

# Awareness of Genetic Polymorphism in Drug Metabolizing Enzymes and Transporters May Promote Personalized Type 2 Diabetes Management [Letter]

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## Dear editor

We read with great interest the study by Williams et al,<sup>1</sup> which shows that the use of personalized medicine in people with type 2 diabetes mellitus (T2D) could improve medication adherence, patient satisfaction, and quality of life. We especially appreciate the viewpoint that factors affecting the intensity of treatment and choice of pharmacotherapy should include medical and patient influences. However, we found one point worthy of discussion and we would like to share our perspectives in the following paragraphs.

Mutations in genes important in drug absorption, distribution, metabolism, and excretion play a critical role in pharmacogenetics of diabetes.<sup>2</sup> There is an extreme need to consider the genetic polymorphism when low efficacy and side effects occur. For example, CYP2C9 is the major metabolizing enzyme responsible for sulfonylureas' biotransformation and the number of CYP2C9\*2 and \*3 alleles is associated with nearly three-fold increased risk of hypoglycemic events.<sup>3</sup> CYP2C8\*3 polymorphisms result in significantly lower exposure and higher clearance of thiazolidinediones (eg, pioglitazone and rosiglitazone), and lower odds ratio of developing edema during rosiglitazone treatment.<sup>4,5</sup> The SLC11B\*1B haplotype reduces plasma concentrations of repaglinide, but has limited effects on the pharmacokinetics of nateglinide.<sup>6</sup> Two genetic variations in SLC22A1 that are in strong linkage disequilibrium increase prevalence of the side effects of metformin in patients with T2D.<sup>7</sup>

Williams et al examined the personal factors, phenotypic characteristics, biomarkers and genetic markers that may have a role in personalizing the management of T2D, and their work is very enlightening and beneficial for the international community. Their recommendations along with our perspectives may provide a more detailed guide for personalized anti-diabetic therapy.

## Disclosure

The authors report no conflicts of interest in this communication.

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