



# 读书报告

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2017年03月19日

# GLUT-2

糖吸收

调节因素

胞内信号分子

葡萄糖敏感性受体及通道蛋白

内分泌及旁分泌

胰岛素

瘦素

肠道内分泌激素

应激和糖皮质激素

ARTICLE IN PRESS

Original Article

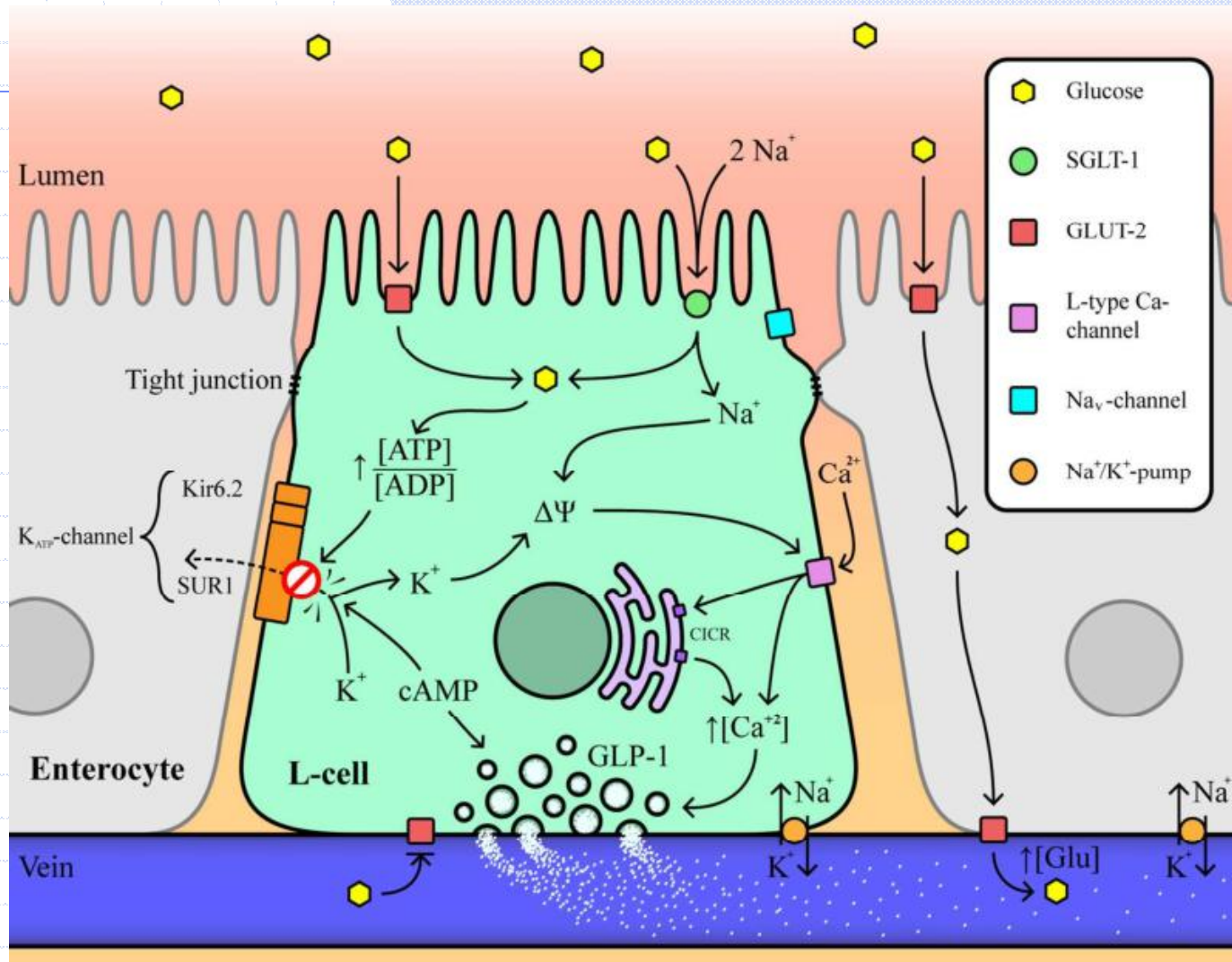


MOLECULAR  
METABOLISM

IF=5.363

# Intestinal invalidation of the glucose transporter GLUT2 delays tissue distribution of glucose and reveals an unexpected role in gut homeostasis

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## **Objective:**

Intestinal glucose absorption is orchestrated by specialized glucose transporters such as SGLT1 and GLUT2. However, the role of GLUT2 in the regulation of glucose absorption remains to be fully elucidated.

## **Methods:**

We wanted to evaluate the role of GLUT2 on glucose absorption and glucose homeostasis after intestinal-specific deletion of GLUT2 in mice (GLUT2<sup>ΔIEC</sup> mice).

## Results:

As anticipated, intestinal GLUT2 deletion provoked **glucose malabsorption** as visualized by the **delay** in the distribution of oral sugar in tissues.

Consequences of intestinal GLUT2 deletion in GLUT2<sup>ΔIEC</sup> mice were **limiting** body weight gain despite normal food intake, **improving** glucose tolerance, and **increasing** ketone body production.



**calorie restriction**

## Results:

Other adaptations to intestinal GLUT2 deletion were **reduced** microvillus length and **altered** gut microbiota composition, which was associated with improved **inflammatory status**.

Moreover, a reduced density of glucagon-like peptide-1 (GLP-1) positive cells was **compensated** by increased GLP-1 content per L-cell, suggesting a preserved enteroendocrine function in GLUT2<sup>ΔIEC</sup> mice.



