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Perinatal programming of intestinal homeostasis following exposure to a high fat diet in male rats offspring

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Objective: This study aimed at studying the effects of a peri-gestational exposure to an obesogenic diet with a prebiotic supplementation (inulin) on the anatomofunctional development of the digestive system and associated metabolic consequences of the growing male offspring.

INTRODUCTION Perinatal period is characterized by developmental phases with high sensitivity to the environmental factors. Among the risk factors, malnutrition or maternal obesity are now recognized to program children's metabolism and promote the occurrence of obesity or type 2 diabetes during postnatal life. This work was dedicated to the peri-gestational exposure of dams to an obesogenic diet (high fat diet, HFD) and the exploration of the prebiotic supplementation benefits

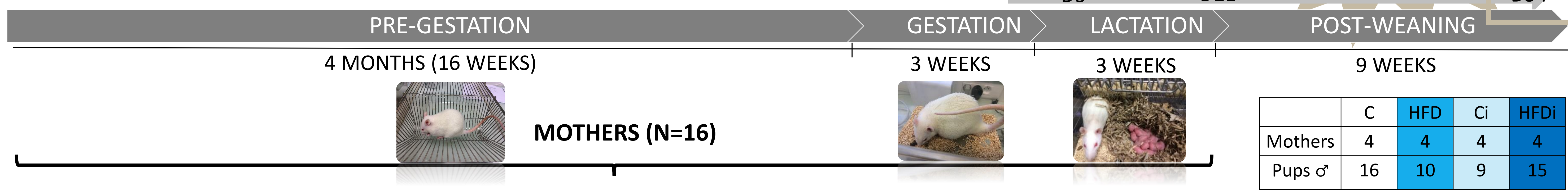
HYPOTHESIS



1. Perinatal HFD : cause of \nearrow the occurrence of obesity, associated with metabolic disorders and disturbances of digestive function in male offsprings ?
2. Prebiotic: limitation of observed disorders induced by the HFD ?



METHODS



HIGH FAT DIET (HFD)

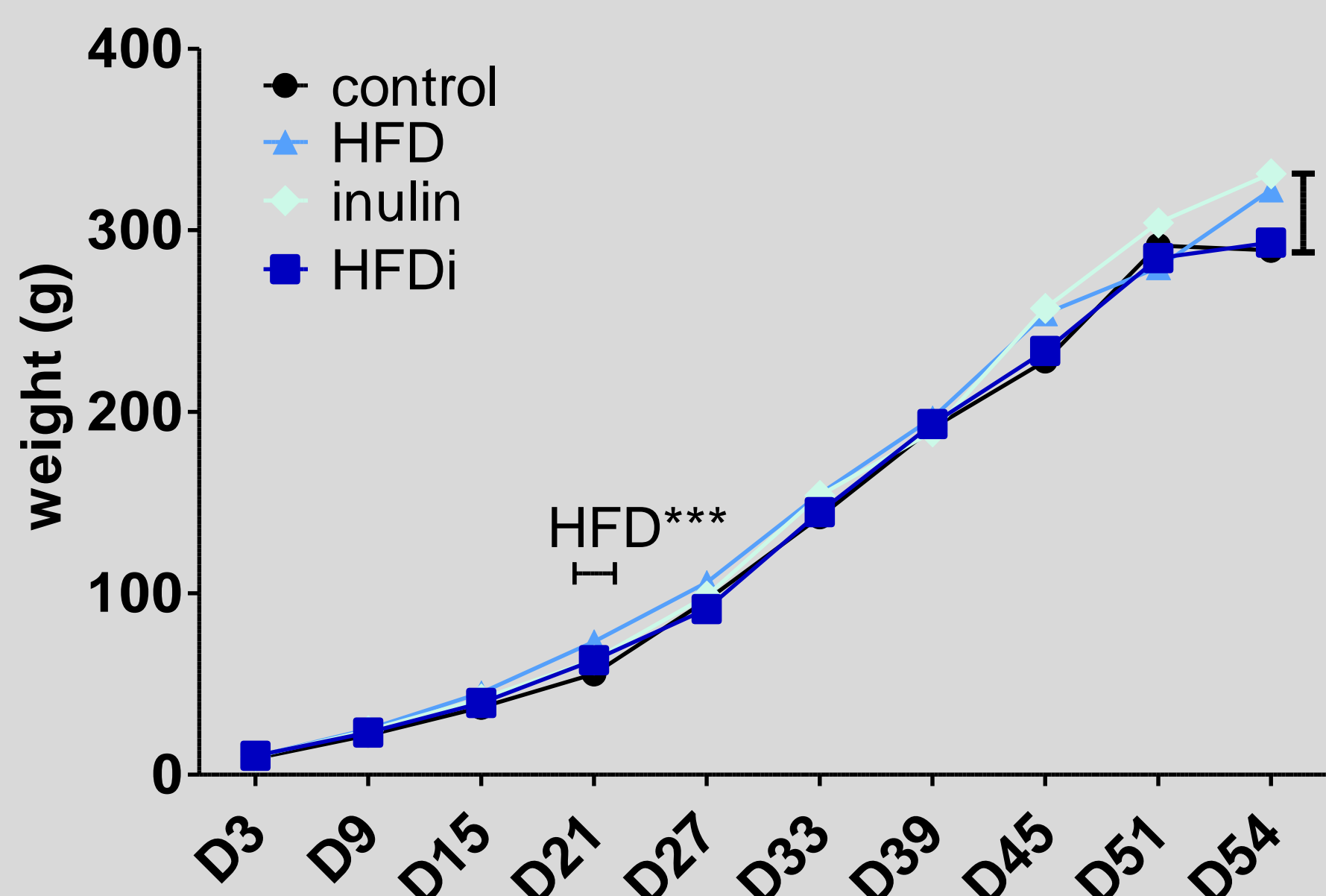
- 60% kcal fat
- 5.21 kcal /g
- D12492 SSMIFF Research Diets

