#### **RESPONSE TO LETTER**

# Thoughtful Response on "The Variants in ADIPOQ are Associated with Maternal Circulating Adipokine Profile in Gestational Diabetes Mellitus" [Response to Letter]

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### **Dear editor**

We are pleased to receive a letter from readers regarding our publication entitled "The Variants in ADIPOQ are Associated with Maternal Circulating Adipokine Profile in Gestational Diabetes Mellitus" (ID: 396238). The purpose of this study was to investigate the association between maternal circulating adipokine levels including adiponectin, adipsin/factor D, lipocalin, and total PAI-1, and resistin and *ADIPOQ* gene polymorphisms (rs266729, rs2241766, and rs1501299) among pregnant women subjects with gestational diabetes mellitus (GDM) and normal glucose tolerance (NGT).

Due to the implications for future research, genome-wide association studies (GWAS) were examined to understand the association between gene polymorphisms and GDM diagnosis/prediction. The genetic determination of GDM that are specific to the Asian population. A significantly elevated future risk of type 2 diabetes is linked to GDM.<sup>1</sup> The metaanalysis demonstrates the role of *ADIPOQ* polymorphism and the risk of GDM among Asian populations.<sup>2</sup> Our study detected polymorphisms that showed the association between *ADIPOQ* +45T/G (rs2241766) and the risk of GDM in Thai pregnant women. However, we did not find an important role for risk factors (age, gestational age, BMI, and blood pressure) in *ADIPOQ* gene polymorphisms. Moreover, a total of 12 gene polymorphisms at ADIPOQ, adipsin, lipocalin-2, PAI-1, resistin, IL-1 $\beta$ , IL-4, IL-17A, TGF- $\beta$ , IL-10, IL-6, and TNF- $\alpha$  were more investigated.<sup>3</sup> The results of this study highlight the need for genetic testing to predict/prevent GDM and the importance of evaluating adipokine/adipocytokine levels in GDM women.

The current study measured five adipokines levels in pregnant women with GDM and NGT. Serum adiponectin levels were significantly lower in the GDM group than in the NGT group. As suggested, various types of adipokines are related to diabetes mellitus pathogenesis. Asprosin is a type of circulating adipokine that is linked to diabetes mellitus and obesity.<sup>4</sup> Previous studies demonstrated a significant relationship between maternal and fetal plasma asprosin levels, both of which increased in normal-weight and obese women with GDM.<sup>5</sup> Therefore, in future studies, the investigation of asprosin levels will be the candidate for measurement in pregnant women with GDM.

The predictive factors of clinical characteristics (maternal age, pre-pregnancy BMI, and increasing body weight) with gestational diabetes mellitus were not found in our study. However, the predictive genetic polymorphisms of *ADIPOQ* +45T/G (rs2241766) are associated with an increased risk of GDM in Thai pregnant women. Raffael Ott et al show that

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gestational diabetes and neonatal outcome are correlated with reduced adiponectin gene expression and DNA methylation in adipose tissues and blood cells.<sup>6</sup>

Much evidence shows the study of adiponectin in humans, mice, rats, and zebrafish. For example, the previous study showed that adiponectin deficiency was correlated with glucose intolerance, hyperlipidemia, and fetal overgrowth in pregnant mice with GDM (adiponectin gene knockout,  $Adipoq^{-/-}$ ).<sup>7</sup> It would be more interesting to study *ADIPOQ* gene polymorphisms in *Macaca fascicularis* model.

## Disclosure

All authors report no conflicts of interest in this communication.

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