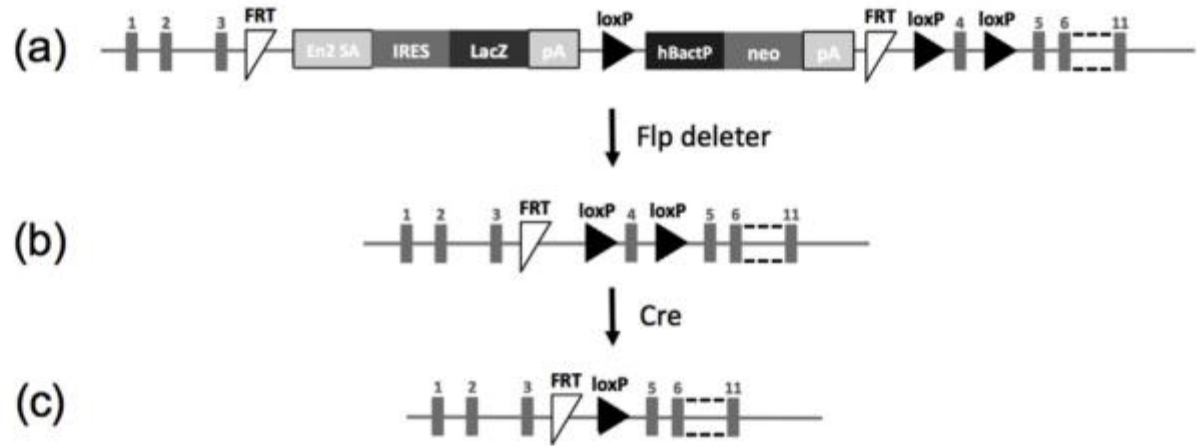
## Conclusions:

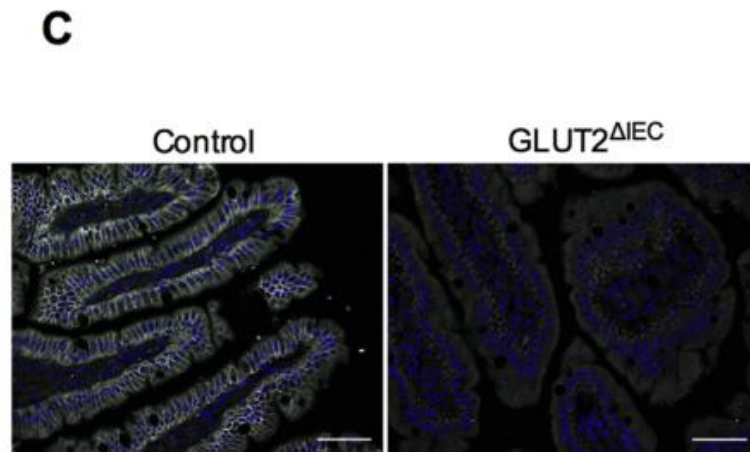
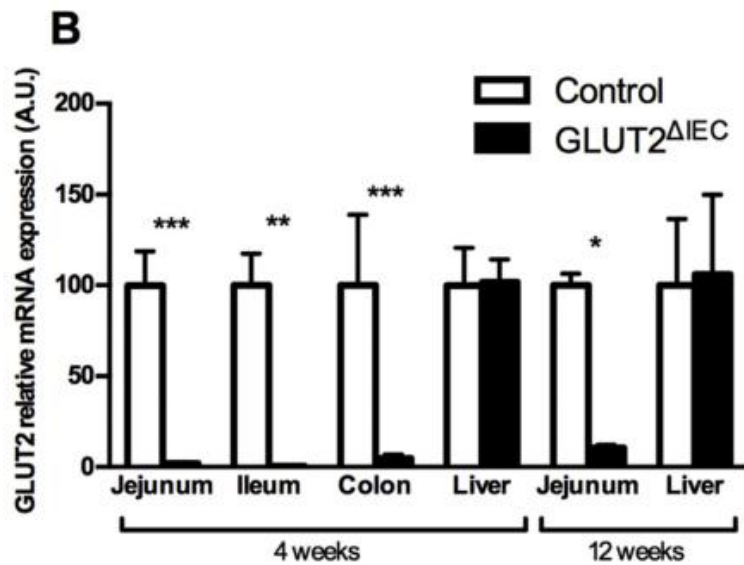
Intestinal GLUT2 modulates glucose absorption and constitutes a control step for the distribution of dietary sugar to tissues.

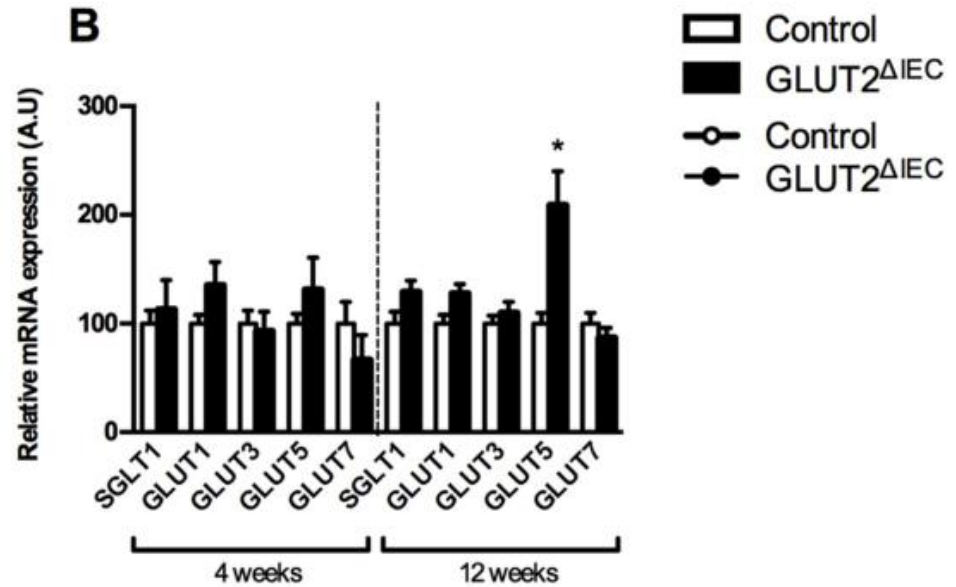
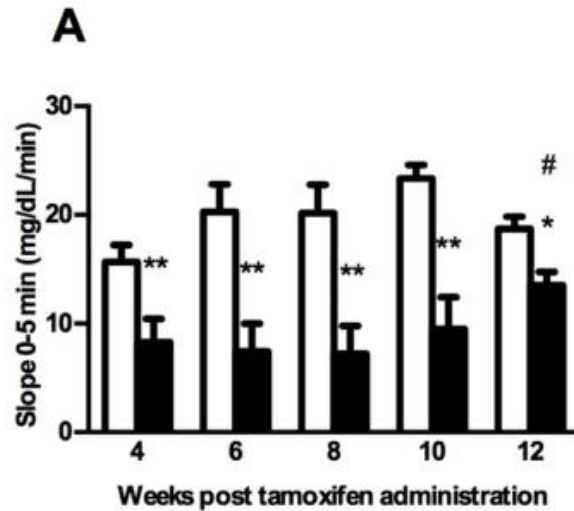
Consequently, metabolic and gut homeostasis are improved in the absence of functional GLUT2 in the intestine, thus mimicking calorie restriction.



