

La glutamine et le grêle de l'agressé

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France

JFN 2013 - Bordeaux



Déclaration d'intérêts:

➤ **Activités de conseil, fonctions de gouvernance, rédaction de rapports**

Non

➤ **Essais cliniques, autres travaux, communications de promotion**

Non

➤ **Intérêts financiers (actions, obligations)**

Non

➤ **Liens avec des personnes ayant des intérêts financiers ou impliquées dans la gouvernance**

Non

➤ **Réception de dons sur une association dont je suis responsable**

Nestlé, Nutricia, Fresenius Kabi, Astra, MSD, Baxter, Bayer, Janssen-Cilag, Roche, Ferring

➤ **Perception de fonds d'une association dont je suis responsable et qui a reçu un don**

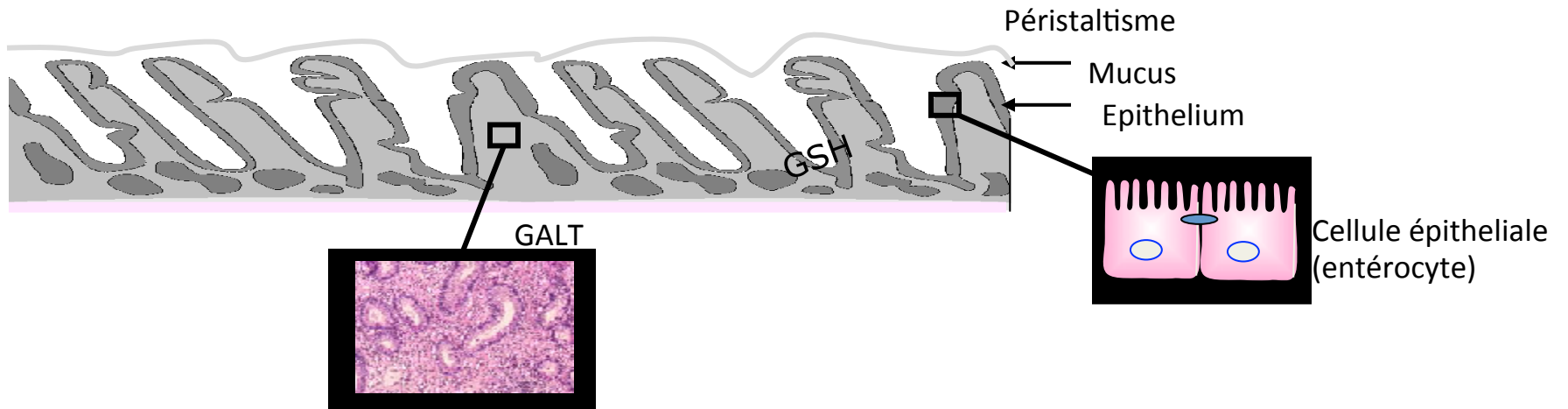
Non

➤ **Détention d'un brevet, rédaction d'un ouvrage utilisé par l'industrie**

Non

Intestin : un organe majeur dans la défense de l'organisme.

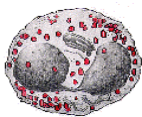
* première barrière de défense de l'organisme



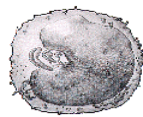
* 60 à 70 % des cellules immunitaires de l'organisme



