

## **Background & Aim**

- Obesity affects a quart of adults and one third of eleven-year-olds are overweighted or obese in Europe (World Health Organization's
- Expansion of obesity is correlated with increased environmental endocrine disruptors, in particular with Bisphenol A (BPA) (Rubin,

### BPA:

Endocrine disruptor (xenoestrogen) : food contaminant and dermal absorption (thermal papers)











Transmitted to the fetus through mother exposure (Schönfelder et al., 2010)

	Maternal blood	Umbilical cord	Amniotic fluid	Placenta	Fetal blood
BPA Concentration (ng/ml)	5.9	1.1	8.3	11.2	1.13

- Correlation between BPA plasma levels, inflammatory markers and visceral obesity in Human adult males (Savastano et al., 2015)
- Long-lasting impacts on immune system development leading to various inflammatory status in adult life (Braniste et al., PNAS 2010; Menard et al., Plos ONF 2014)
- Food intolerance development at adulthood after perinatal exposure (Menard et al., FASFB 2014)



Endocrine disrupting chemicals and immunometabolism

### > Aim of this study :

### In mice perinatally exposed to BPA

- 1. To show, at different life stages, the inflammatory status that correlates with metabolic disorders
- 2. To investigate predictive immune markers of susceptibility to obese phenotype

### Perinatal BPA exposure contributes to obese phenotype in male mice at adulthood: an immunological point of view

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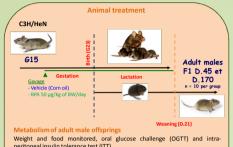
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### Methods & Results

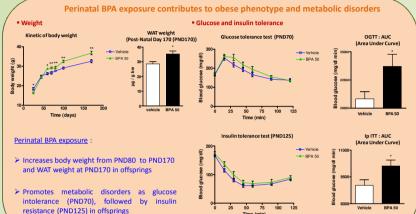


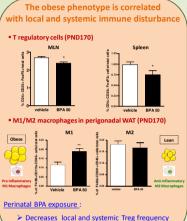
peritoneal insulin tolerance test (ITT)

Frequency of T regulatory subsets in Mesenteric Lymph Nodes (MLN) and spleen and M1/M2 macrophages in perigonadal White Adipose Tissue (WAT)

Cytokine level in supernatant of primary cells (MLN and spleen) after in vitro anti-CD3/CD28 restimulation for 4 days

IgA and pIgR level (feces), antimicrobial activity test. GuIDA (microbiome





## Increases M1 macrophage frequency in WAT

PND170

## An inflammatory environment precedes obese phenotype at adulthood in perinatally-exposed mice to BPA Perinatal BPA exposure > Increases inflammatory cytokine production by immune cells from spleen and MLN at PND45 in offsprings > At PND170, local inflammatory markers normalized, except systemic IL-17 inflammation

# Perinatal exposure to BPA impairs local IgA production and antimicrobial activity leading to dysbiosis Antimicrobial activity Intestinal microbiome > Perinatal BPA exposure reduces IgA and pIgR production in feces at PND45, associated with a decreased antimicrobial activity and reduction of Bifidobacterium population

### Perinatal BPA exposure has multiple impacts in male offsprings:

### Metabolic disorders

Lean phenotype

- Increased body and WAT weight

PND45

- Glucose intolerance
- Insulin resistance

#### > Immunologic disturbance

- Decreased intestinal and systemic Treg
- Increased pro-inflammatory M1 macrophages

### > Local and systemic inflammation

Increased IFN-y and IL-17 production after in vitro anti-CD3/CD28 restimulation

### > Reduced host defenses

- Decreased IgA secretion via decreased pIgR
- Decreased antimicrobial activity

### > Intestinal dysbiosis

Pronounced decrease of Bifidobacterium in gut

Perinatal exposure to BPA evokes immunologic disturbances that precede obese phenotype in mature mice

-These early immune disturbances occur concomitantly to decreased host defenses towards intestinal bacteria and induced dysbiosis

Conclusion

In conclusion, impact of BPA on immune system may increase susceptibility to metabolic disorders in perinatally-exposed individuals