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## PART 3

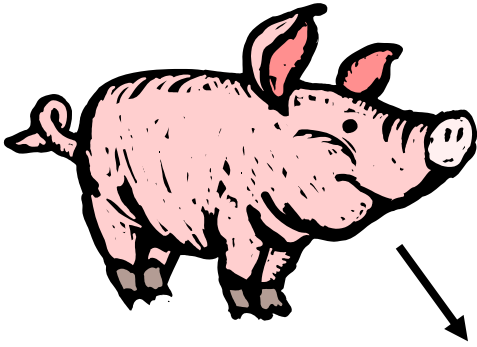
# Effects of DON on intestinal immunity

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# Introduction



**Intake of DON contaminated-feed**

## **MAY AFFECT THE INTESTINE IMMUNE FUNCTIONS**

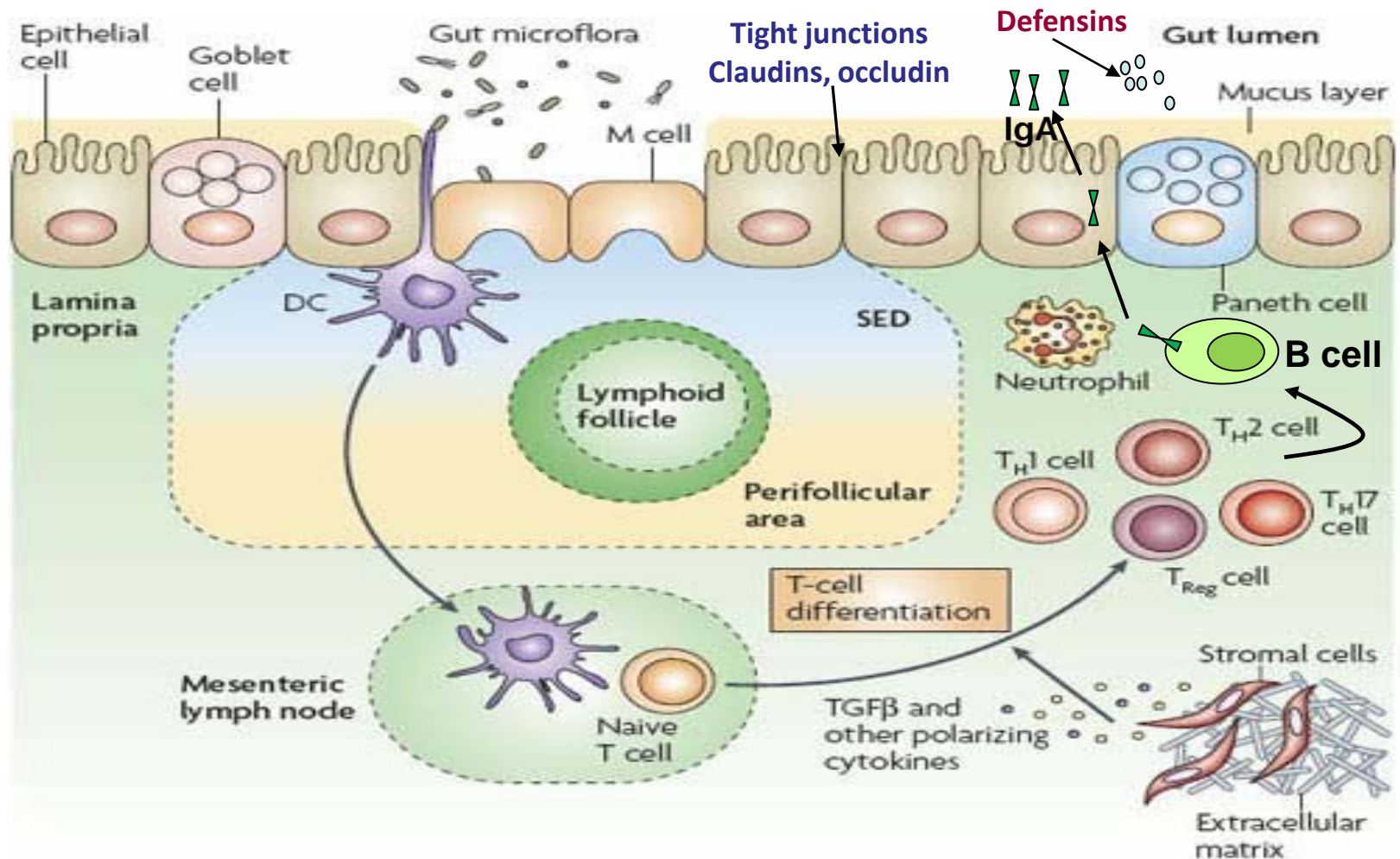
- Natural defences of epithelium (mucin production, intestinal mucosal permeability );
- Immune functions that are regulated by different cytokines, chemokines and other factors (PGE2, ROS, etc.)

Recent studies have shown that DON intake may:

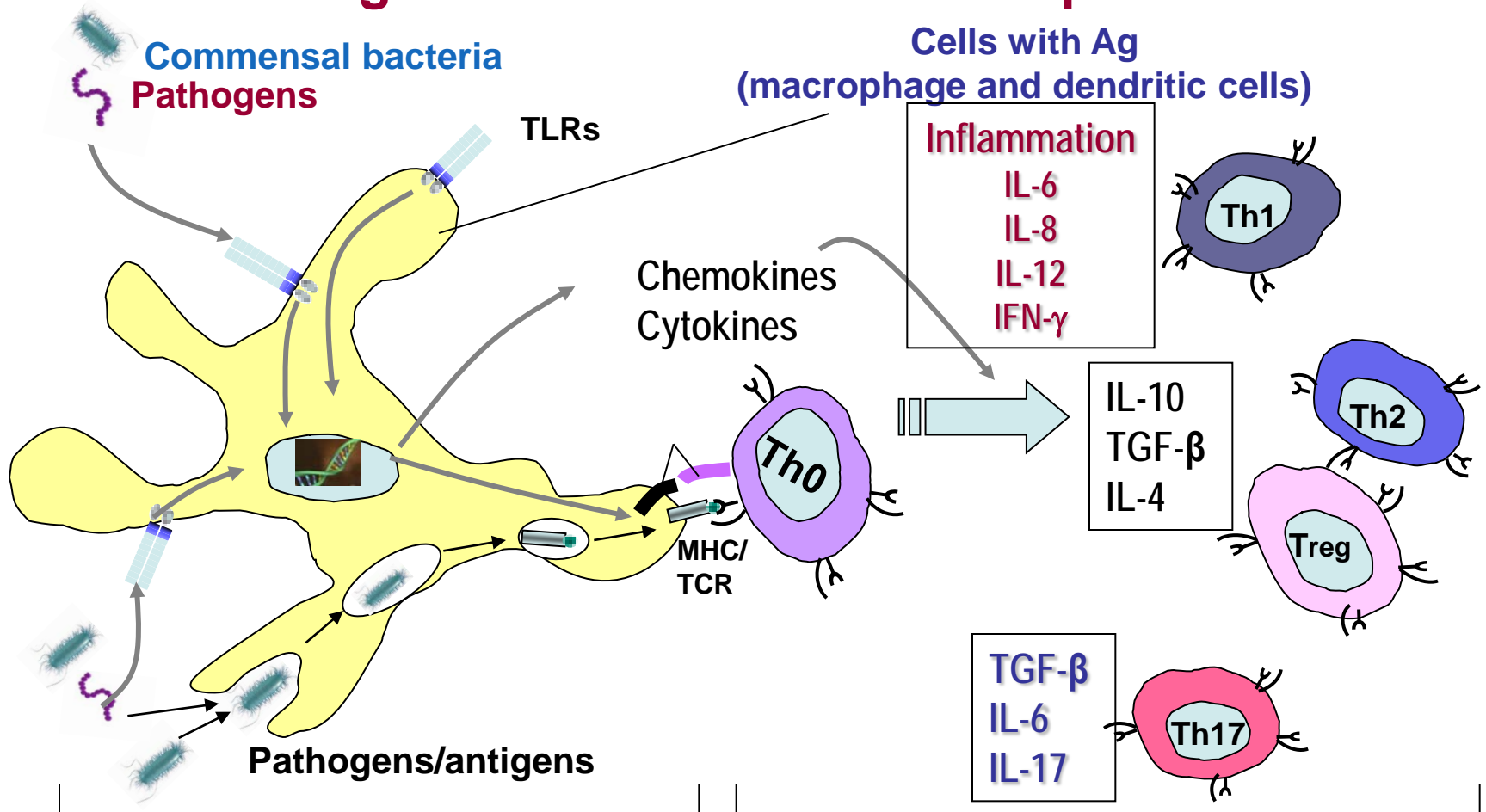
- Increase expression of several cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IFN- $\gamma$ , IL-6 and IL-10) at the jejunum and ileum level (Bracarense et al., 2012); or
- Decrease expression of IL-1 $\beta$  and IL-8 (Becker et al. 2011)

