Physiogenex
THE METABOLIC DISEASES EXPERTS

High fat diet mouse - Prebiotics

A dedicated nutritional animal model to demonstrate that your prebiotics impact metabolic parameters in adapted animal models

Key benefits

- ✓ Validate beneficial effects of your prebiotics on : body weight and adipose tissue weight gain, glucose intolerance and insulin resistance, hepatic insulin signalling, inflammation
- ✓ Dedicated nutritional animal model to demonstrate that your compound improves both early or established diabetes

ANIMAL MODEL

- Background strain: C57Bl6/J mouse
- Diet: High Fat Diet
- Reference compounds: prebiotic, GLP-1, DDP IV inhibitor

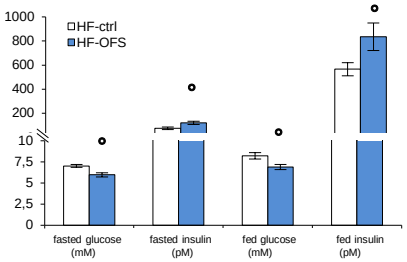
SCIENTIFIC RELEVANCE

Prevention – Oligofructose (OFS)

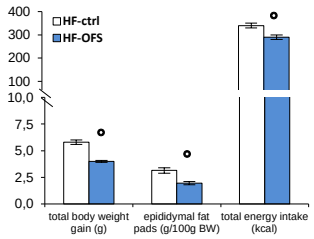
1 - **Impaired insulin secretion** (4 weeks high fat diet):

- OFS **decreases plasma glucose** and **increases plasma insulin levels** (both fasted and fed conditions)
- OFS **lowers body weight gain, epididymal fat pads and total energy intake**

Fasted/fed plasma glucose and insulin



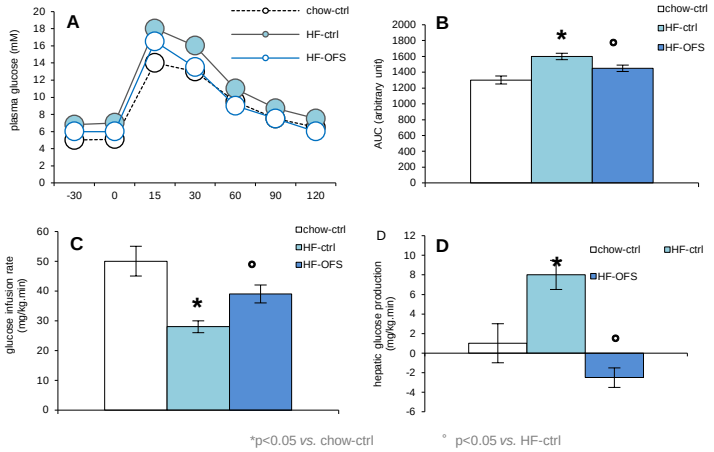
Body weight gain, epididymal fat pads and energy intake



° p<0.05 *vs.* HF-ctrl

- OFS **reduces glucose intolerance**
- OFS **improves insulin sensitivity**

Oral glucose tolerance test (A, B) and hyperinsulinemic euglycemic clamp (C, D)



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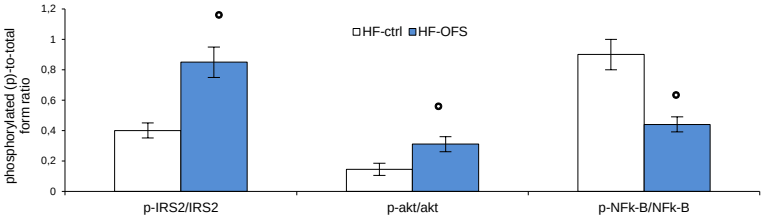
- Oligofructose **stimulates insulin signaling pathway**