**A**





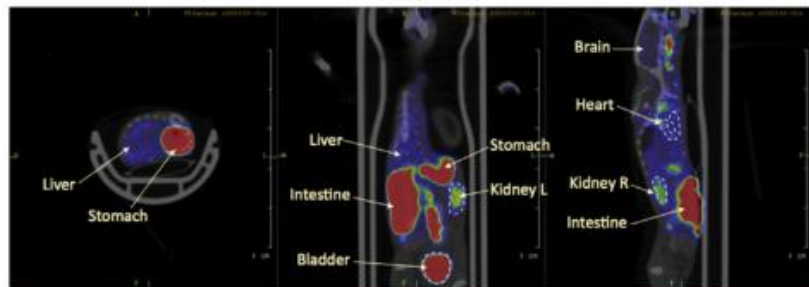


**C**

Figure 2: GLUT2<sup>ΔIEC</sup> mice display glucose malabsorption.

C

Control

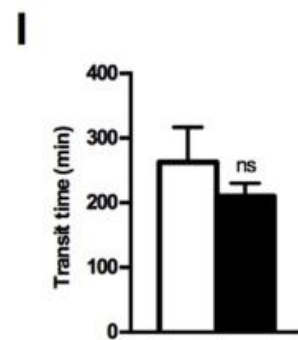
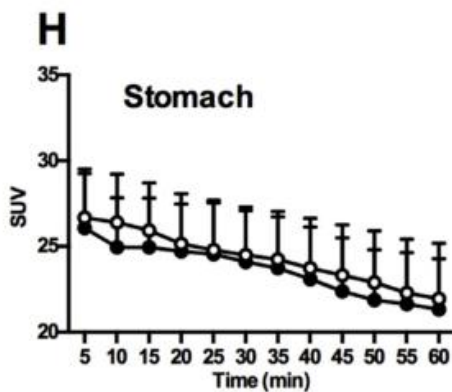
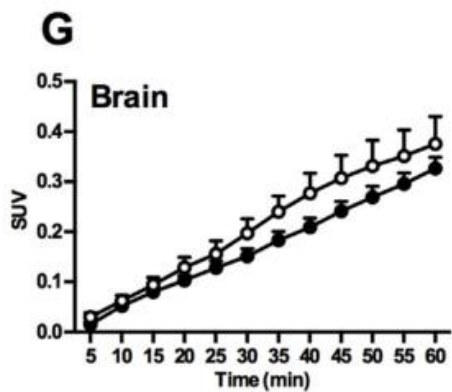
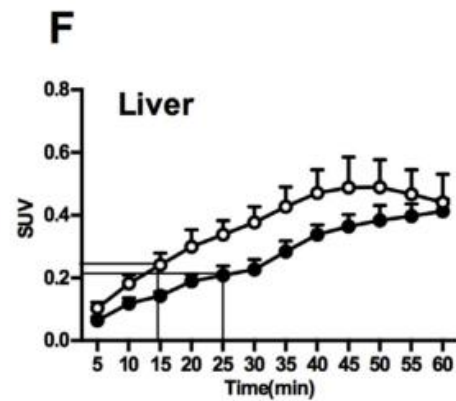
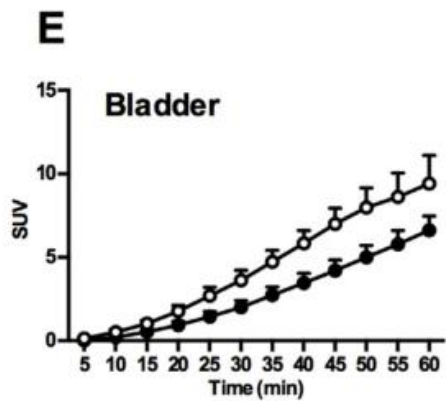
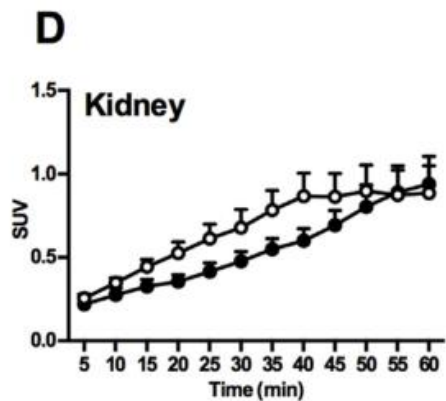