INULIN (i)

- Food fiber (β 2-1 fructane)
- Prebiotic effect

RESULTS

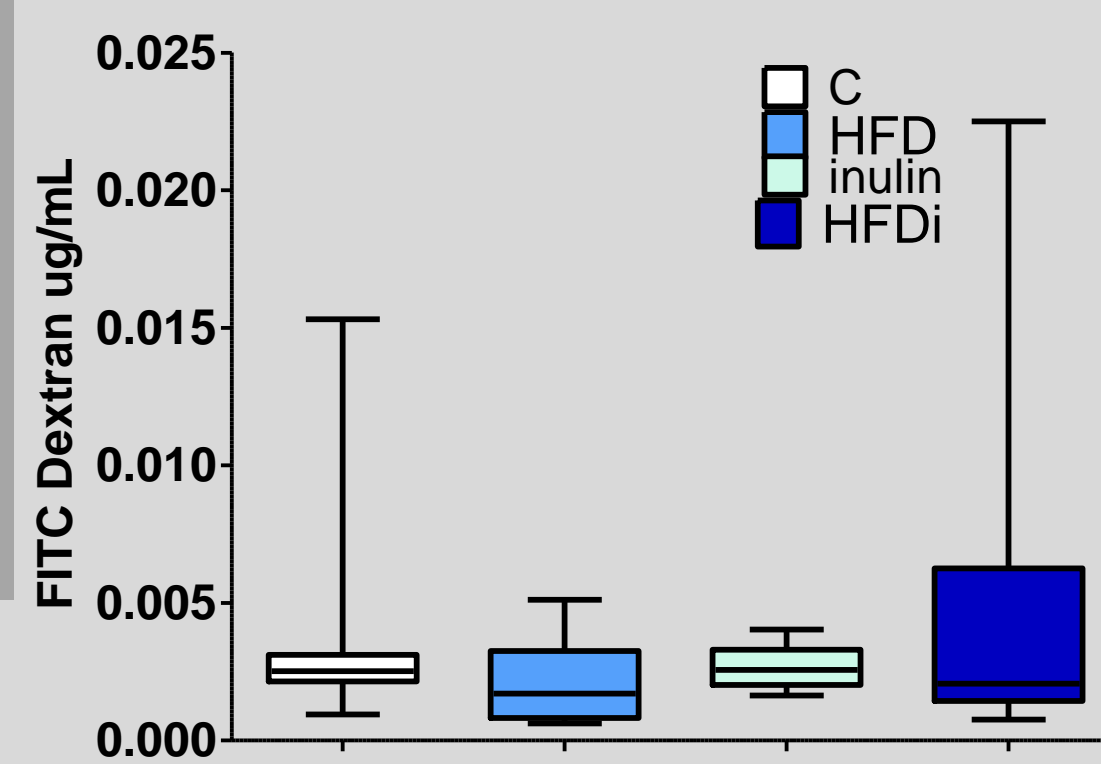
WEIGHT



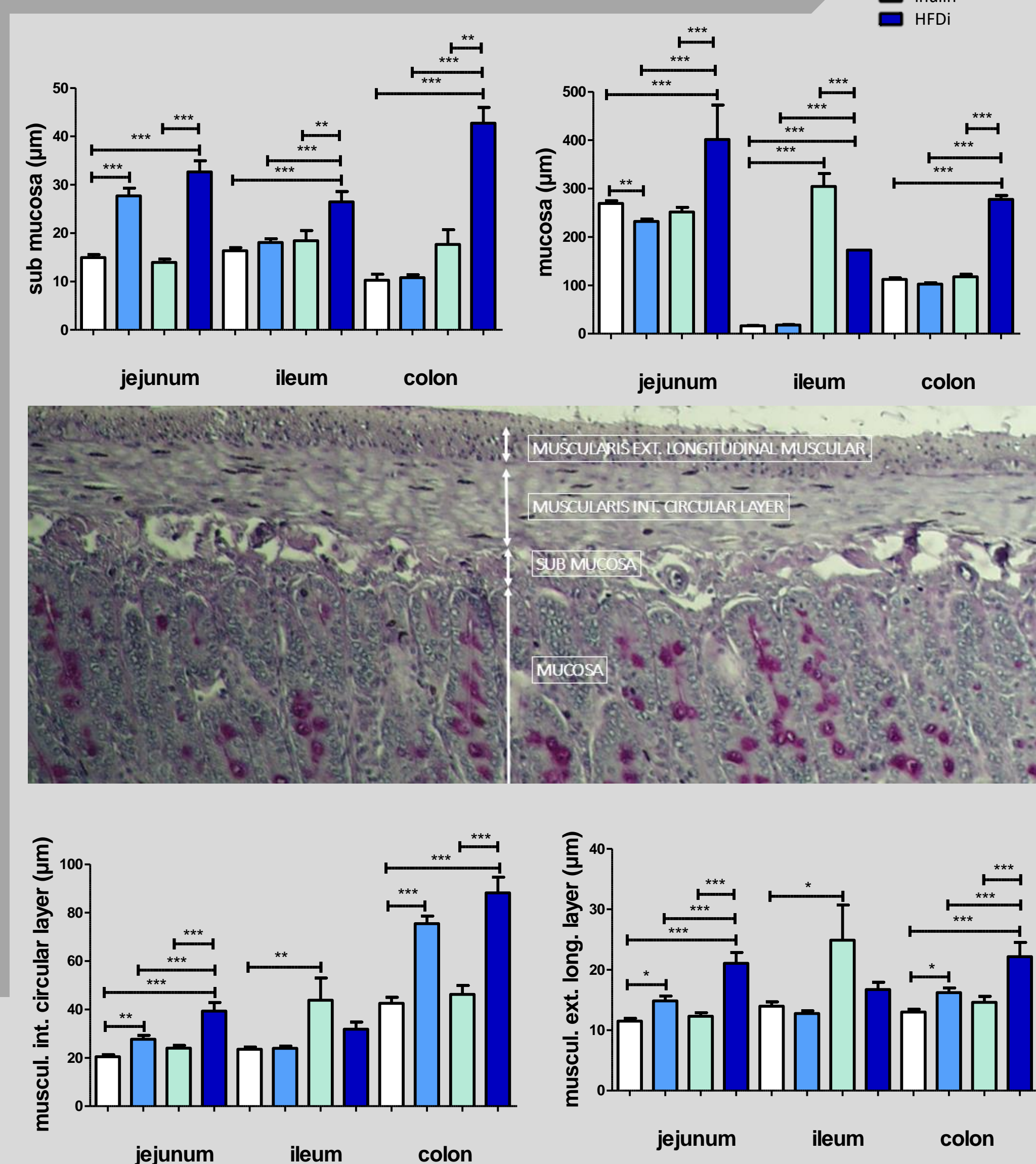
METABOLIC ASSAYS

	HFD	Ci	HFDi
Total cholesterol (mmol/L)	\emptyset	\emptyset	\emptyset
TG (mmol/L)	\emptyset	\nearrow^*	\emptyset
HDL (mmol/L)	\emptyset	\emptyset	\emptyset
LDL (mmol/L)	\emptyset	\searrow^{**}	\searrow^*
Glucose (mmol/L)	\nearrow ind	\emptyset	\emptyset
Insulin (uU/L)	\emptyset	\emptyset	\emptyset
IGF1/weight	\emptyset	\emptyset	\emptyset
Leptin	\nearrow ind	\emptyset	\emptyset

INTESTINAL PERMEABILITY



INTESTINAL LAYERS THICKNESSES



GENE EXPRESSION

	JEJUNUM	ILEUM	COLON
MUC2	HFD \searrow^{***} with or without inulin	HFD \searrow^* with inulin	HFD \searrow^{***}
MUC3	HFD \searrow with * or without inulin**	\emptyset	HFD \searrow^{***}
TLR4	HFD \nearrow ind with and without inulin	HFD \searrow^* with inulin	HFD \searrow^{***}