Neutrophiles



Eosinophiles



Monocytes

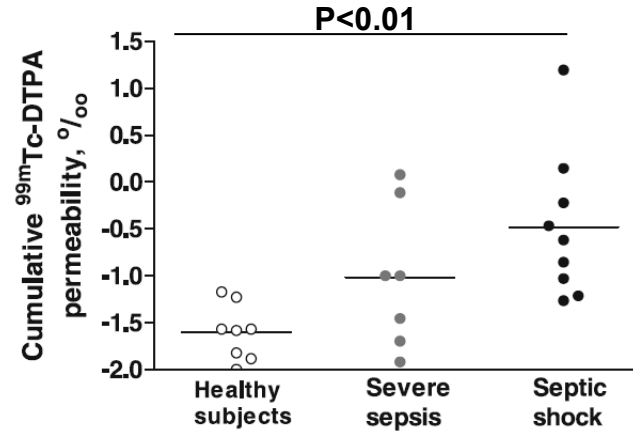
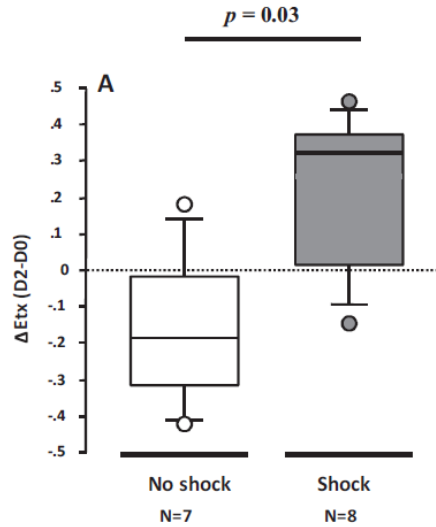