4 weeks

12 weeks

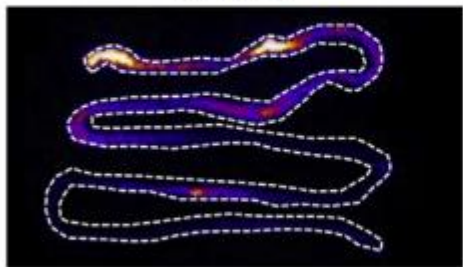
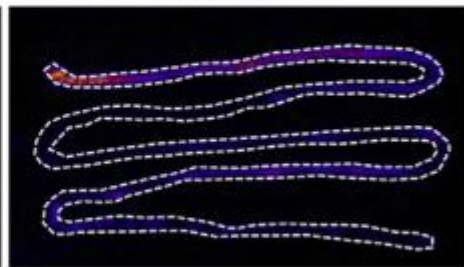
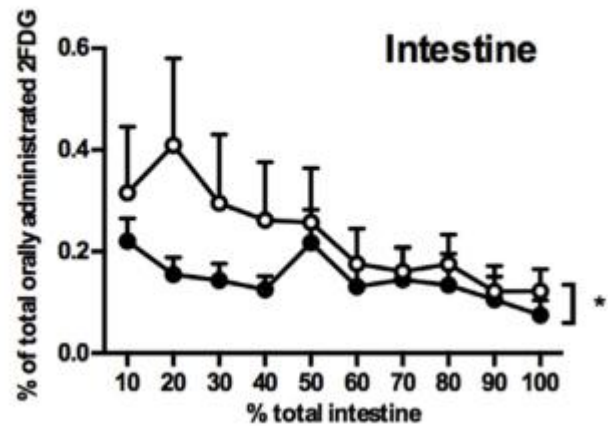
GLUT2<sup>ΔIEC</sup>

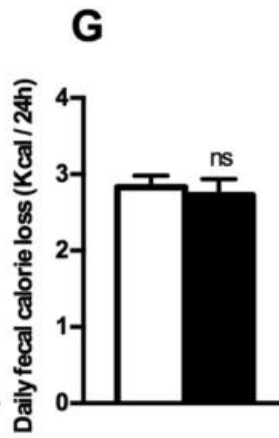
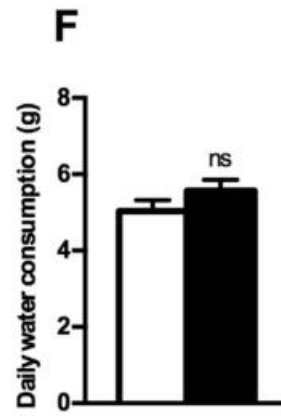
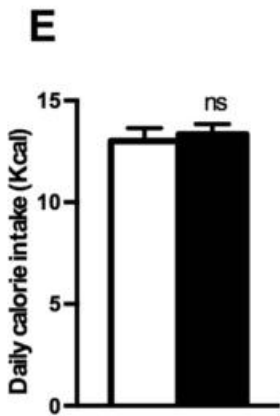
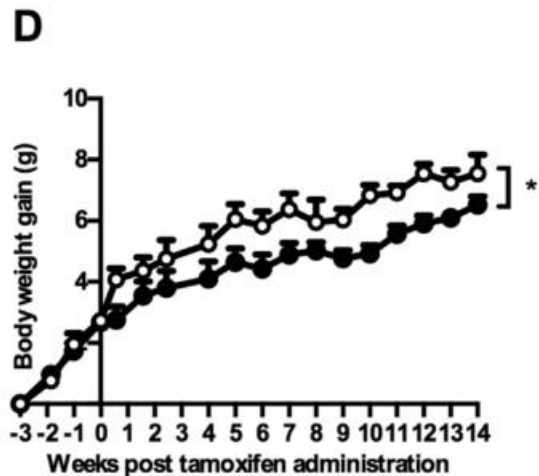
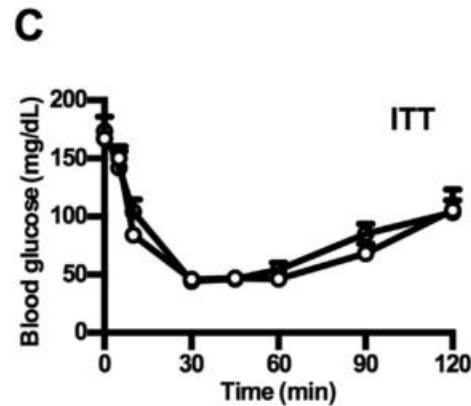
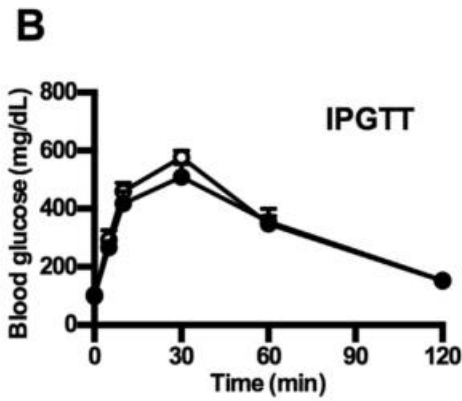
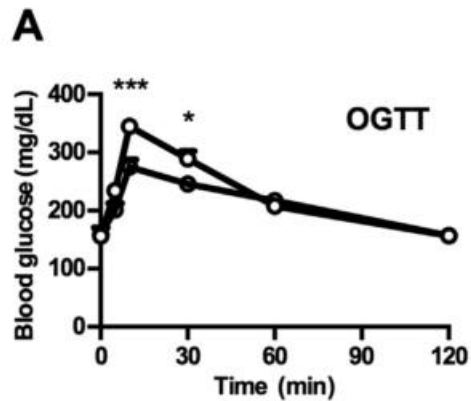