**Effects of DON on intestinal immune response  
are still not well understood**

# Intestine is the main interaction site between the immune system, microorganisms and other antigens including mycotoxins



# Immune cells and cytokines involved in the regulation of the immune response



Innate immunity

Adaptative immunity

Different  
bacteria



Different  
signals



Different  
responses

# Study objectives

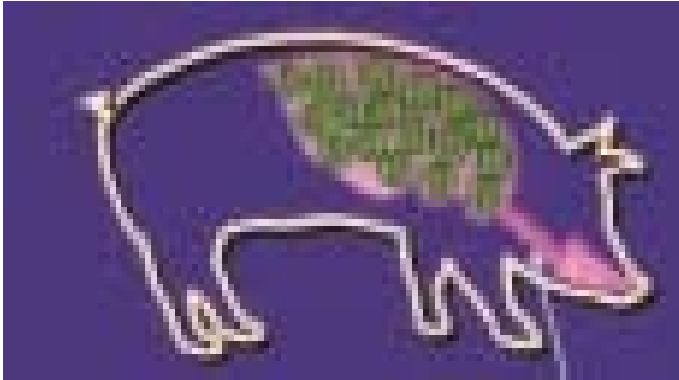
**Evaluate the influence of DON-contaminated feed on:**

- **Growth**
- **Antibody response against ovalbumin (OVA)**
- **Chemokines production: IL-8, CXCL10** (attraction and control of activation status of immune system cells)
- **Proinflammatory cytokines production:**  
**IL-1 $\beta$ , IL-6, TNF- $\alpha$**

## **Study objectives – cont.**

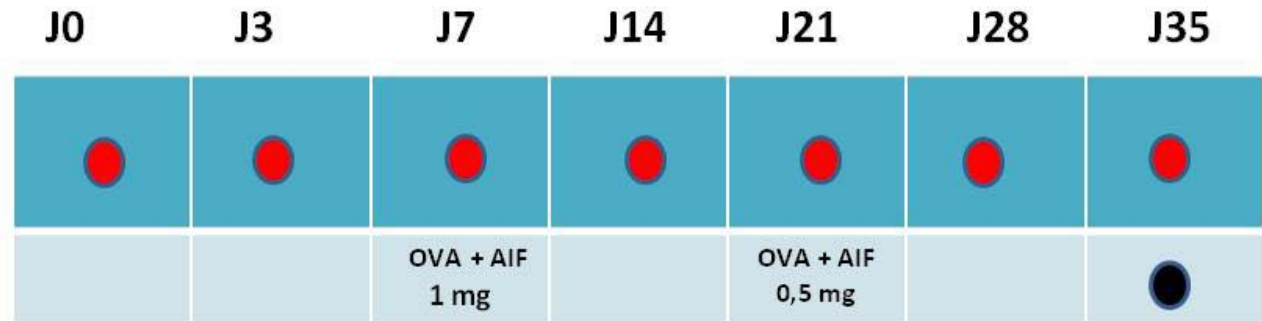
- Enzyme expression involved in the metabolism of oxygen reactive species (ROS) at the intestine level (SOD3, GPX3)**
- Cytokines production involved in the regulation of Th1 (IFN- $\gamma$ ), Th2 (IL-4) and Treg (IL-10) responses**
- Intestinal barrier function (occludin and claudins 3 and 4) and antimicrobial peptide production ( $\beta$ -defensin-1)**

# Animals and treatments



DON (ppm/kg)	PIGS (n)
0	8
1.5	8
3.5	8

- ✓ Weight gain
- ✓ Ab production against OVA

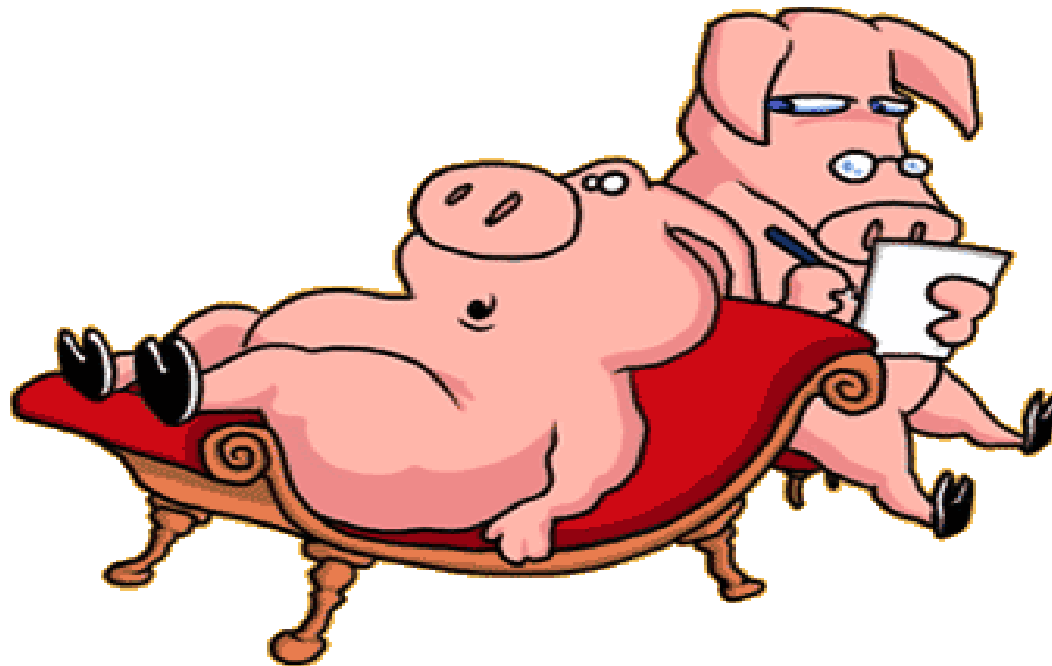


● Blood sample    ● Euthanasia

Euthanasia

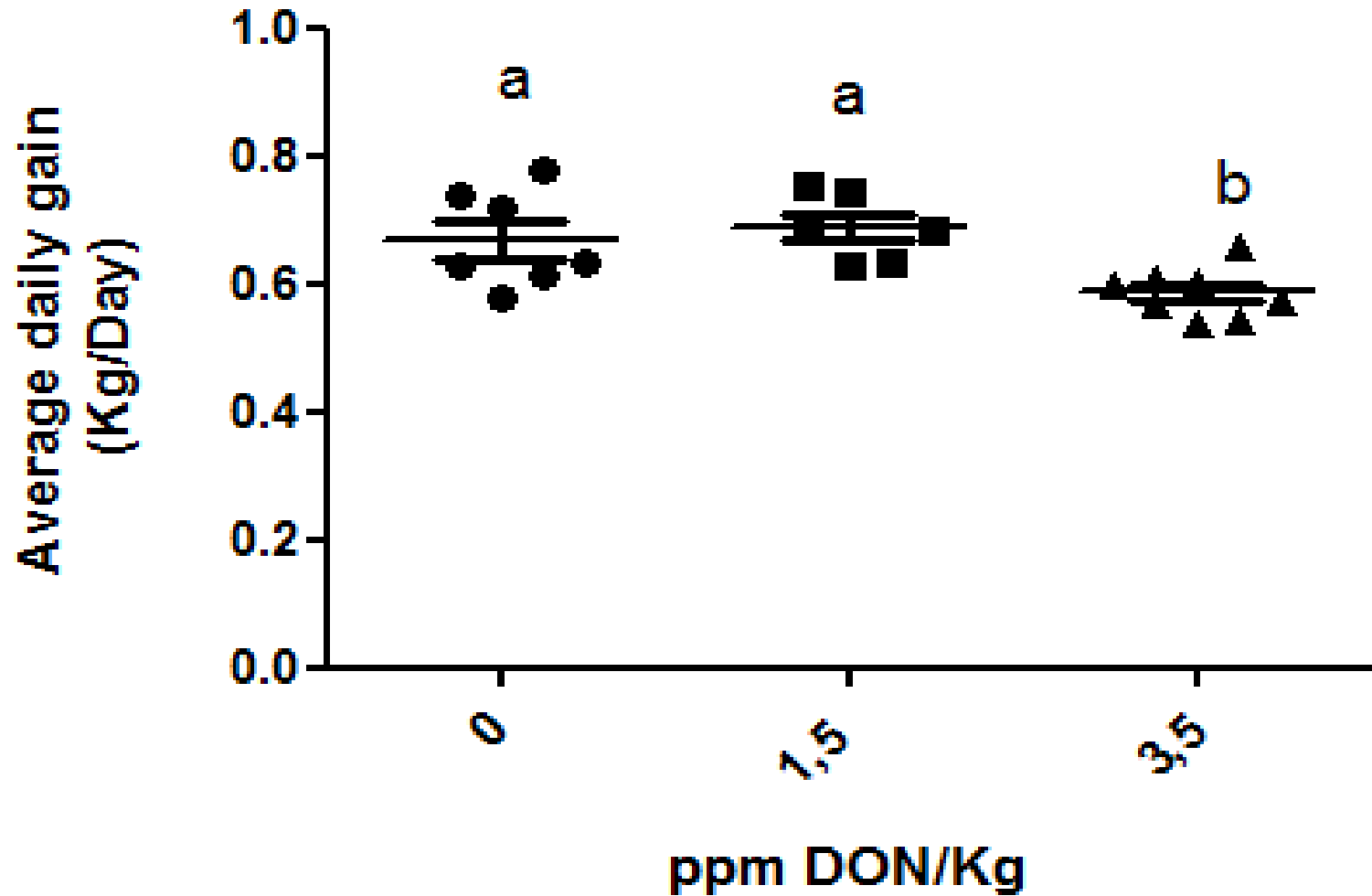
- ✓ Genes expression using qPCR (jejunum and ileum)

