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Perinatal programming of intestinal homeostasis following exposure to low dose of chlorpyrifos in male rats offspring

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Objective: This work was aimed at studying the effects of a peri-gestational exposure of dams to a low dose of pesticide (chlorpyrifos) with a prebiotic supplementation (inulin) on the anatomo-functional development of the digestive system and associated metabolic consequences of the growing male offspring.

INTRODUCTION

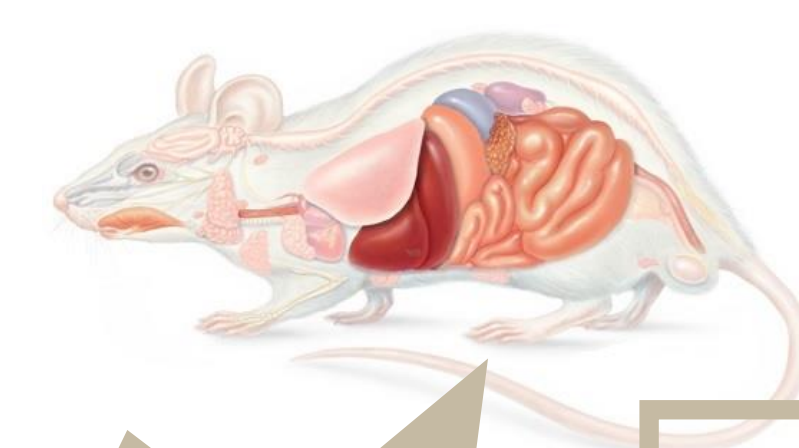
Perinatal period is characterized by a succession of developmental phases with high sensitivity to environmental factors. Among the risk factors, pesticide exposure is now recognized to reprogram children's metabolism and promote the occurrence of obesity or type 2 diabetes.

This work was dedicated to the peri-gestational exposure of dams to a low dose of pesticide (chlorpyrifos, CPF) and the exploration of the prebiotic supplementation benefits