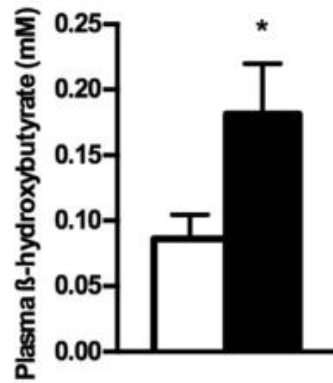
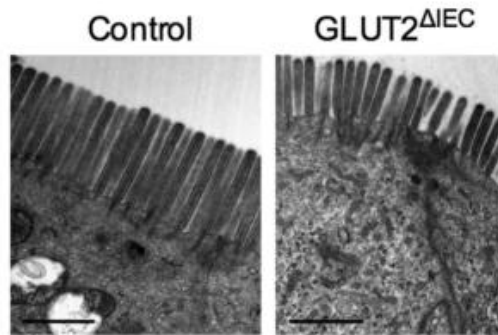
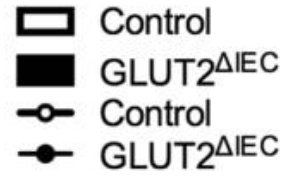
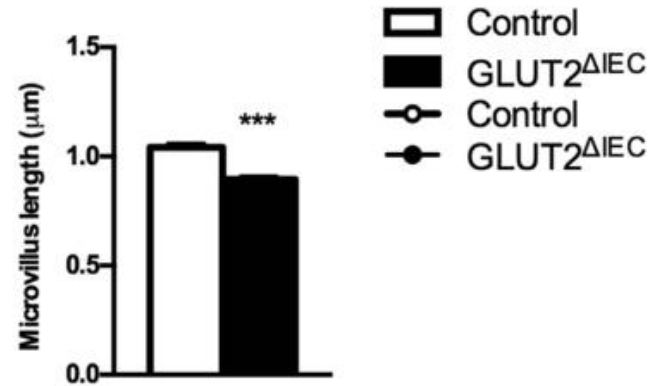


**J**

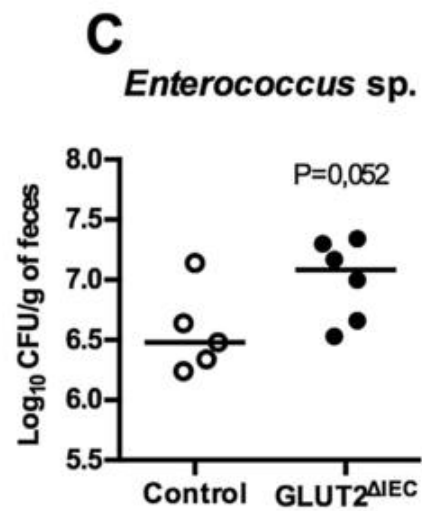
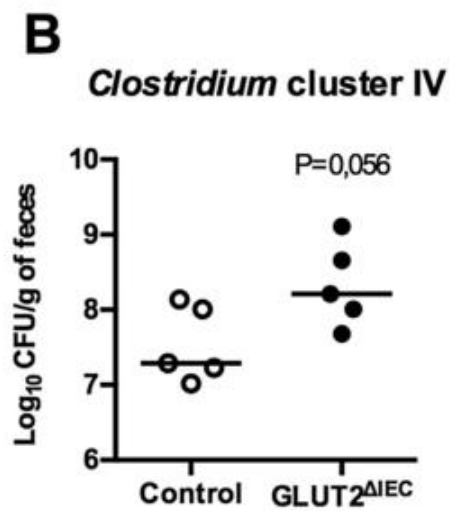
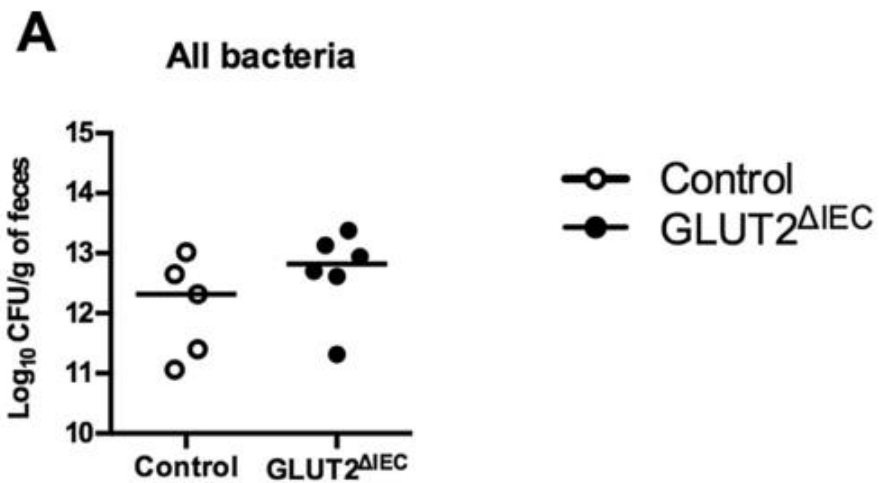
Control

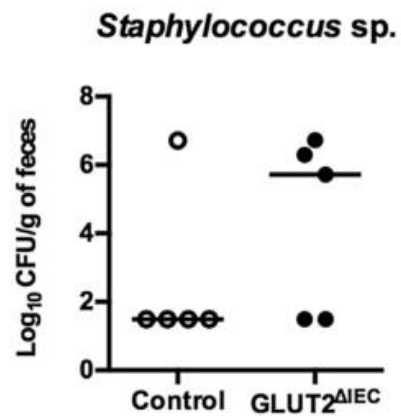
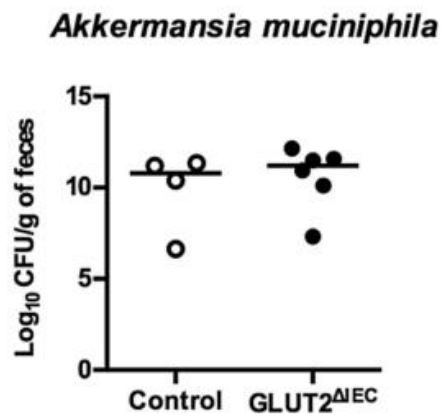
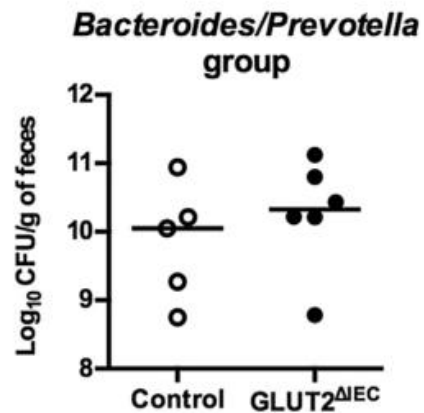
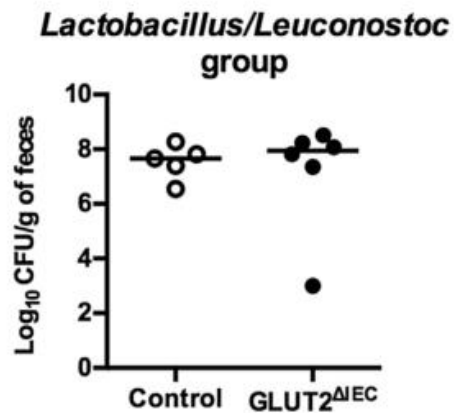
GLUT2 $\Delta$ IEC**K**

