complications. Further studies are necessary to evaluate the effect of the extract on other aspects related to the pathology.

Diabetes Mellitus and Glucose Metabolism

DYSREGULATED METABOLIC RESPONSE

Effects of Sodium Glucose Cotransporter 2 Inhibitor on Renal Renin-Angiotensin-Aldsoterone System

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Objective: The renoprotective effect of sodium glucose cotransporter 2 inhibitor (SGL2i) has been reported in diabetic patients. Local renin-angiotensin-aldosterone system (RAAS) is activated in diabetes mellitus and hypertension. We examined the effects of SGL2i on the RAAS in the obese diabetic rats fed a high salt diet. **Methods:** Zucker-diabetic rats (ZDR) and control rats were fed a high or normal salt diet and were treated with canagliflozin for 8 weeks. Blood pressure (BP), blood glucose (BG), PRA, plasma aldosterone (PAC), urinary albumin excretion (UAE), urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG), gene expression of angiotensinogen in the kidney were measured. **Results:** ZDR febd a high salt diet showed high BP, increased UAE and urinary 8-OHdG and elevated angiotensinogen mRNA levels. Treatment with canagliflozin significantly decreased BP, BG, UAE, urinary 8-OHdG and and renal angiotensinogen mRNA levels compared with control rats (p&lt0.05). **Discussion and Conclusion:** The closer mechanism of renoptotection of SGL2i in diabetes mellitus is unclear. We have reported that the repoprotective effects of type 2 angiotensin receptor antagonist or mineralocorticoid receptor blocker were partly due to the decreased RAAS in the kidney. Decreased renal RAAS by the treatment with canagliflozin may contribute to the renoprotection in DZR.

Diabetes Mellitus and Glucose Metabolism

DYSREGULATED METABOLIC RESPONSE

Efficient Restoration of Beta Cell Dedifferentiation by Calorie Restriction With High Fat/Low Carbohydrate Diet in Obese Diabetes Model and the Possible Role of GLP-1

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In type 2 diabetes, pancreatic beta cells are gradually 'exhausted' and fall into beta cell dysfunction, which proceeds more severe insulin dependence. Among the proposed mechanisms of beta cell dysfunction such as endoplasmic reticulum stress and oxidative stress, the beta cell heterogeneity has attracted the researcher's interest recently. In 2012, Talchai et al. revealed that the beta cells were dedifferentiated in diabetic mice model, and nowadays it is considered as one form of the beta cell heterogeneity and is observed broadly among diabetic animal models and human patients. Previously we showed that food restriction had the best effect to restore beta cell gene expression in obese diabetic model mice, among the known diabetic treatments which we tested. In the current study, we aimed to unveil the molecular basis in the improvement of beta cell dedifferentiation during the calorie restriction. First, we utilized the high-fat/low carbohydrate diet (HF) or low-fat/high carbohydrate (HC) diet, to determine whether fat restriction or sugar restriction reduces the beta cell dedifferentiation in obese mice. When calorie intake was restricted evenly, both HF diet and HC diet decreased the body weight and hyperglycemia in db/db mice equally. Albeit the same metabolic profile, db/db group fed with HC diet had more enlarged islets and more dedifferentiated beta cell features than db/dbs fed with HF diet, which indicated the compensatory beta cell response in HC diet group. Moreover, HC diet group showed more severe fatty liver than HF diet group, along with the elevated synthesis and accumulation of triglycerides and cholesterol in liver. It is speculated that the insulin resistance in liver might impact on the beta cell dedifferentiation. Next, we analyzed the effect of glucagon-like peptide 1 (GLP-1) on beta cell dedifferentiation, since GLP-1 is secreted more from intestine by protein and fat intake, rather than by sugar intake. Also, increasing number of reports have suggested the improving effect of GLP-1 on beta cell dysfunction and fatty liver. Indeed, GLP-1 administration altered the reduced beta cell/alpha cell ratio in db/db mice, which indicated the restoration of beta cell heterogeneity. We are now investigating if GLP-1 administration reimburse the beta cell dedifferentiation in db/db mice fed with HC diet, to illuminate the role of incretins in beta cell dedifferentiation induced by unbalanced nutrition during diet. Also, we will present the RNA sequencing data of the liver in db/db mice fed with HF and HC diet, to elucidate the key molecules and genes which connect the beta cell function and metabolic state in liver.

Diabetes Mellitus and Glucose Metabolism

DYSREGULATED METABOLIC RESPONSE

Identification of Sortilin Alternatively Spliced Variants in 3T3L1 Adipocytes

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Type 2 diabetes mellitus (T2DM) is a chronic and progressive metabolic disease with no cure. Adipocytes play a crucial role in glycemic regulation and take up circulating glucose in response to insulin signaling. In T2DM, translocation of major glucose transporter 4 (Glut4) from