Phosphorylated-to-total from ratio determined by Western blot

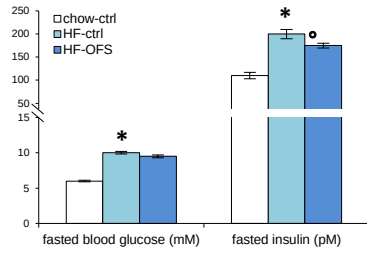


° p<0.05 *vs.* HF-ctrl

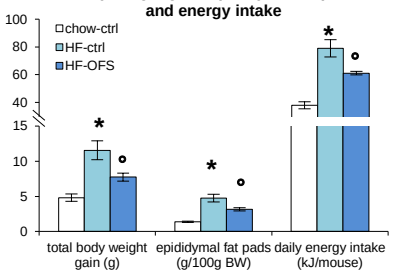
2 - **Impaired insulin action** (14-weeks high fat diet):

- OFS **decreases hyperinsulinemia and improves insulin sensitivity**
- OFS **reduces total body weight gain, epididymal fat pads and energy intake**

Fasted plasma glucose and insulin



Body weight gain, epididymal fat pads and energy intake



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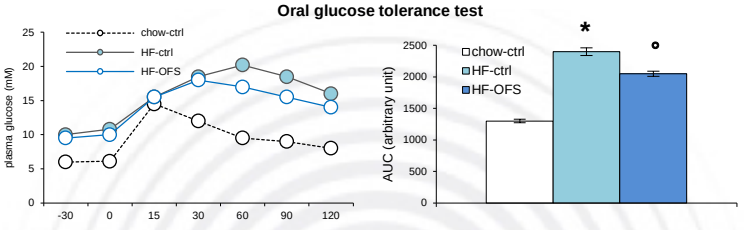
- OFS **reduces glucose intolerance** in diabetic mice
- OFS **reduces inflammation** in diabetic mice

Oral glucose tolerance test



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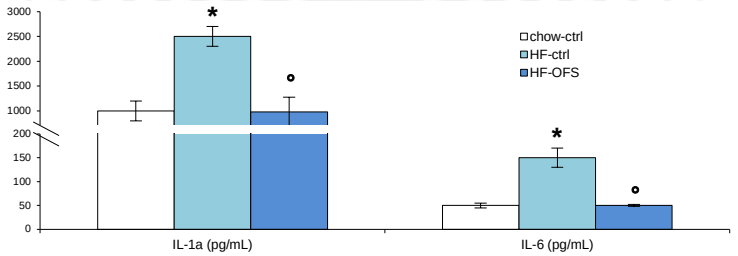
Inflammation markers IL-1a and IL6 plasma levels



*p<0.05 *vs.* chow-ctrl ° p<0.05 *vs.* HF-ctrl

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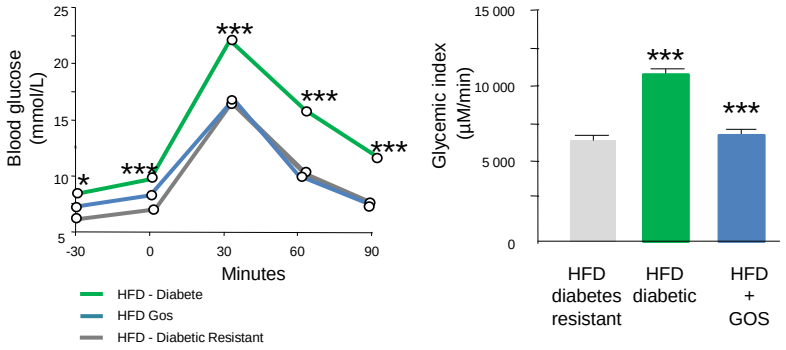
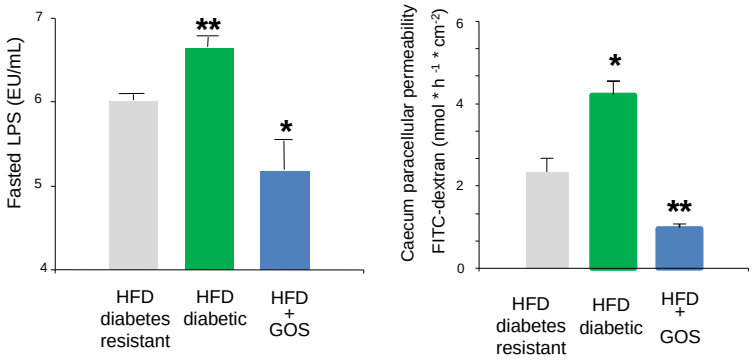
Prevention – Dietary fibres (GOS)