Lymphocytes

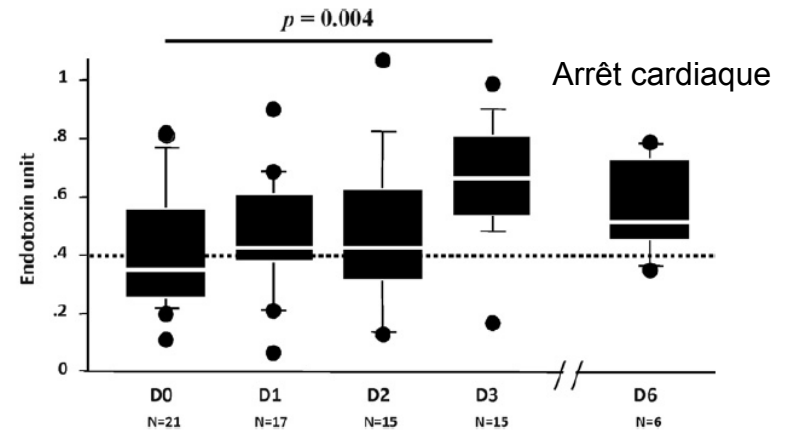


Mastocytes

Perméabilité intestinale

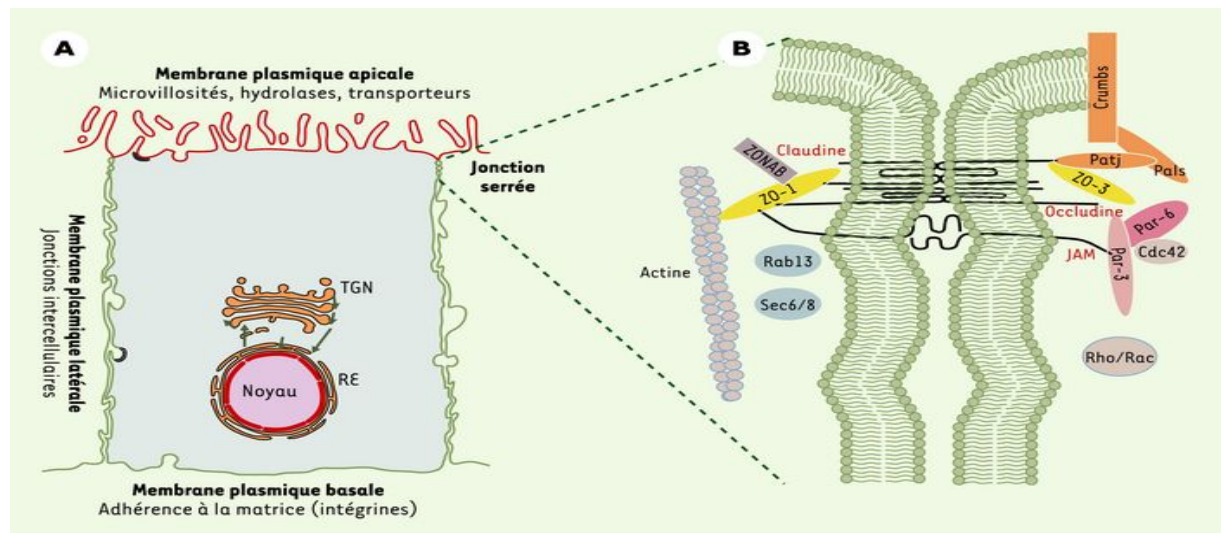
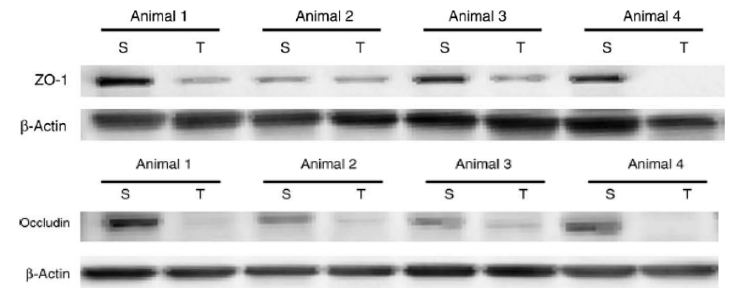
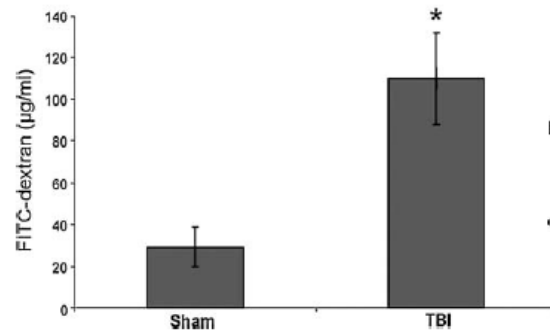
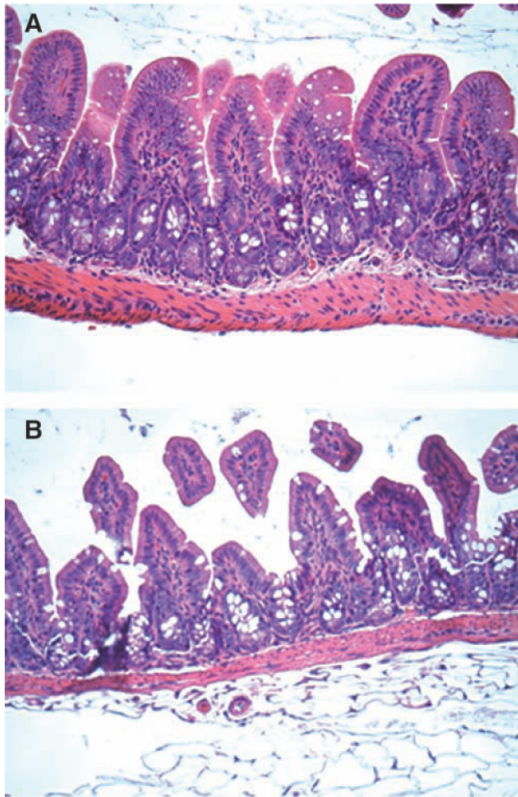


