Letter

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An *In Vitro* Model to Probe the Regulation of Adipocyte Differentiation under Hyperglycemia (*Diabetes Metab J* 2013;37:176-80)

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The investigation of the role of high glucose in adipocyte differentiation has an important conceptual implication. It can explain the metabolic dysregulation of obesity through the direct link between hyperglycemia and increase in adiposity.

In the article entitled "An *in vitro* model to probe the regulation of adipocyte differentiation under hyperglycemia," Shilpa et al. [1] reported that 105 mM high glucose inhibited differentiation of adipocyte and stimulated proliferation of preadipocyte. This study is of great interest in that very high glucose enhanced the risk of adiposity in 3T3-L1 cells. This concept is also demonstrated in other cell types. High glucose drives the differentiation of stem cells into adipocytes by increasing the expression of adipocyte specific proteins such as SREBP-1C, GLUT-4, and PPAR-γ [2]. Also high glucose activates an adipogenic differentiation in pancreatic β-cells. Besides, this study well agrees with many previous reports about an important role for protein kinase C (PKC) in diabetes and in adipogenesis. PKC appears to be involved in oxidative stress. Recently, PKC β has been found to recruit the 66-Kd Shc which triggers reactive oxygen species (ROS) production [3].

However, this study has some points to be discussed. First, the 105 mM (1,890 mg/dL) glucose concentration is not a physiologic concentration found in human except in hyperosmolar hyperglycemic state. Thus, it might be a stretch to argue that the effect of very high glucose concentration such as 105 mM on the adipogenesis can explain the pathogenesis of obesity. While 25 mM concentration of glucose was used as a control, it is already a high concentration which is somewhat similar to diabetic condition. Chuang et al. [4] demonstrated that 25 mM glucose condition enhanced adipogenesis and lipid accumulation in mesenchymal stem cells compared with the condition of 5.5 mM glucose. Perhaps the reason why they used 25 mM glucose as a control is that it is the glucose concentration employed at a conventional protocol of differentiation of 3T3L1 cell is 25 mM at all stages. However, if the author used the 5 to 6 mM glucose as a control, it would be more acceptable design explaining the effect of chronic hyperglycemia condition on adipogenesis. Lin et al. [5] studied about whether 4 mM of glucose could differentiate 3T3L1 cell. They showed smaller lipid droplets in oil red O stain and, more insulin sensitive signaling in phosphorylation of Akt under 4 mM glucose condition. The 25 mM glucose induced insulin resistance and increased ROS, proinflammatory cytokine, and resistin gene expression, even though larger lipid droplets was observed than at 4 mM glucose condition.

Second, 105 mM glucose has high osmolarity, which can induce osmotic stress. There is a need for mannitol control to exclude the effect of high osmolarity. If there is a difference between the effect of 105 mM glucose versus mannitol control, it can clearly demonstrate that whether the increase of oxidative stress, cytokine gene expression, nuclear factor-κB, or tumor necrosis factor-α, is due to very high concentration of glucose

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itself or due to high osmolarity.

CONFLICTS OF INTEREST

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

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