# Results

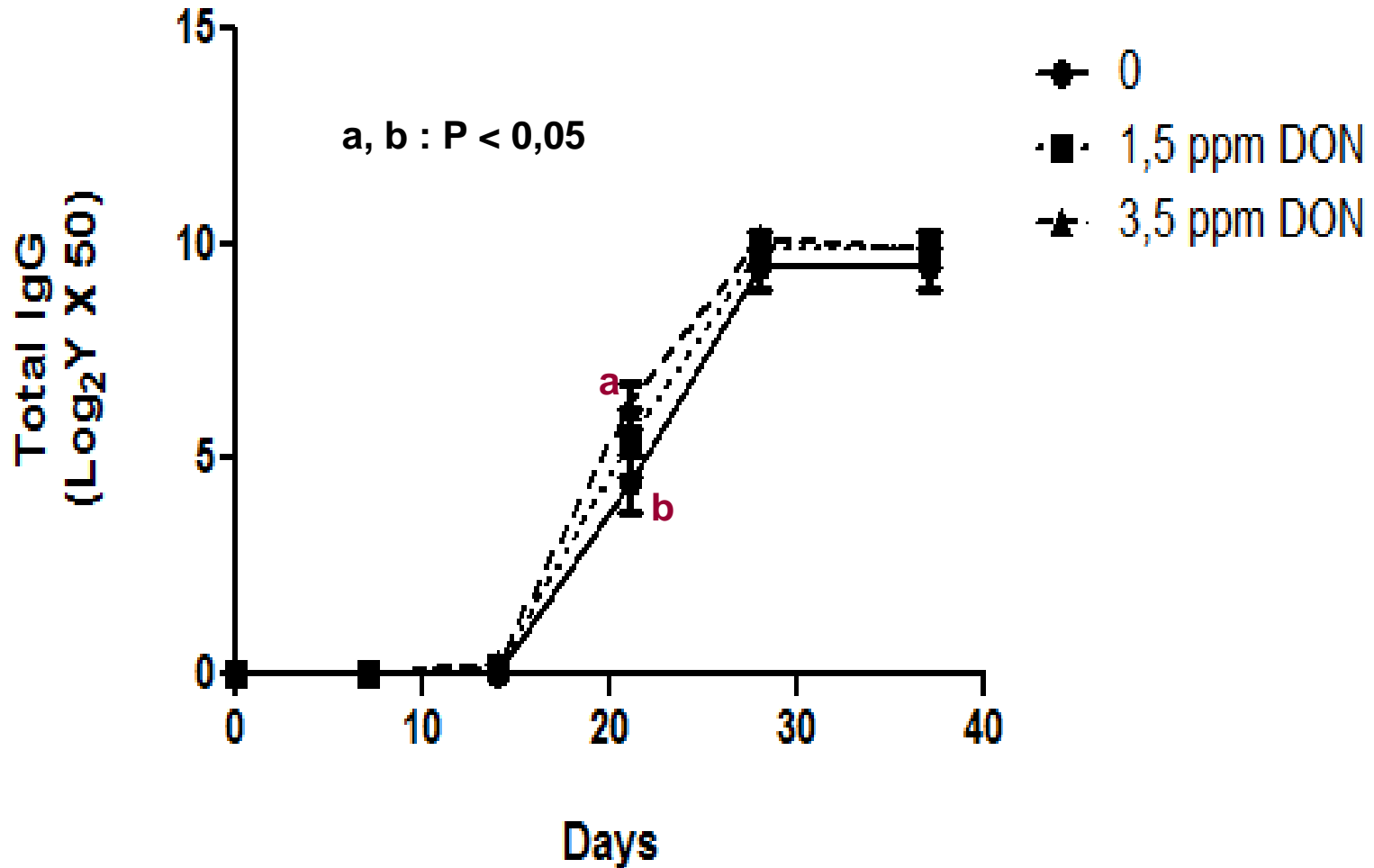




# Pigs daily gain is decreased by DON

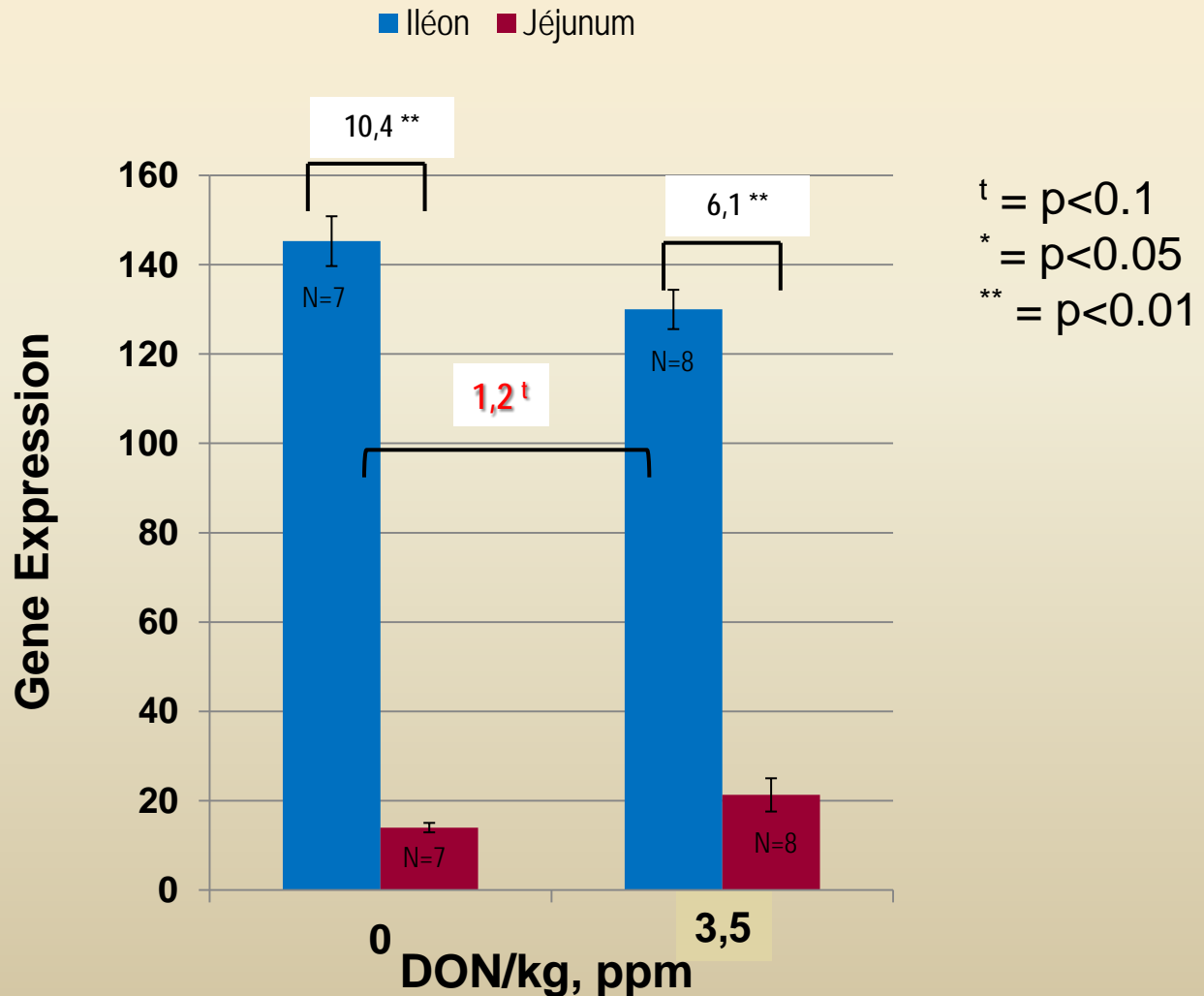


# Antibody response against OVA is increased by DON



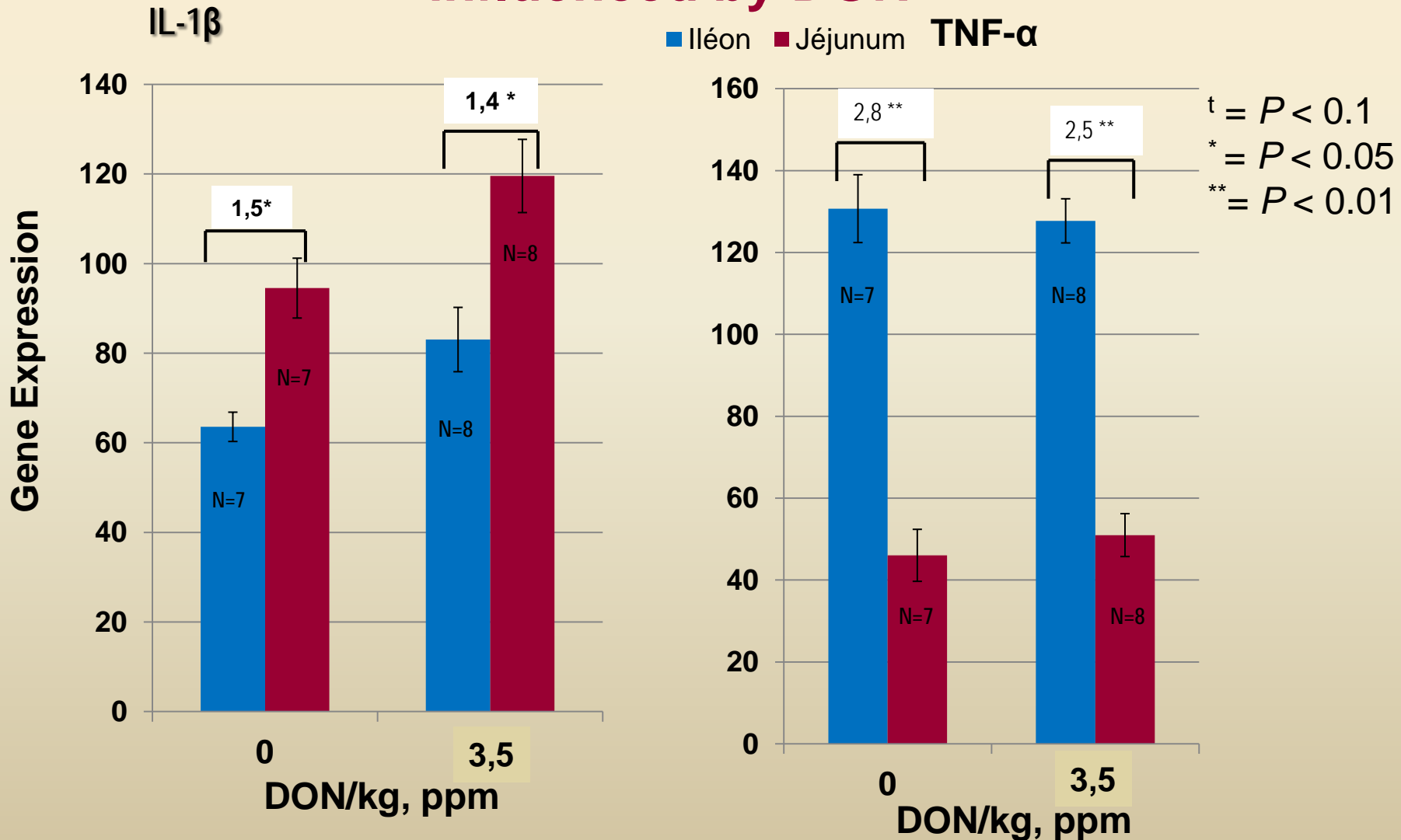