Jorgensen et al, 2006

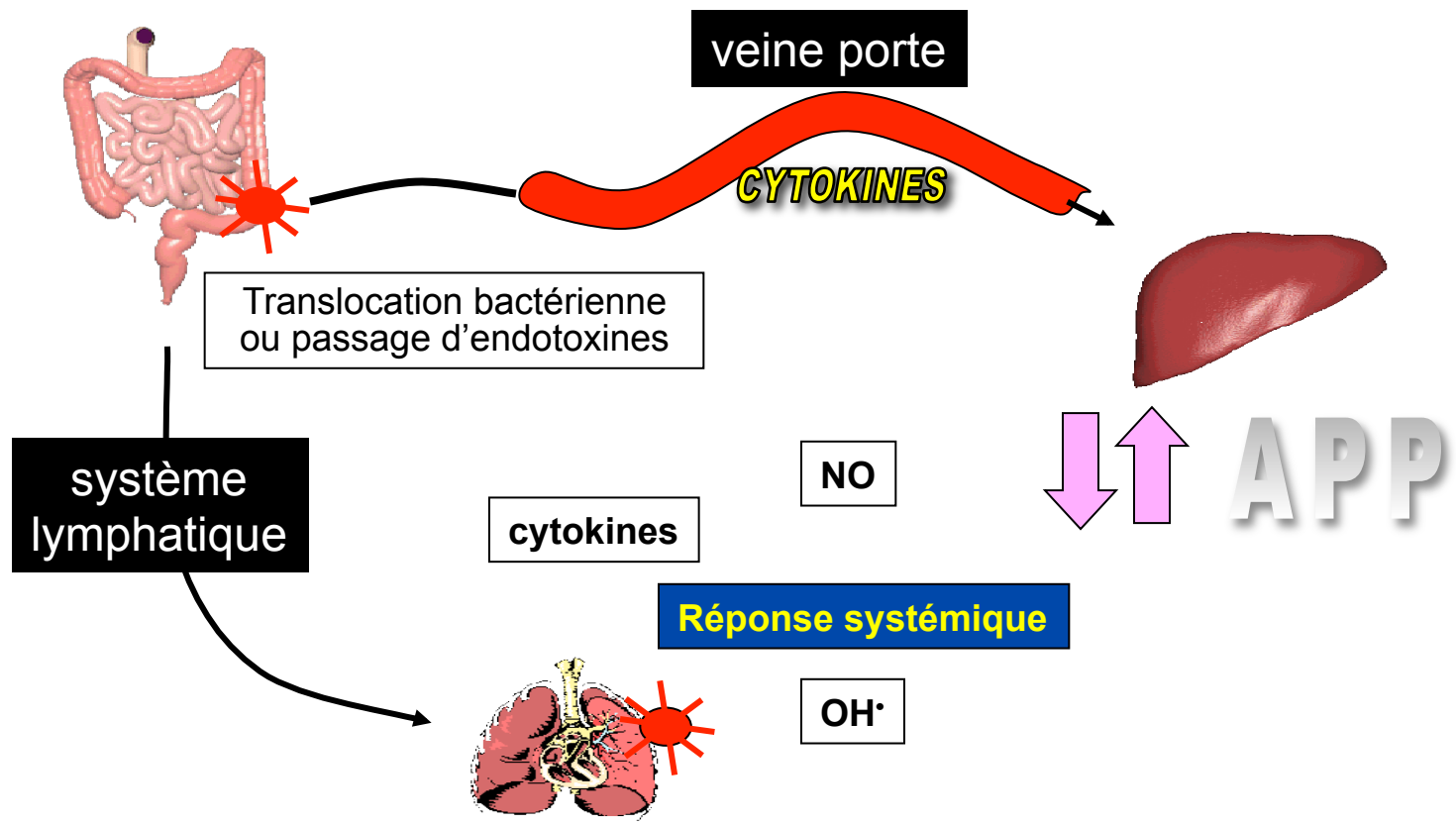


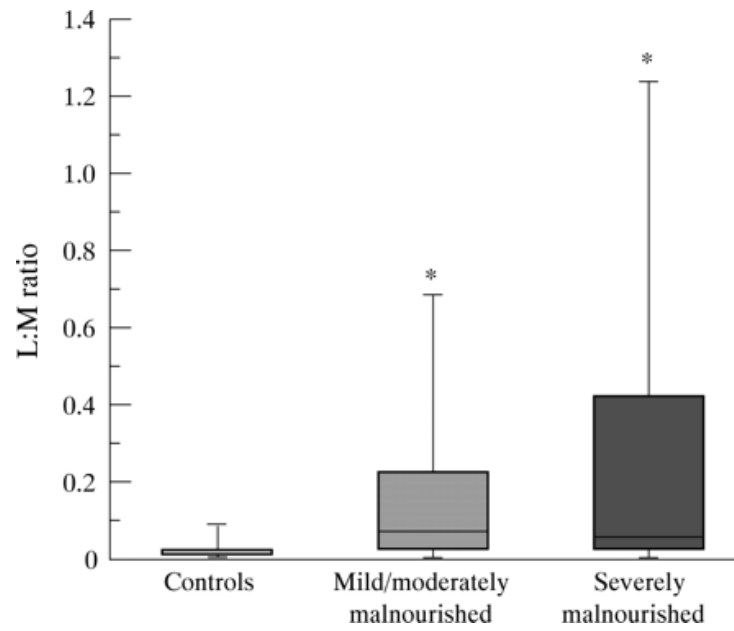
Grimaldi et al, 2013

Perméabilité intestinale: modèle de traumatisme crânien

