

Short Communication

Similarities and differences in beta cell mass between Caucasians and Japanese in the face of obesity and diabetes

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The prevalence of type 2 diabetes (T2DM) is markedly increasing, the incidence of diabetic complications and the cost of treatment remain major issues throughout the world. Recent studies showed that β -cell deficit is a core feature of T2DM [1]. Even in the obese subjects with T2DM, beta cell function and mass are reduced [2]. Preservation or recovery of beta cell mass (BCM) is therefore an important therapeutic strategy for T2DM. However, the physiological changes in BCM during the development of T2DM remain less clear. In adult humans, BCM increases by approximately 20%–50% in obese nondiabetic individuals in the Caucasian population [3]. While, we and another Japanese study reported that no significant increase in BCM was observed in obese nondiabetic adults in the Japanese population [4,5]. The mean BMI of Japanese patients with T2DM is $<25\text{kg/m}^2$, suggesting that about half of patients with T2DM are not even overweight (*i.e.*, $\text{BMI} \geq 25\text{kg/m}^2$, the definition of obesity in Asian countries). In contrast, most patients of Caucasians with T2DM are obese, and the mean BMI of patients with T2DM is $\sim 30\text{kg/m}^2$. Considering the similar incidence of T2DM despite less degree of obesity in Japanese compared with Caucasians [6], these findings suggest that β -cell regenerative capacity may differ between Japanese and Caucasians. Because of the limited capacity of β -cell regeneration in Japanese, excess β -cell workload could be induced in individuals with less obesity compared with Caucasians.

We have recently examined that interaction between the effects of diabetes and obesity on BCM by using surgically resected pancreas samples in 99 Japanese individuals [7]. Of these, 49 patients had been diagnosed with T2DM or pancreatic diabetes before operation. In

addition, a questionnaire on a family history of diabetes and history of obesity was conducted. As a result, in patients with diabetes mellitus (DM groups), BCM was decreased by 46% compared with age- and BMI-matched nondiabetic patients (NDM group). The reduction in BCM in Japanese patients with DM group was consistent with our prior report using autopsy pancreas [4]. Regarding the effects of obesity on BCM in patients with and without diabetes, no difference in BCM between lean and obese subjects was observed in the NDM and DM groups (Obesity was defined as body mass index (BMI) of 25kg/m^2 or greater). Similarly, there were no significant correlations between BCM and BMI, duration of obesity or maximum BMI in the NDM and DM group. These findings suggest that the increase in BCM in the face of insulin resistance is extremely limited in the Japanese (Figure 1), and the ethnic difference in BCM could be attributable to lower maximum insulin secretory ability in Japanese compared with Caucasians. We also assessed the effect of a first-degree family history of diabetes on BCM. Although there was no significant difference in BCM between patients with and without a family history of diabetes, in the DM group islet density was significantly decreased in patients with a family history compared with those without. We have previously reported that islet number rather than islet size is a major determinant of BCM, and islet density was negatively correlated with plasma glucose level in nondiabetic humans [8]. Reduced islet density yet greater islet size has also been reported in nondiabetic subjects with the TCF7L2 polymorphism who are susceptible to T2DM [9]. Together with these prior studies, the present study suggests that a genetic factor is associated with T2DM susceptibility through reduced islet number. Genome-wide association studies have currently detected genetic loci associated with T2DM, most of which are assumed to relate to the β -cell [10,11], also indicating the importance of β -cells in the pathogenesis of T2DM. It has also been reported that BCM was decreased by 20–40% in patients with impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) [12], suggesting that BCM is related to glucose intolerance even prior to the development of T2DM.

Given the fact that Japanese have even less beta cell functional capacity compared with Caucasians, the importance of treatment as well as prevention strategy for T2DM aiming to preserve or recover functional BCM should be emphasized in the Japanese population. Further studies are needed to determine genetic and environmental

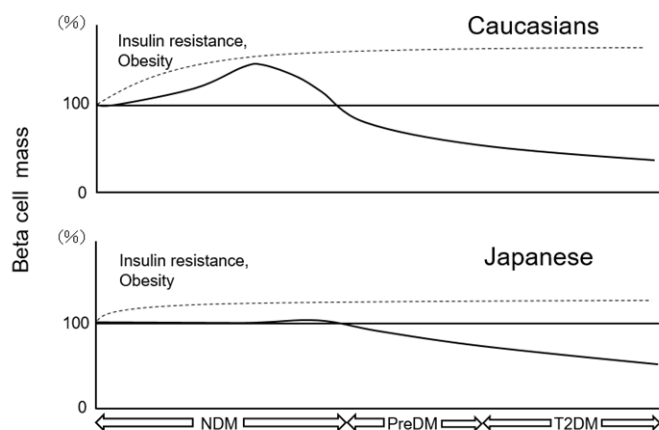


Figure 1. Hypothesis for change in beta cell mass during the development of insulin resistance and abnormal glucose tolerance [NDM: Non-diabetic; PreDM: Prediabetes; T2DM: Type 2 diabetes. BCM increases to adapt to the increased demand in obese nondiabetic individuals in the Caucasian population, while BCM in the face of insulin resistance is extremely limited in the Japanese. With progression to prediabetes and overt diabetes, progressive decline of BCM underlies the disease].

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factors regulating BCM in humans and clarify the underlying mechanisms of the ethnic difference in β -cell change in response to obesity.

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