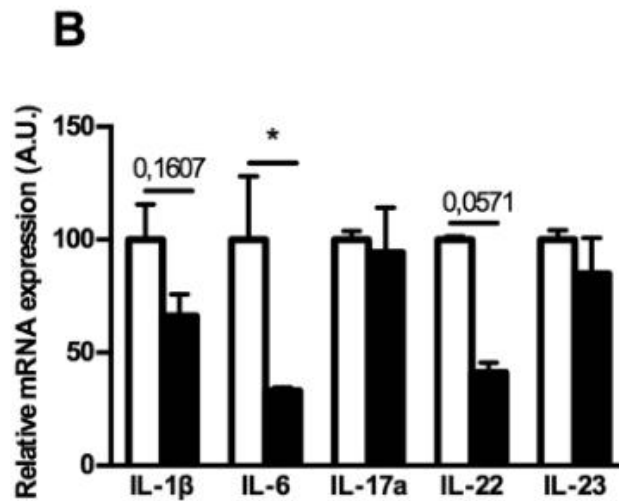
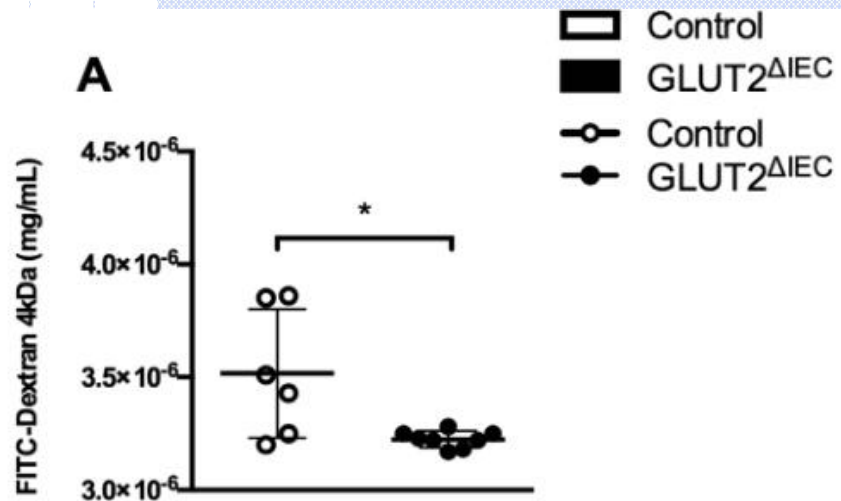


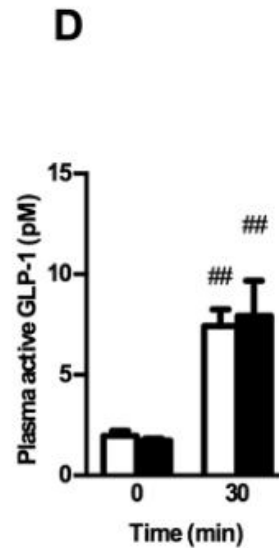
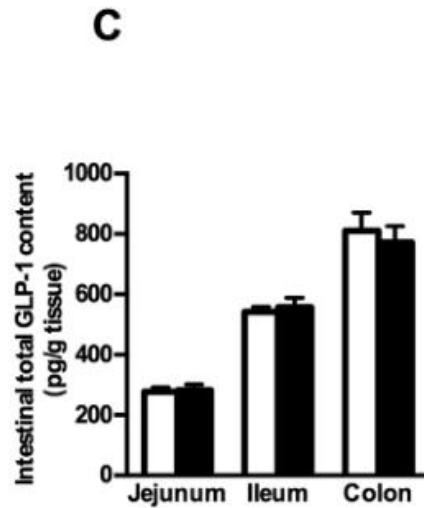
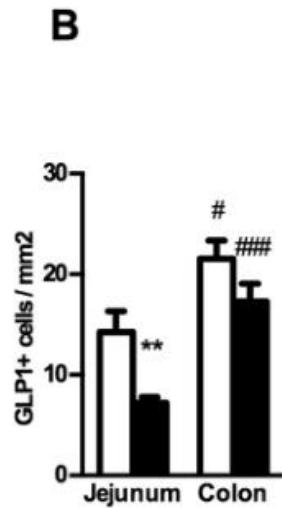
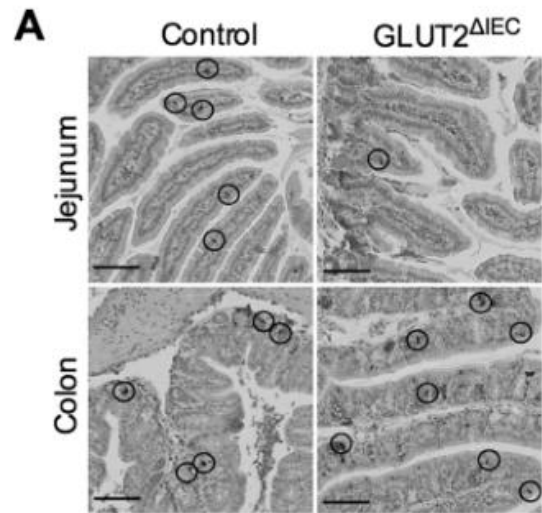
**H****I****J**