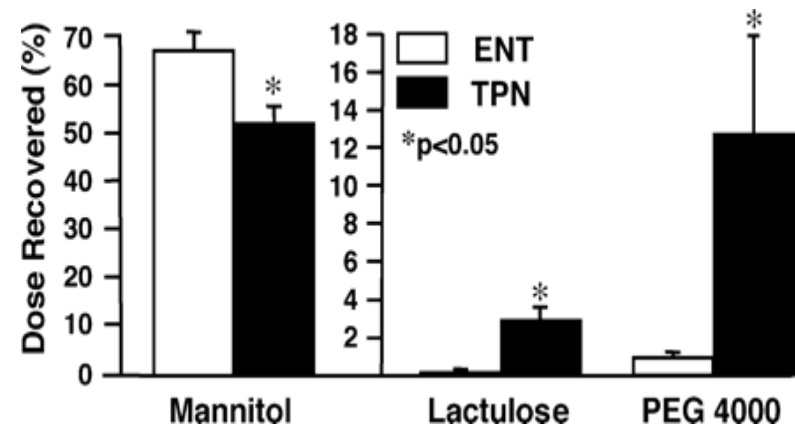


Bansal et al, 2009





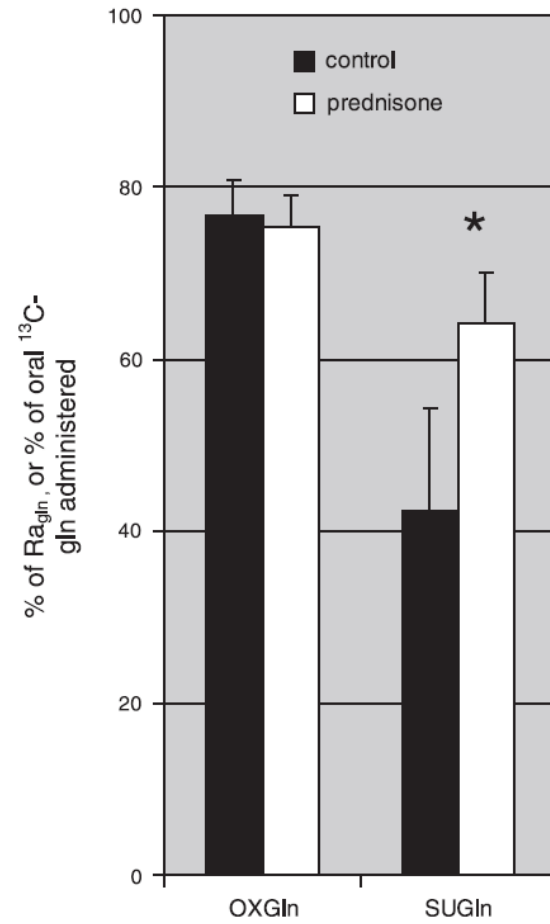
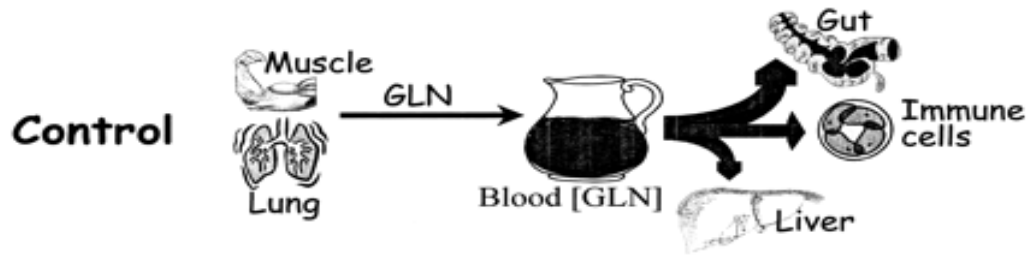
Welsh et al, 1998