# Proinflammatory cytokine

DON tends to decrease expression of IL-6 in ileum



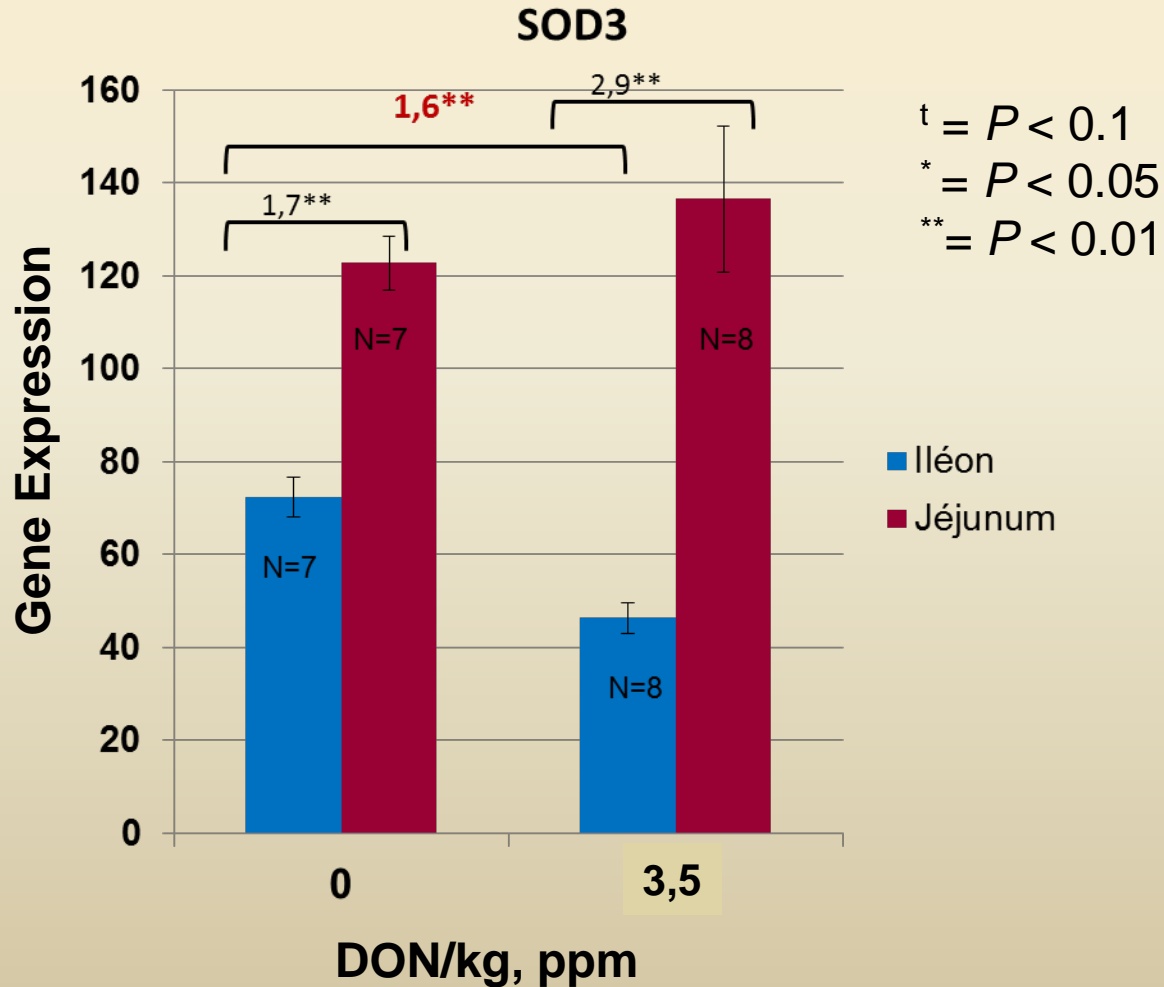
# Proinflammatory cytokine

## Expression of IL-1 $\beta$ and TNF- $\alpha$ are not influenced by DON



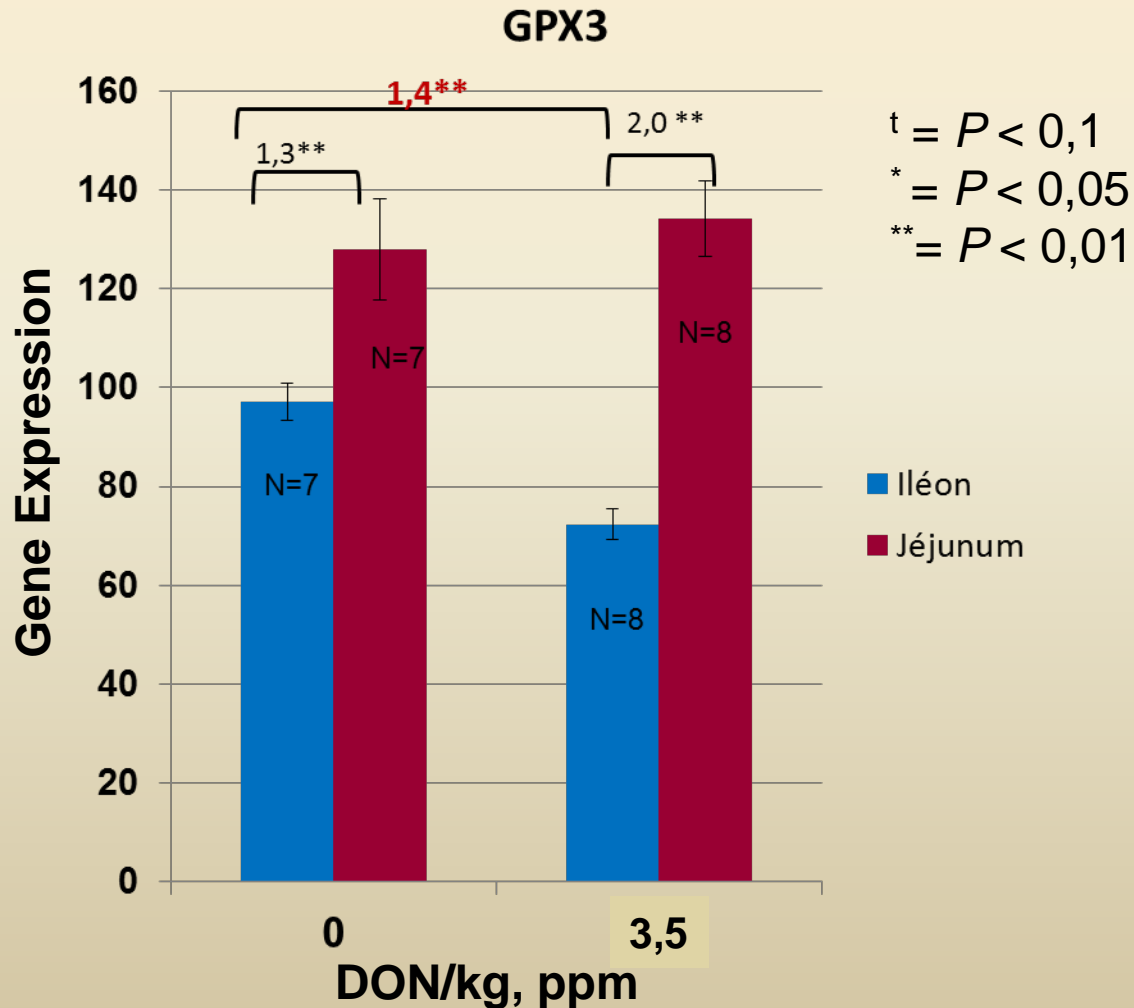