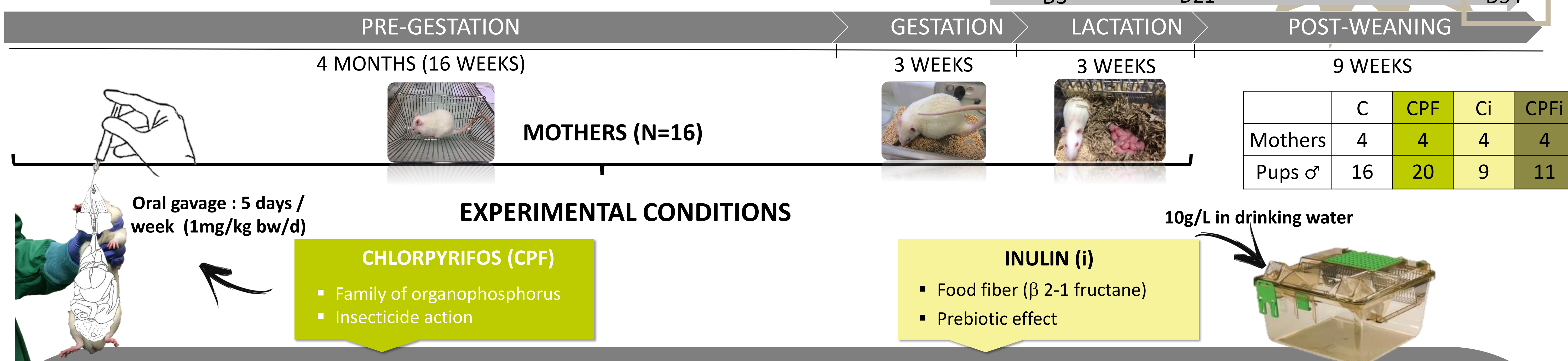
HYPOTHESIS



1. Chlorpyrifos : 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 pesticide ?

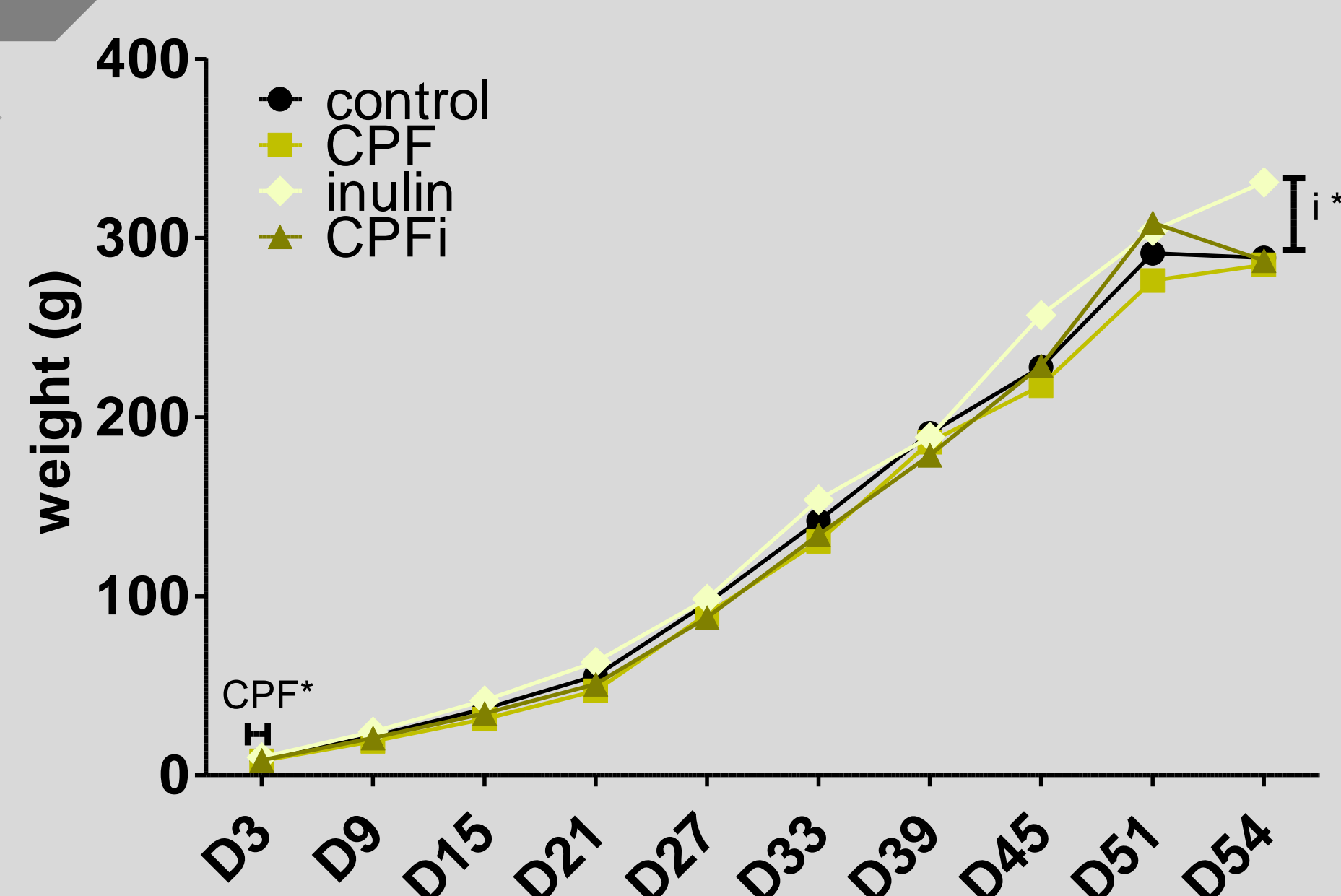


METHODS



RESULTS

WEIGHT

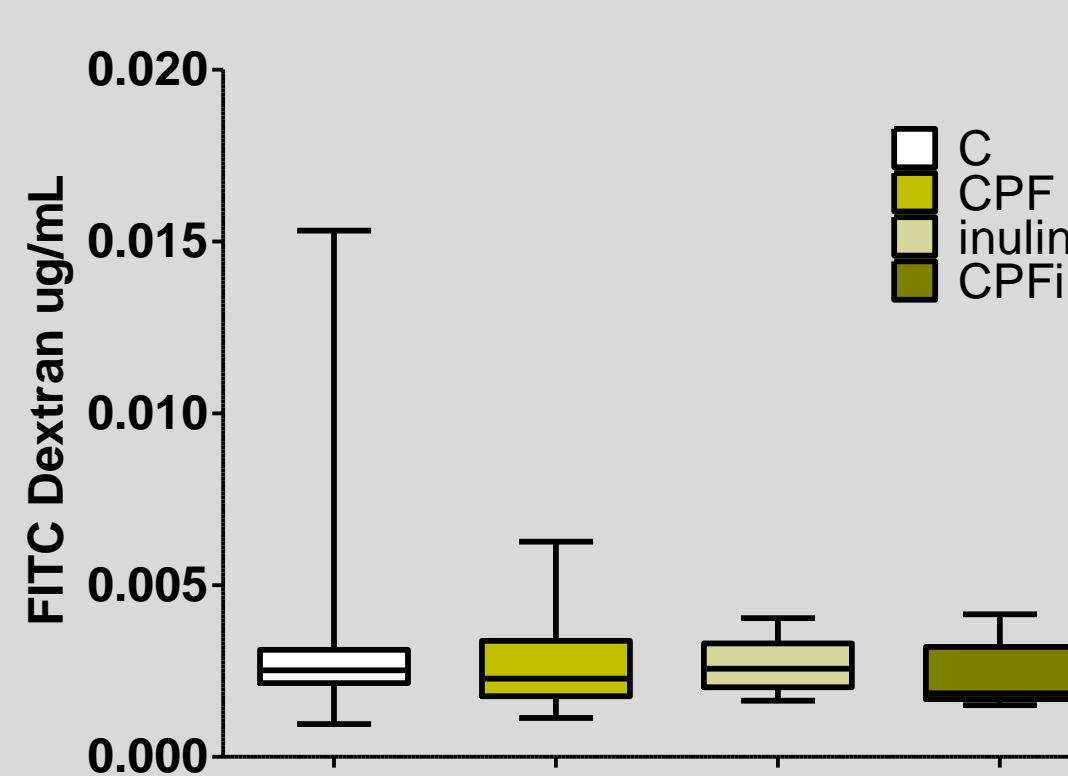


METABOLIC ASSAYS

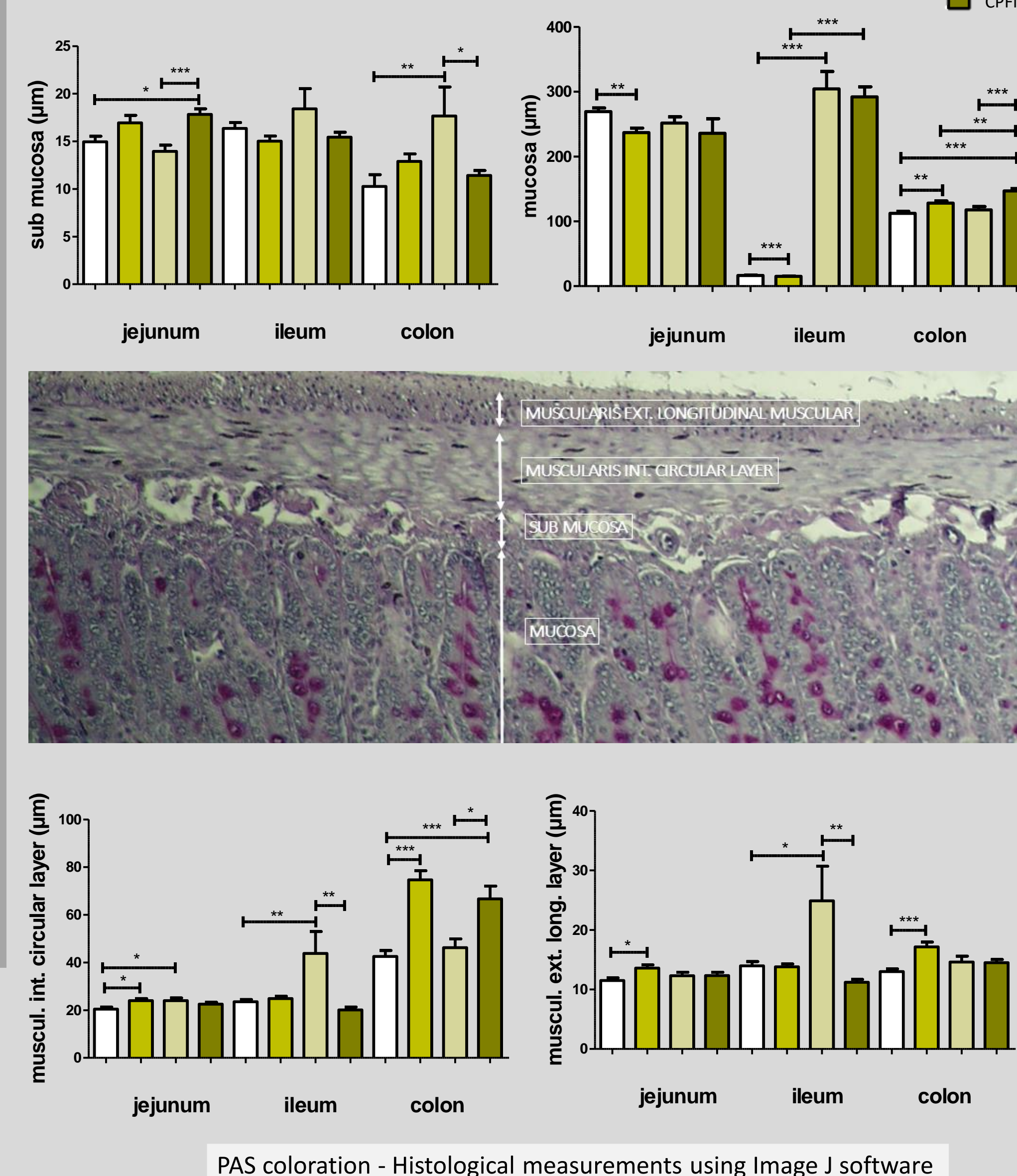
	CPF	Ci	CPFi
Total cholesterol (mmol/L)	\emptyset	\emptyset	\emptyset
TG (mmol/L)	CPF ind \nearrow	\nearrow^*	\emptyset
HDL (mmol/L)	\emptyset	\emptyset	\emptyset
LDL (mmol/L)	\emptyset	\searrow^{**}	\searrow^*
Glucose (mmol/L)	\emptyset	\emptyset	\emptyset
Insulin (μ U/L)	\nearrow ind	on CPF rats \searrow^{***}	\searrow^*
IGF1/weight	\searrow^{**}	\searrow^{**}	\emptyset
Leptin	\searrow ind	\emptyset	\emptyset

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