Kansagram et al, 2003

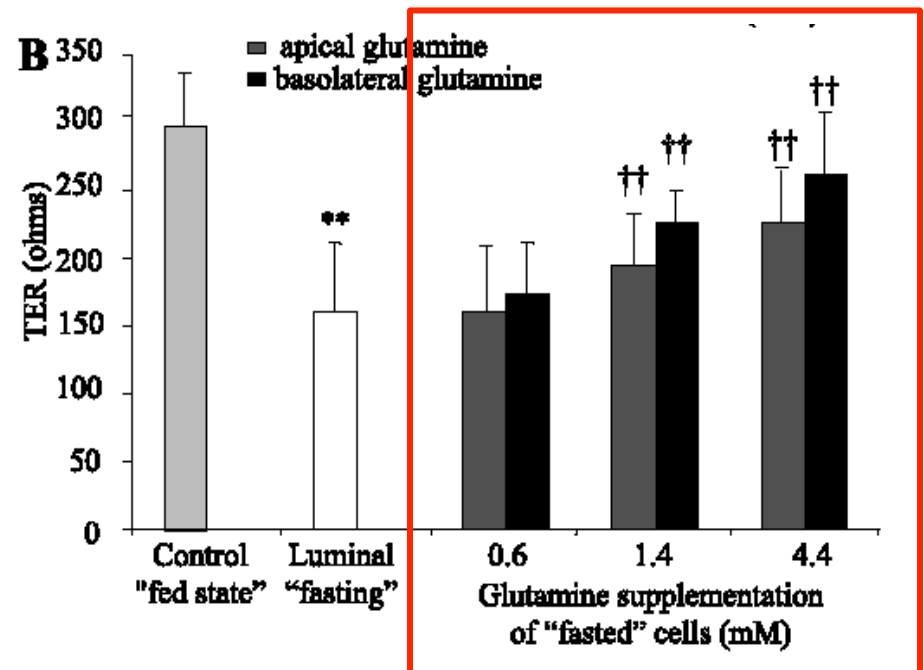
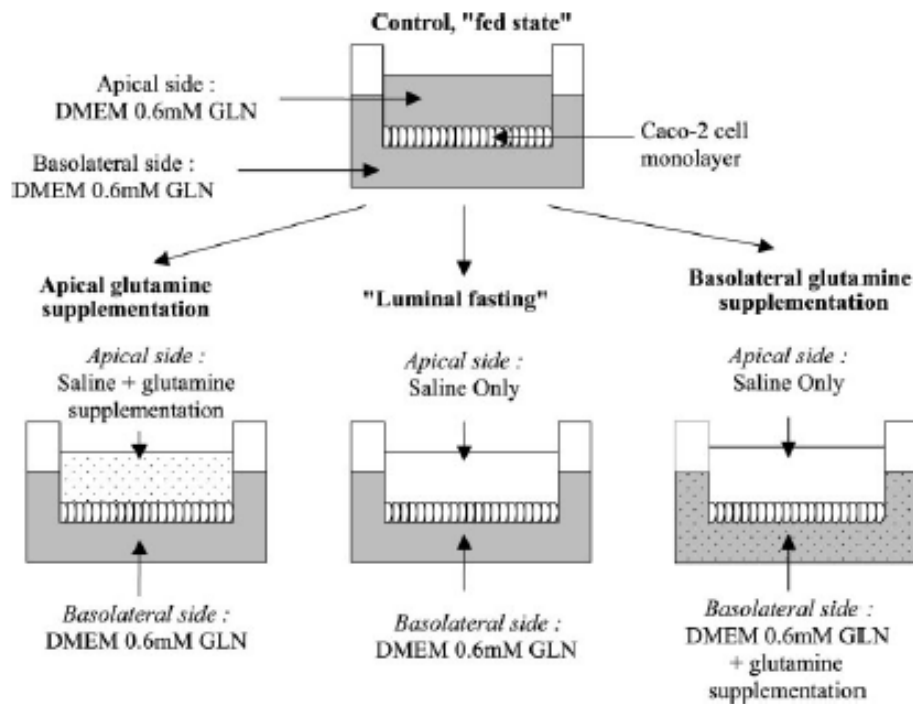
Flux interorganes de glutamine chez le sujet sain et au cours d'un sepsis