# Reactive Oxygen Species

Expression of superoxide dismutase is decreased in the ileum by DON



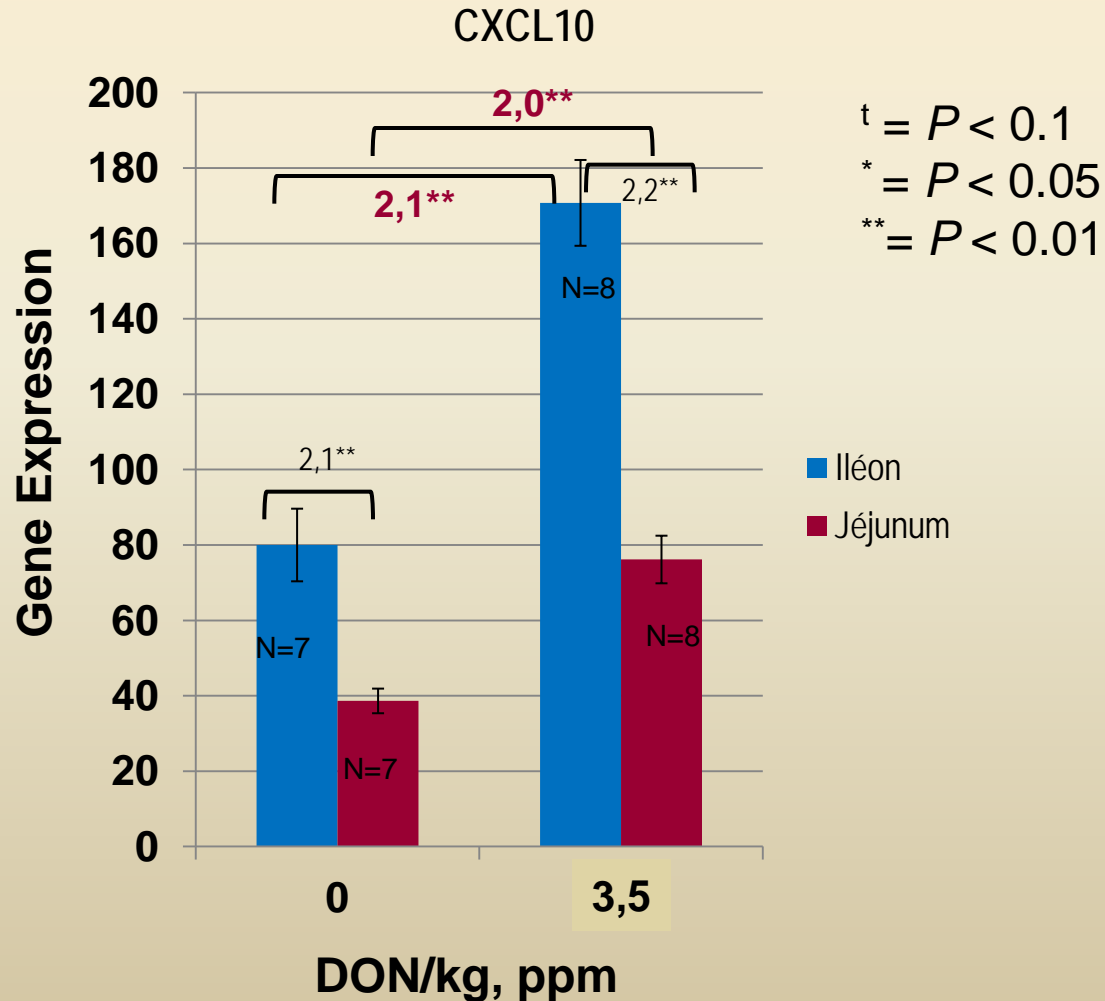
# Reactive Oxygen Species

Expression of glutathione peroxidase is decreased in the ileum by DON