- GOS **prevents the occurence of diabetic phenotype**



* p <0.05 GOS *vs* diabetic *** p<0.001 GOS *vs* diabetic

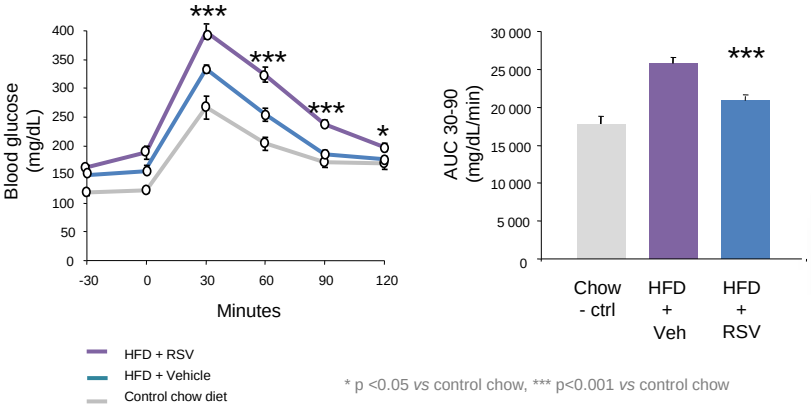
- GOS **prevents increase in plasma LPS levels and lowers paracellular permeability**



Therapeutics: Resveratrol

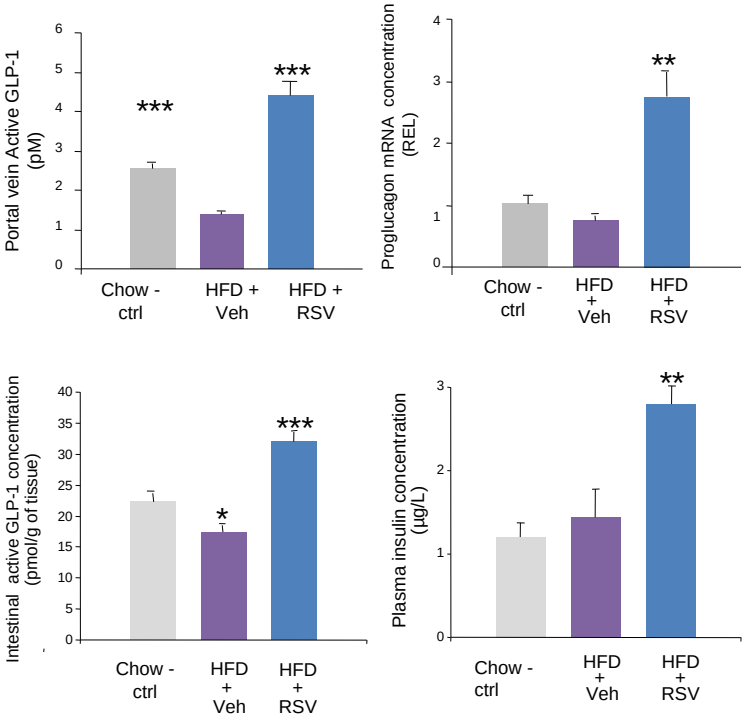
Resveratrol:
- a potent anti-diabetic agent at high doses
- has **a prebiotic effect on gut microbia** (Dao et al, 2011)

In mice fed a 5-week high fat diet (HFD 70%), **resveratrol reduces glucose intolerance** without affecting fasting glycemia.



* p <0.05 *vs* control chow, *** p<0.001 *vs* control chow

Resveratrol **increases levels of GLP-1 and insulin.**



** p <0.01 *vs* control chow, *** p<0.001 *vs* control chow

ADD-ON STUDIES

• Intestinal microflora characterization in partnership with **Vaiomer** :

Metagenomics, Transcriptomics, Proteomics and Metabolomics

REFERENCES

Delmée E et *al*. Life Sci. 2006 Aug 1;79(10):1007-13.
Dao TM et *al*. PLoS One. 2011;6(6).

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