(D'après Karinch A et Souba W 2001)

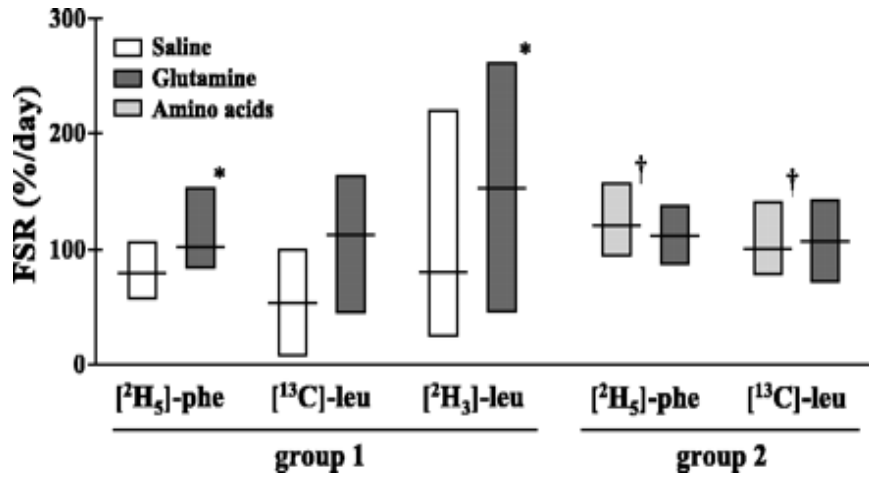


Thibault et al, 2008

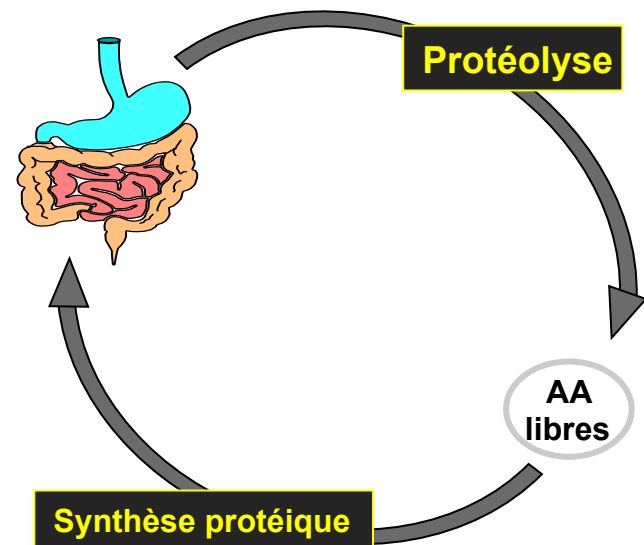
Perméabilité intestinale



LeBacquer et al, 2003



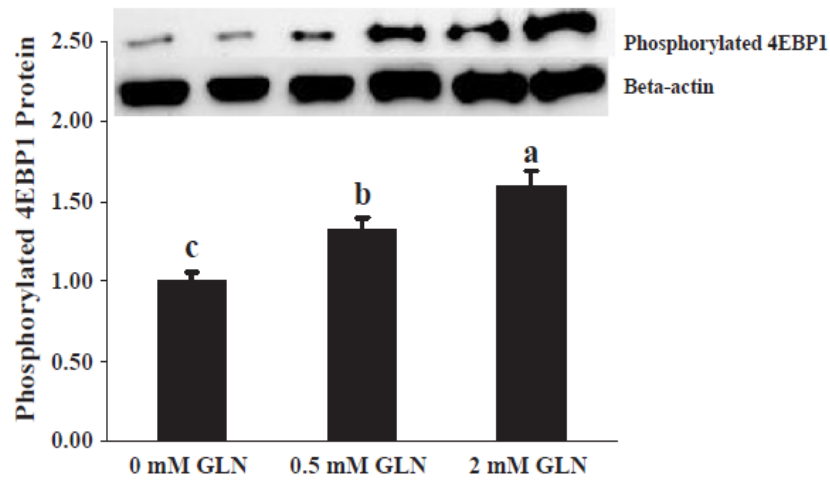
Coëffier et al, 2003



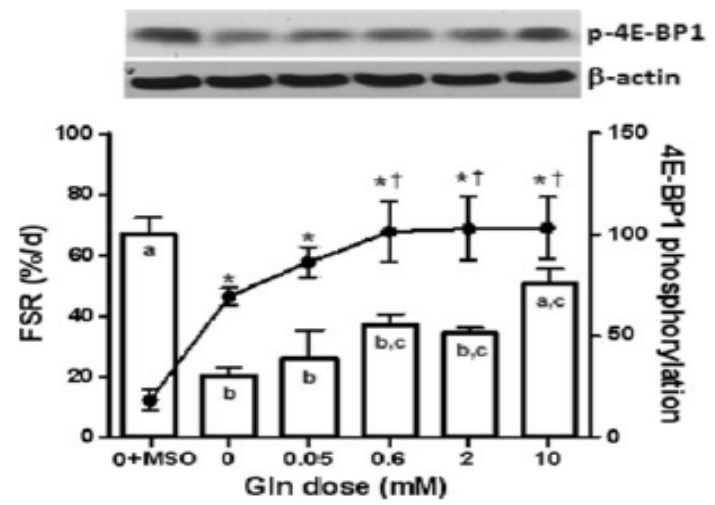
→ 50% des protéines sont renouvelées par jour.

Table 1 Effects of individual amino acids on intestinal protein synthesis and involved signaling pathways

Models		Protein synthesis	Signaling pathways	References
<i>Glutamine</i>				
In vitro, HCT-8 cells (human)				Boukhettala et al. (2012)
	Supplementation	Increased	↑ mTOR	