INTESTINAL PERMEABILITY



INTESTINAL LAYERS THICKNESSES



GENE EXPRESSION

	JEJUNUM	ILEUM	COLON
MUC2	CPF \searrow^*	\emptyset	CPF \searrow^{**} with and without inulin
MUC3	CPF \searrow^{***}	CPF \nearrow^{**}	CPF \searrow^{***}
TLR4	CPF \nearrow^{**}	Inulin on CPF rats \searrow ind	CPF \searrow^{**} with and without inulin

EPITHELIAL TIGHT JUNCTIONS PROTEINS

	JEJUNUM	ILEUM	COLON
CLAUDINE 4	CPF \searrow^{***} Inulin \searrow^{***}	CPF \nearrow^{***}	\emptyset
OCCLDINE	\emptyset	\emptyset	CPF \searrow^{***} Inulin \searrow^{***} Inulin \nearrow ind on CPF rats

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)

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 a pesticide during the peri-gestational period presented:

- Developmental alterations : a lower birth weight and a \searrow in plasma levels of factors involved in growth and metabolism (IGF1 and leptin).
- Modification of the intestinal epithelial permeability : underexpression of tight junctions proteins in some intestinal segments
- Disturbance of intestinal barrier function : a reduced expression of MUC2 and MUC3 genes
- 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 colon) and \searrow of mucosa thickness (jejunum and ileum).
- We suggest that the pesticide slows down fetal and postnatal development (especially the digestive system) and may cause digestive function alterations such as an increase of intestinal permeability, and probably some impacts on intestinal motility.

THANKS

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