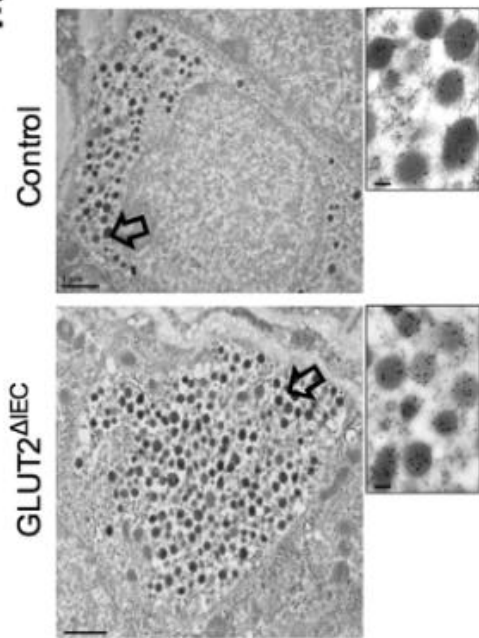
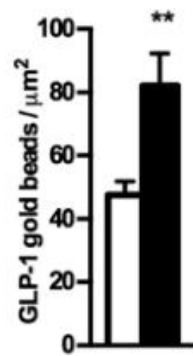
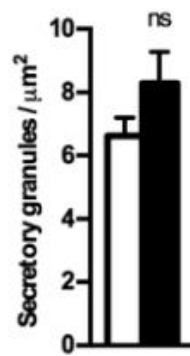
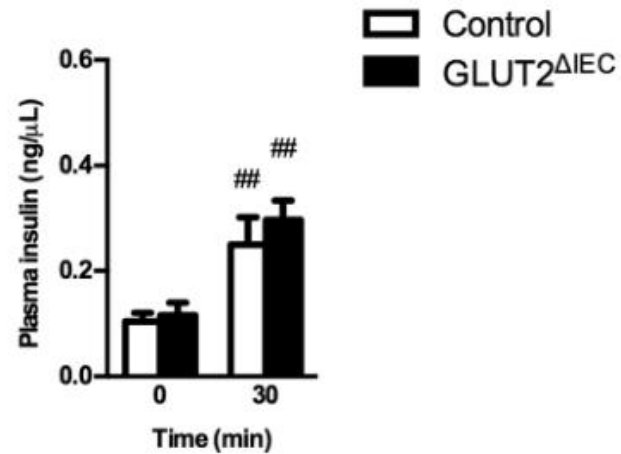




**D****E****F****G**

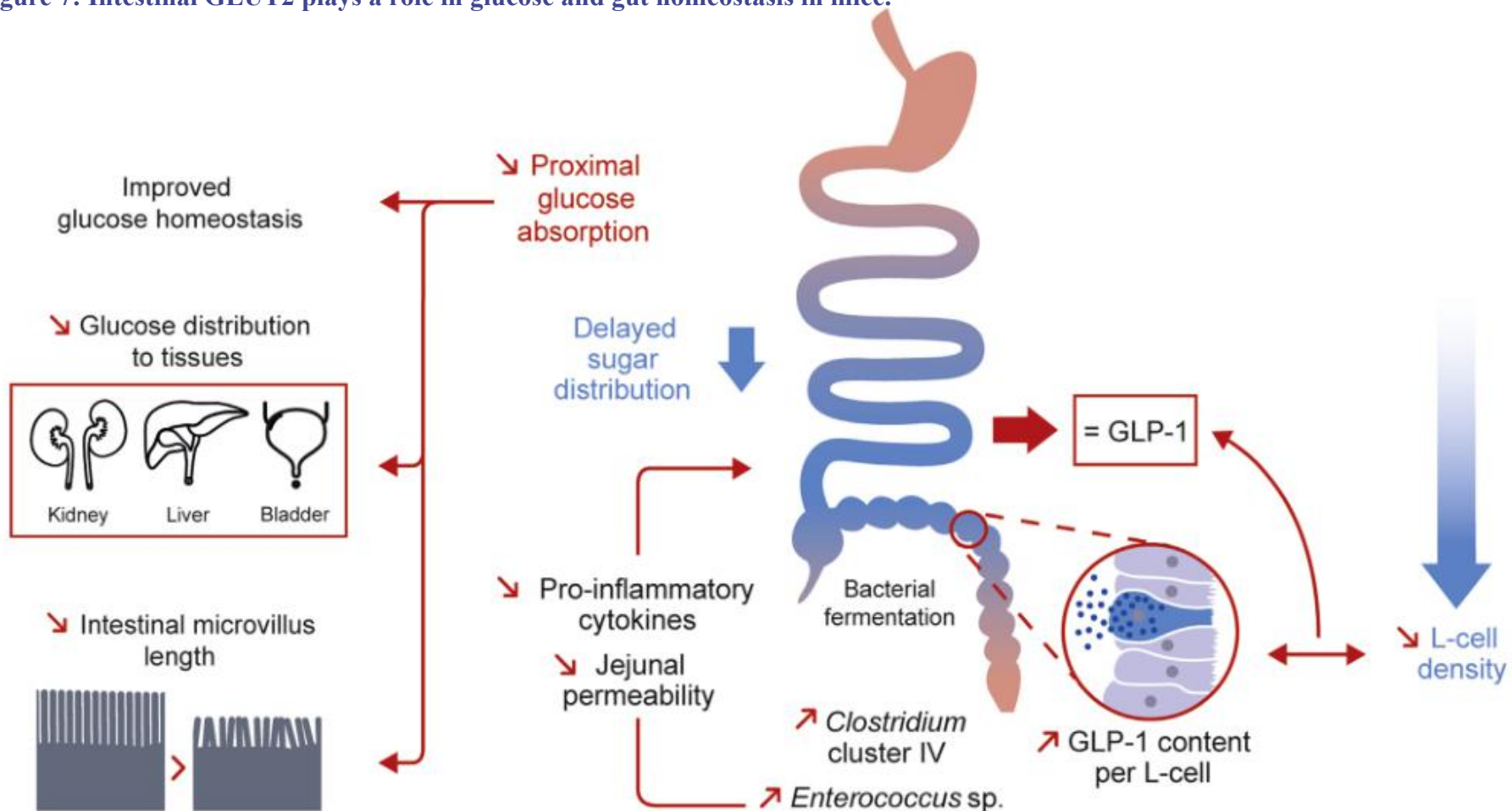




**E****F****G****H**

Control  
GLUT2 $\Delta$ IEC

Figure 7: Intestinal GLUT2 plays a role in glucose and gut homeostasis in mice.



