with Sex-Specific Effects for Type 2 Diabetes Mellitus and Glycemic Traits in a Korean Population (*Diabetes Metab J* 2014;38:375-87)

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We greatly appreciate your thoughtful comments and suggestions on our article entitled "Genome-Wide Association Study Identifies Two Novel Loci with Sex-Specific Effects for Type 2 Diabetes Mellitus and Glycemic Traits in a Korean Population," which was published in the *Diabetes & Metabolism Journal* [1].

Chronic alcohol intake is associated with type 2 diabetes mellitus (T2DM) as an independent risk factor, and it has also been considered to be related with increased adipogenesis, impaired glucose tolerance, and insulin resistance [2]. However, the underlying molecular mechanisms behind physiological and pathological entities have not been fully explored.

In our study, we conducted the approximate conditional analysis on multiple diverse effects. We confirmed that the associated signals of two variants (rs11065756 and rs2074356) in *CCDC63* and *C12orf51* were only slightly diminished after adjustment for alcohol consumptionin T2DM, fasting plasma glucose, and homeostatic model assessment-B traits, indicating that there was no evidence for the substantial attenuation in statistical causal inference. These results suggested that the newly identified T2DM loci were not simply secondary to the alcohol effects.

Indeed, a previous genome-wide study showed that the two loci were predominantly associated with the amount of alcohol consumed in two population-based cohorts including heavy drinkers (~40%) [3]. Several studies have reported that moderate alcohol intake is associated with decreased risk of T2DM [4-6]. Recent studies have demonstrated that alcohol intake is associated with widespread changes in DNA methylation as an epigenetic factor [7,8]. Given the phenotypic and genotypic heterogeneity between T2DM and alcohol intake, further integrated multianalyses will be needed to determine influence of metastable epialleles on T2DM risk [9]. Taken together, our findings suggest that the two novel variants influencing T2DM have impacts on alcohol-independent T2DM risk. The identification of these loci provides additional clues regarding the pleiotropic effects associated with variation in the 12q24 region of the human genome.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Go MJ, Hwang JY, Park TJ, Kim YJ, Oh JH, Kim YJ, Han BG, Kim BJ. Genome-wide association study identifies two novel Loci with sex-specific effects for type 2 diabetes mellitus and glycemic traits in a korean population. Diabetes Metab J 2014;

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38:375-87.
2. Pietraszek A, Gregersen S, Hermansen K. Alcohol and type 2 diabetes. A review. Nutr Metab Cardiovasc Dis 2010;20:366-75.
3. Baik I, Cho NH, Kim SH, Han BG, Shin C. Genome-wide association studies identify genetic loci related to alcohol consumption in Korean men. Am J Clin Nutr 2011;93:809-16.
4. Koppes LL, Dekker JM, Hendriks HF, Bouter LM, Heine RJ. Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies. Diabetes Care 2005;28:719-25.
5. Fueki Y, Miida T, Wardaningsih E, Ito M, Nakamura A, Takahashi A, Hanyu O, Tsuda A, Saito H, Hama H, Okada M. Regular alcohol consumption improves insulin resistance in healthy Japanese men independent of obesity. Clin Chim Acta 2007; 382:71-6.
6. Conigrave KM, Hu BF, Camargo CA Jr, Stampfer MJ, Willett WC, Rimm EB. A prospective study of drinking patterns in relation to risk of type 2 diabetes among men. Diabetes 2001;50: 2390-5.
7. Philibert RA, Plume JM, Gibbons FX, Brody GH, Beach SR. The impact of recent alcohol use on genome wide DNA methylation signatures. Front Genet 2012;3:54.
8. Simmons RA. Programming of DNA methylation in type 2 diabetes. Diabetologia 2013;56:947-8.
9. Drong AW, Lindgren CM, McCarthy MI. The genetic and epigenetic basis of type 2 diabetes and obesity. Clin Pharmacol Ther 2012;92:707-15.