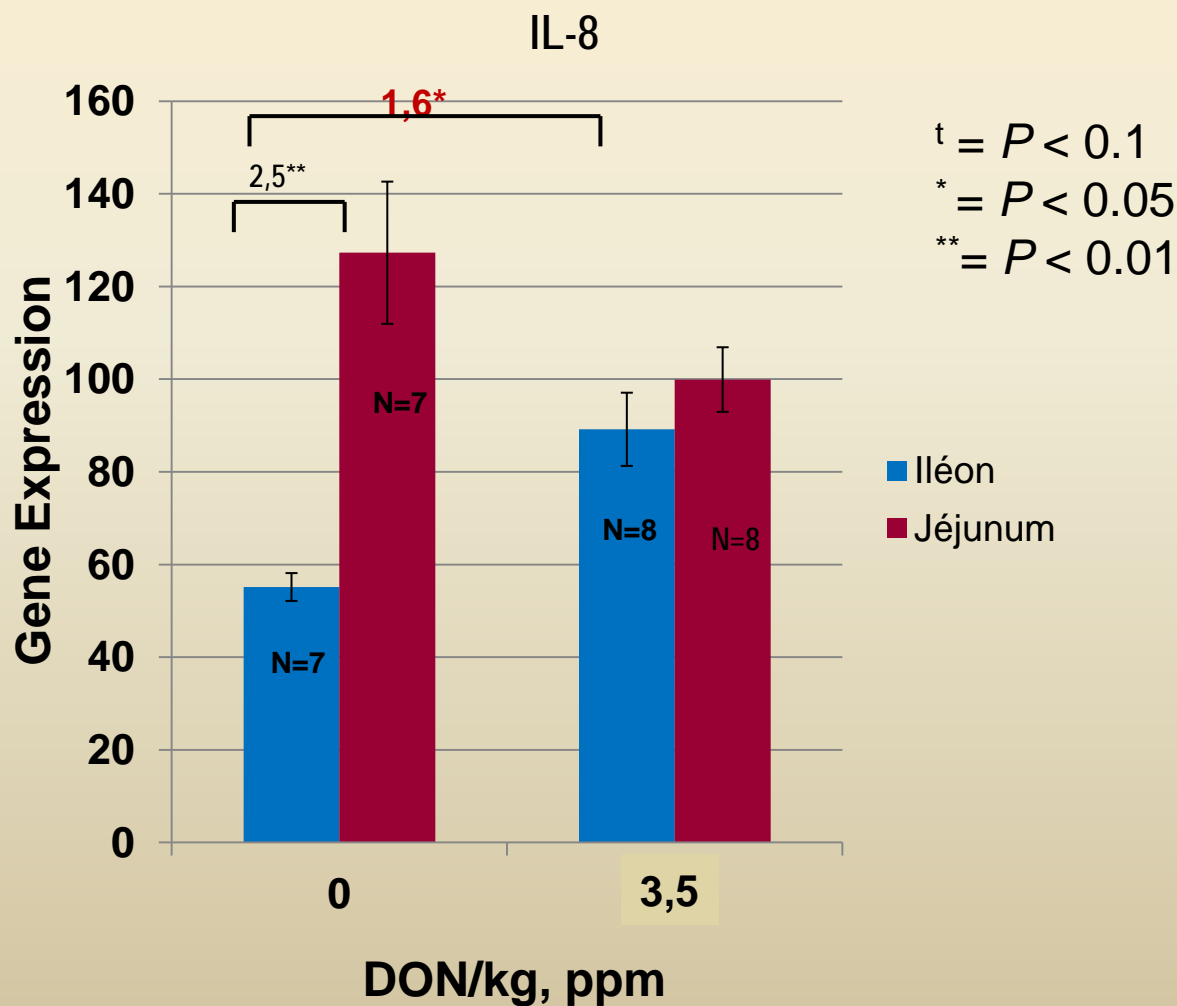
# Chemokine

## Expression of CXCL10 in jejunum and ileum is increased by DON



# Chemokine

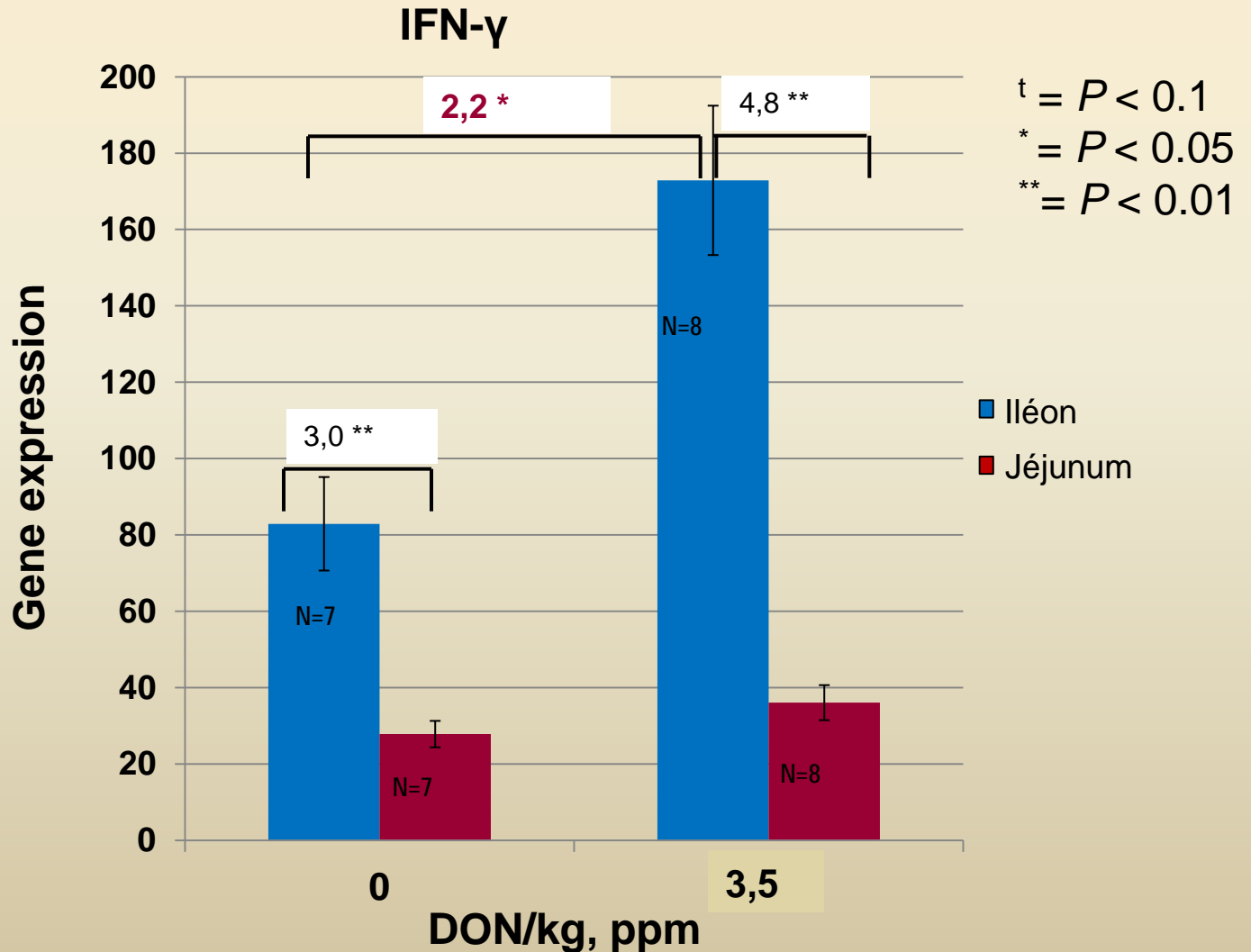
## Expression of IL-8 in ileum is increased by DON