EPITHELIAL TIGHT JUNCTIONS PROTEINS

	JEJUNUM	ILEUM	COLON
CLAUD	Inulin \searrow^{**}	HFD \nearrow^{**} with and without inulin	HFD \nearrow^{**} with inulin
INE 4	Inulin \nearrow^{**} on HFD pups	\emptyset	Inulin \nearrow^{**} on HFD pups
OCCLU	HFD \searrow^*	\emptyset	HFD \nearrow with*** and without inulin
DINE	Inulin \nearrow^{**} on HFD pups	\emptyset	Inulin \nearrow^{**} on HFD pups

RT PCR : Expression of genes coding for mucin 2 and 3 and TLR4 receptor proteins and proteins involved in tight junctions constitution (standardization gene: GAPDH)

COBAS Automaton (Roche) and Rat ELISA (Fisher Scientific Thermo Kit)

PAS coloration - Histological measurements using Image J software

Kruskal Wallis with Dunn's post test or ANOVA with Bonferroni's post test ; GraphPad Prism version 5.00 - * p<0,05; ** p<0,01; *** p<0,001

CONCLUSIONS

Pups from dams in contact with an HFD during the peri-gestational period presented:

- **Overweight** : a higher weight at young adult age (D21 until D60)
- Modification of the **intestinal epithelial permeability** : overexpression of tight junctions proteins
- Disturbance of **intestinal barrier function** : a reduced expression of MUC2 and MUC3 genes and alteration of TLR4 gene expression
- Impacts on **organs development and growth (digestive system)** : \nearrow of circular and longitudinal muscle layers thicknesses (jejunum and colon), \nearrow of submucosa thickness (jejunum and ileum) and \searrow of mucosa thickness (jejunum and colon).
- We suggest that HFD administration in the mothers (dams) might increase the occurrence of obesity and may cause alterations of digestive functions in the offsprings.

THANKS

Animal team, PlatAnN animal facility platform, and Aurélie Corona, laboratory technician PériTox UMR-I-01, Amiens, France

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