Intestinal inactivation of GLUT2 in mice reduces proximal intestinal absorption of glucose. This sugar malabsorption modifies body homeostasis by means of

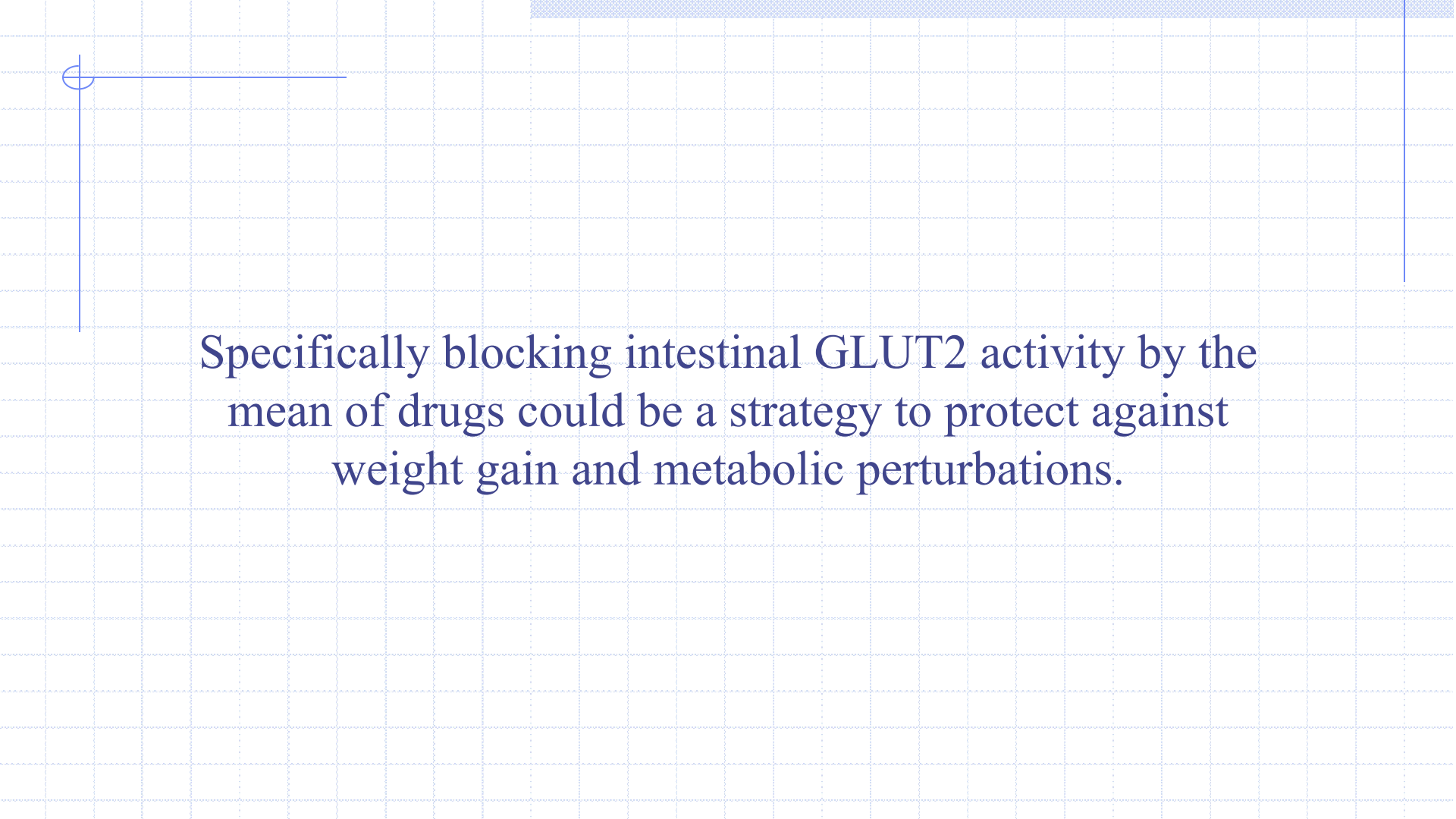
- 1) improving glucose homeostasis,
- 2) delaying tissue distribution of glucose to peripheral tissues
- 3) reducing intestinal microvillus length, which could result in a global nutrient malabsorption, mimicking caloric restriction.

Our hypothesis is that blocked proximal glucose absorption causes an increased glucose delivery to distal intestine, giving new fermentable energy sources to the distal gut microbiota.

Thus, we observed increased levels of commensal *Clostridium cluster IV* and *Enterococcus* sp. in our model. These bacteria show positive impact on gut homeostasis, including a reduced expression of pro-inflammatory cytokines through butyrate production and reduced gut permeability.

Surprisingly, intestinal GLUT2 invalidation leads to a strong loss in enteroendocrine L-cell density, with no impact on GLP-1 plasma levels thanks to increased GLP-1 content per GLUT2<sup>ΔIEC</sup> L-cell.



A decorative graphic consisting of a blue circle at the top left, a horizontal blue line extending to the right, and a vertical blue line extending downwards. The background is a light blue grid pattern.

Specifically blocking intestinal GLUT2 activity by the mean of drugs could be a strategy to protect against weight gain and metabolic perturbations.

感悟



方法

扩展



# THANKS