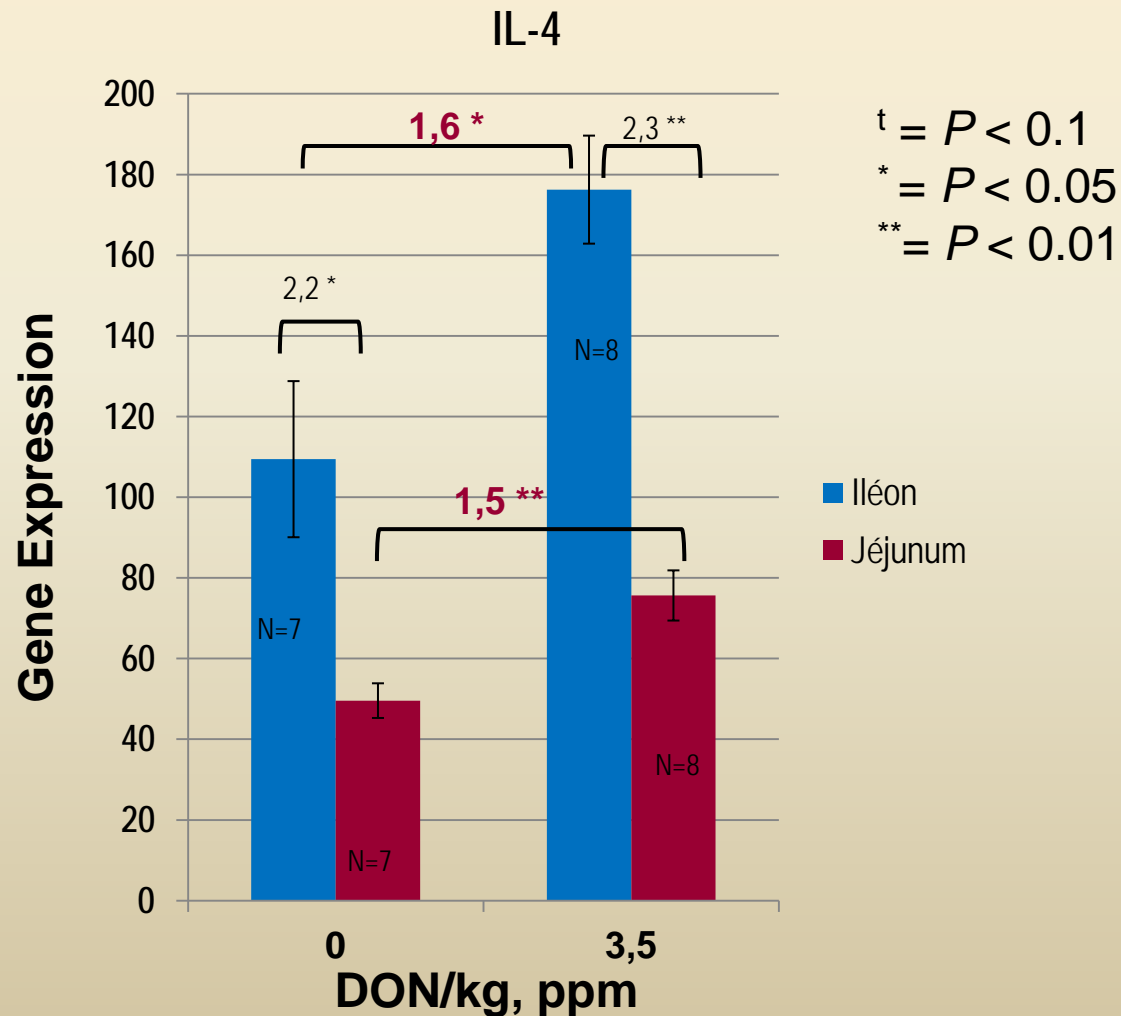
# Th1 response

Expression of IFN- $\gamma$  in ileum is increased by DON



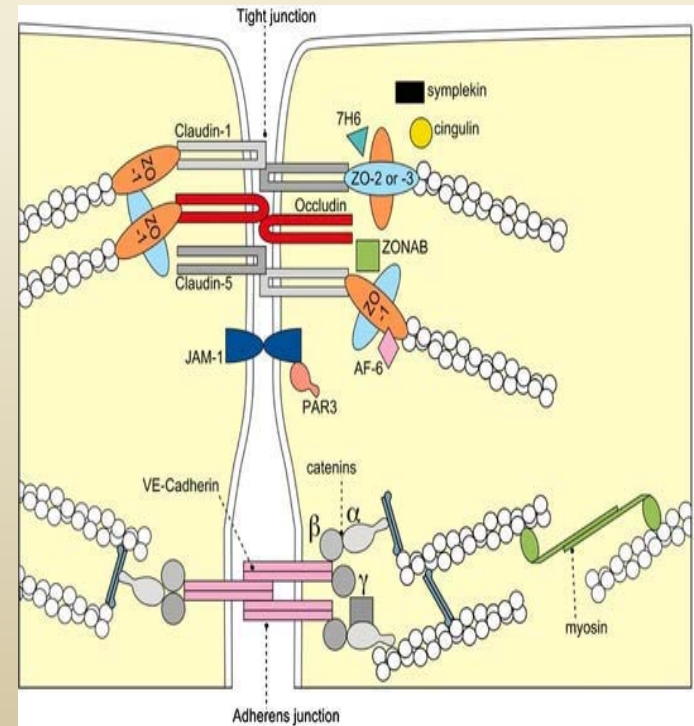
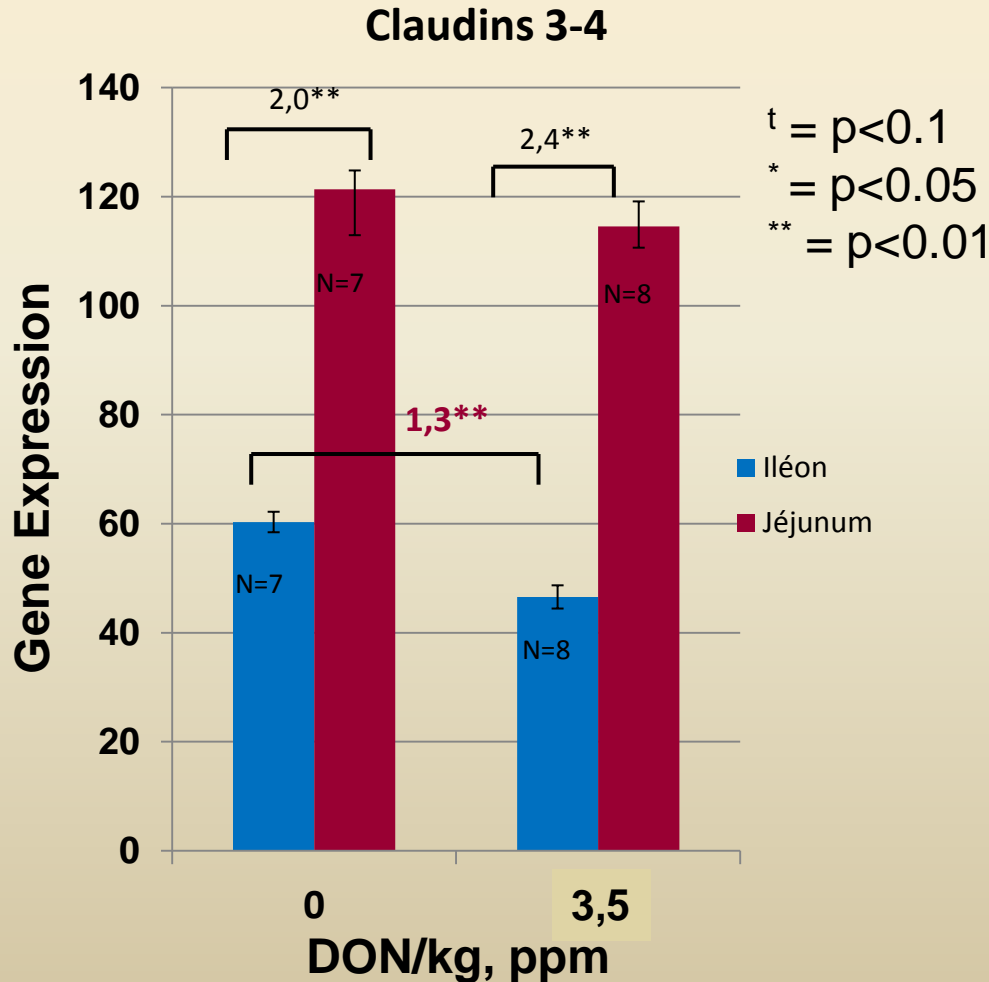
# Th2 response

