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**SUN-665**

Peripheral CB1 Blocker Improves Metabolism in DIO Mice Independent of Hepatic FGF21

Obesity is associated with an overactive endocannabinoid system, and selective blockade of $CB_1R$ in peripheral tissues, including the liver, reverses HFD-induced metabolic abnormalities by restoring normal lipid and glucose homeostasis. Fibroblast growth factor-21 (FGF21) has emerged as a major endocrine regulator derived from the liver that reduces adiposity and hepatic steatosis and improves glucose tolerance and insulin sensitivity, with changes similar to those induced by $CB_1R$ blockade. Here we investigated whether FGF21 mediate the metabolic effects of CB1R blockade in DIO mice.

In C57BL/6J wild-type mice, HFD caused a robust increase in hepatic *Fgf21* mRNA and serum FGF21 levels, which were reversed by chronic $CB_1R$ blockade to levels observed in STD or vehicle-treated hepatocyte-specific $CB_1R^{-/-}$ ($LCB1^{-/-}$) mice, indicating activation of $CB_1R$ in the liver is largely involved in HFD-induced "FGF21-resistant" state. In contrast, the expression of the FGF21 receptor *Fgfr1* and co-receptor β-klotho (*Klb*) were dramatically reduced by HFD in both epididymal fat and brain tissue in wild-type mice, and these effects were reversed by peripheral $CB_1R$ antagonist JD5037 treatment.

To address whether FGF21 mediated the metabolic effects of $CB_1R$ blockade, we repeated JD5037 treatment in liver-specific $FGF21^{-/-}$ (FGF21-LKO) mice. Surprisingly, JD5037 treatment was almost equally effective in both HFD-fed wild-type and in FGF21-LKO mice in reducing body weight and hepatic steatosis, attenuating hyperinsulinemia and hyperleptinemia. The current data suggest that peripheral $CB_1R$ blockade in obese mice improves insulin sensitivity and energy expenditure independently of hepatic FGF21.

# Diabetes Mellitus and Glucose Metabolism

## CLINICAL AND TRANSLATIONAL GLUCOSE METABOLISM AND DIABETES

### *Utility of Continuous Glucose Monitoring in Children with Type 1 Diabetes: Is HbA1c Enough?*

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**MON-625**

Utility of continuous glucose monitoring in children with Type 1 diabetes: Is HbA1c enough?

**Introduction:** Type 1 diabetes is an autoimmune condition resulting in insulin deficiency that requires daily insulin therapy and self-monitoring of blood glucose. Continuous glucose monitoring (CGM) systems allow for measurement of interstitial fluid glucose levels in a continuous fashion to identify variations and trends that are not feasible with conventional self-monitoring. Hemoglobin A1C (HbA1C) is the method used to assess adequate glycemic control and relates to future risk of developing complications. Current evidence has shown improvement in HbA1C with concomitant use of CGM in adults over 25 years of age with Type 1 diabetes, whereas studies in children and adolescents have failed to show this. However, it is important to note the limitations in HbA1C use as it is a marker of average blood glucose over 3 months but does not reflect glycemic variability. More recent data has suggested that factors such as time in range (TIR), which can be determined with CGM use, are also associated with decrease risk of diabetes complications.

**Methods:** The goal of our study was to analyze the change in HbA1C levels after using a CGM (DEXCOM G4, G5, G6) over a 6-month period in pediatric patients with Type I diabetes. Two HBA1c levels 3 months apart from 92 patients were collected before using a CGM and two while using a CGM. Results were compared by using a dependent samples t-test. IBM SPSS 25.0 was used for data analysis.

**Results:** Preliminary analysis indicates the average change in HBA1C among the patients (N=92) before (-0.08 ± 1.16) and while using the CGM (0.12 ± 1.00) was not significantly different ($t$ (79) = -1.27, $p$ = 0.21). The average change in HBA1C was also not significantly different ($p$>0.05) among the patients before and while using the CGM for gender (males and females), age groups (0-7 years, 8-14 years, and 15-24 years), and generations of DEXCOM used (G4, G5, and G6).

**Conclusion:** As has been shown in other studies, we did not find a significant change in HbA1c after CGM use for 6 months in our patients. While HbA1C is a reflection of blood sugars over a 3-month period, it does not provide information about glycemic excursions. Metrics derived from CGM use, such as TIR, can provide actionable information which we did not address in our study. There have been reports of the association between TIR and long-term complications of diabetes. Most data comes from studies in adults and pediatric data is lacking. We propose that future studies must look into CGM metrics such as TIR to better define glycemic control in pediatric patients with diabetes mellitus.

# Diabetes Mellitus and Glucose Metabolism

## METABOLIC INTERACTIONS IN DIABETES

### *Murine Cecal Ligation and Puncture (CLP) Perturbs Phosphorylation of Insulin Receptor Substrate 2 (IRS-2)*

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**SUN-651**

**Abstract:** Hyperglycemia is a characteristic finding in sepsis, and its presence worsens outcome (1). Patients with sepsis need larger doses of insulin to reduce glucose levels. This abnormality has been termed "insulin resistance" but the molecular mechanism by which sepsis attenuates the insulin signaling pathway is unknown. Previous work has