Expression of IL-4 is increased in the jejunum and the ileum by DON



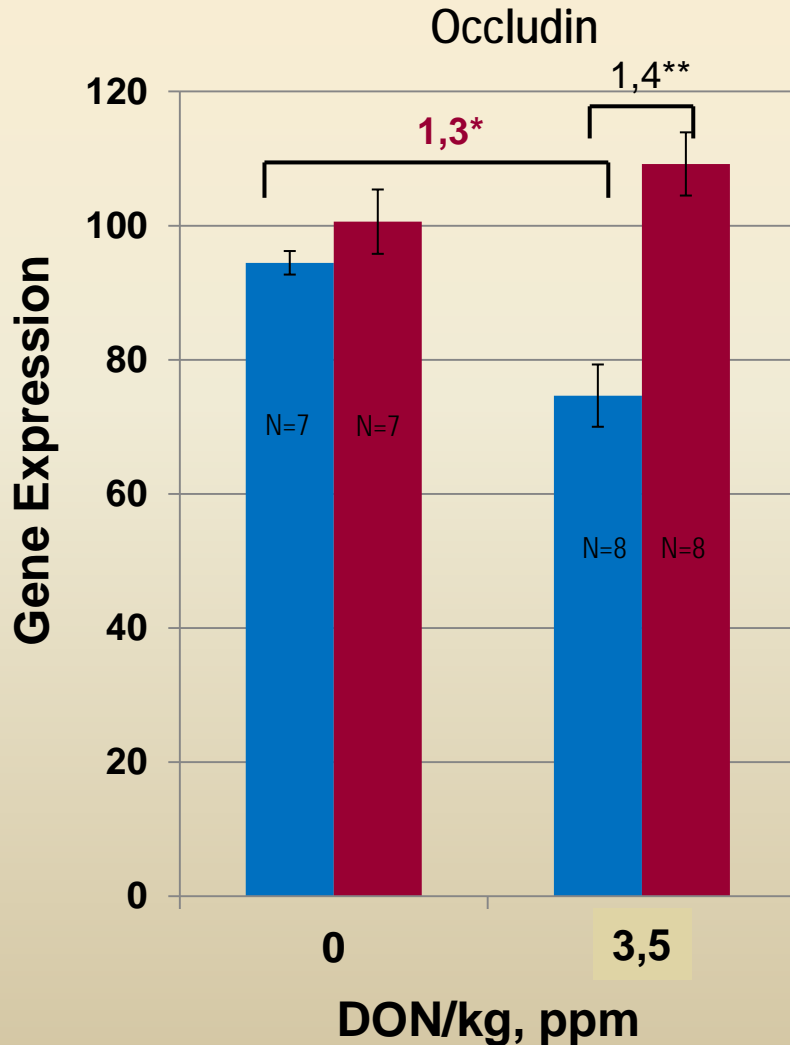
# Barrier function

DON reduces expression of claudins 3 and 4 in the ileum

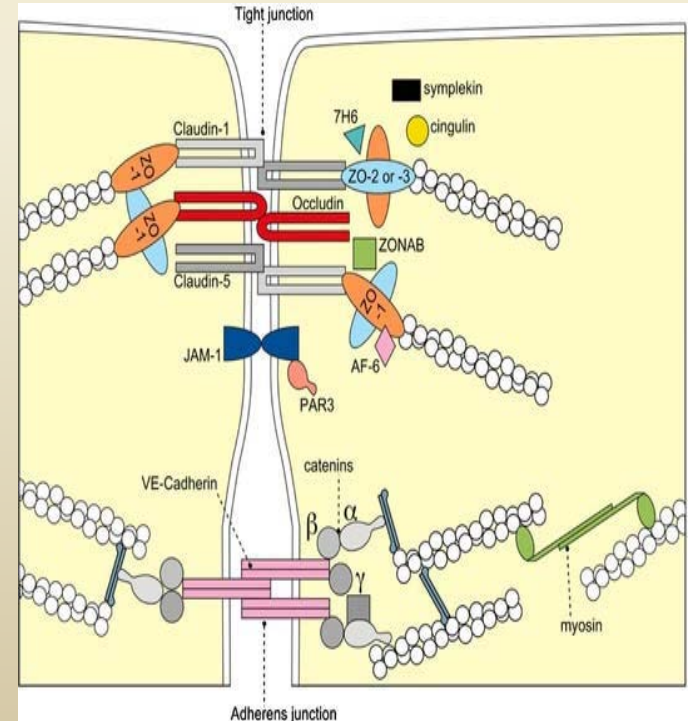


# Barrier function

## Expression of occludin is decreased in ileum by DON

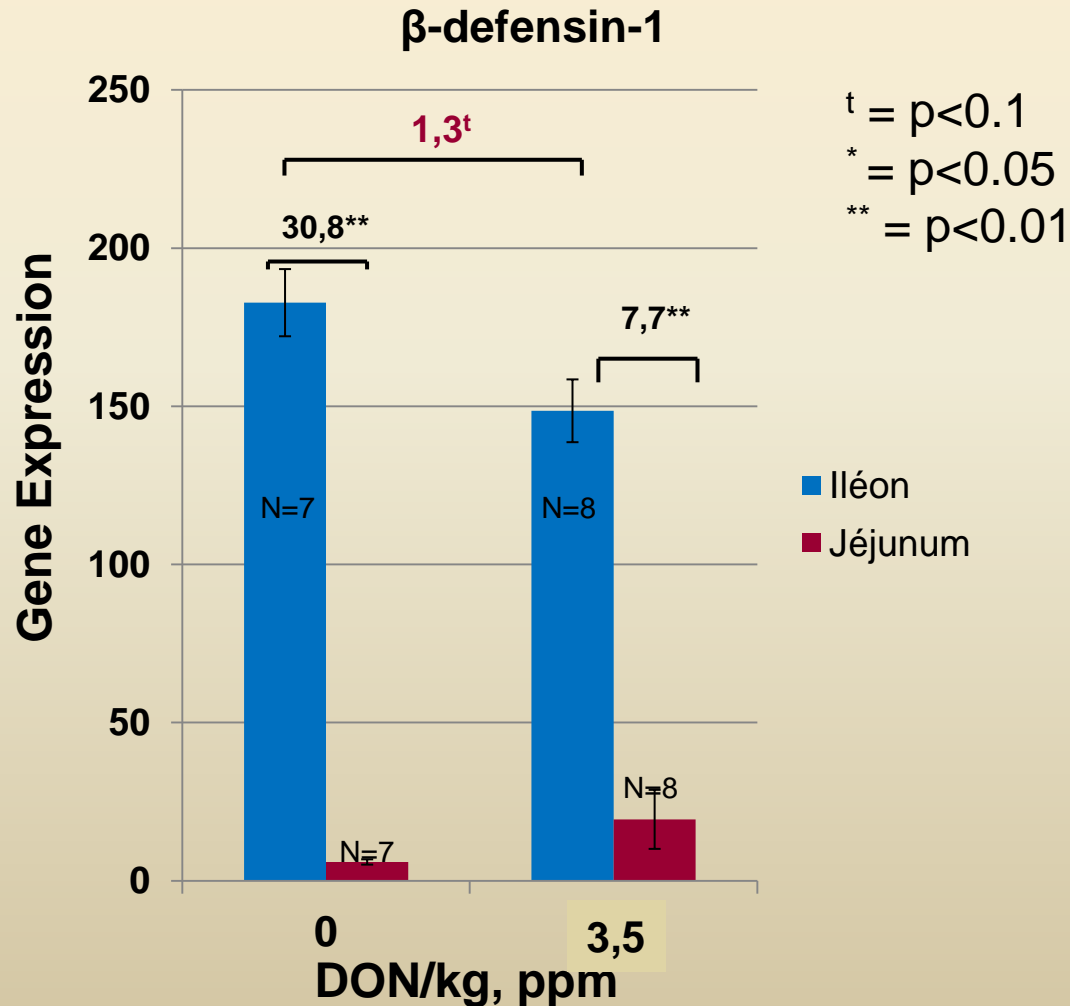


t =  $p < 0.1$   
 \* =  $p < 0.05$   
 \*\* =  $p < 0.01$



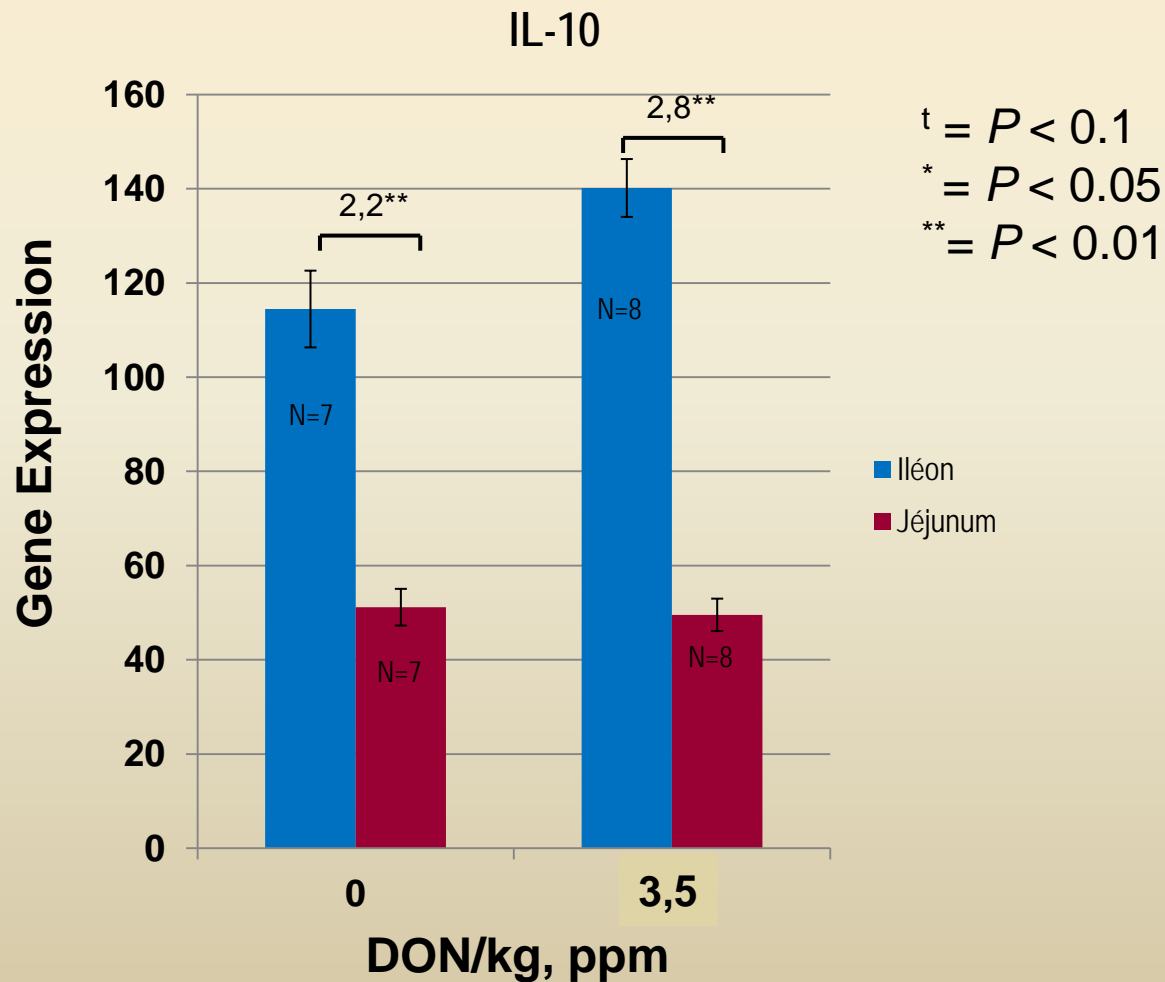
# Antimicrobial peptide

DON tends to decrease expression of  $\beta$ -defensin-1 in ileum



# Treg response

Expression of IL-10 is not influenced by DON



## Conclusions – Part 3

- **At the ileum level, intake of DON**
  - Tended to decrease expression of IL-6 while these of TNF- $\alpha$  and IL-1 are not affected;
  - Decreased expression of two enzymes (SOD3 and GPX3) involved in the metabolism of oxygen reactive species;
  - Increased expression of IFN- $\gamma$  (Th1 response) and IL-4 (Th2 response);
  - Decreased of expression of claudins and occludin, tight junction proteins that play a role in the intestinal permeability.

## **Conclusions – Part 3 (cont.)**

- **At the jejunum level, only the expressions of CXCL10, NOS2 (data not shown) and IL-4 were increased by DON.**
- **There are important differences between ileum and jejunum concerning the expressions of cytokines, chemokines, enzymes and other peptides.**





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**Thank you for  
your attention**

**Questions?**

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