In vitro, IPEC-1 cells (porcine)				Xi et al. (2012)
	Supplementation	Increased	↑ mTOR	
In vitro, Caco-2 cells (human)	Supplementation	Increased	–	Le Bacquer et al. (2003)
In vitro, isolated enterocytes (rat)	Supplementation	Increased	–	Higashiguchi et al. (1993)
Jejunal segment (piglets)	Supplementation	Decreased	–	Adegoke et al. (2003)
In vivo, healthy humans	Supplementation	Increased	–	Coeffier et al. (2003a)
In vivo, malnourished rats	Supplementation	Unaffected	–	Tannus et al. (2009)
In vivo, hypercatabolic dogs	Supplementation	Increased	–	Humbert et al. (2002)

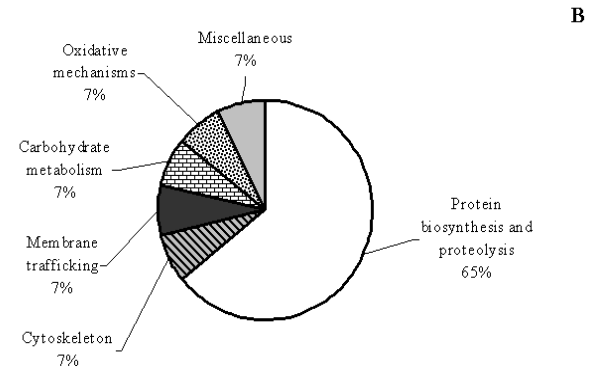
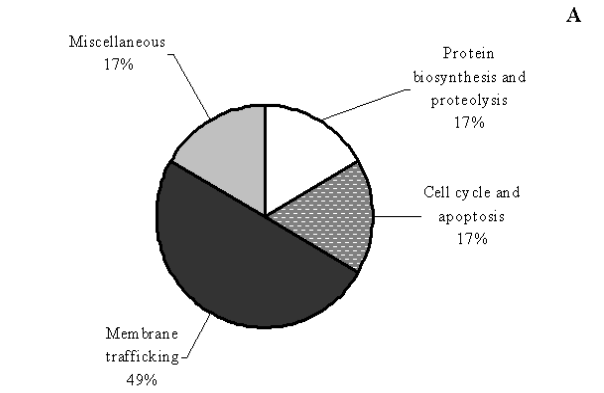
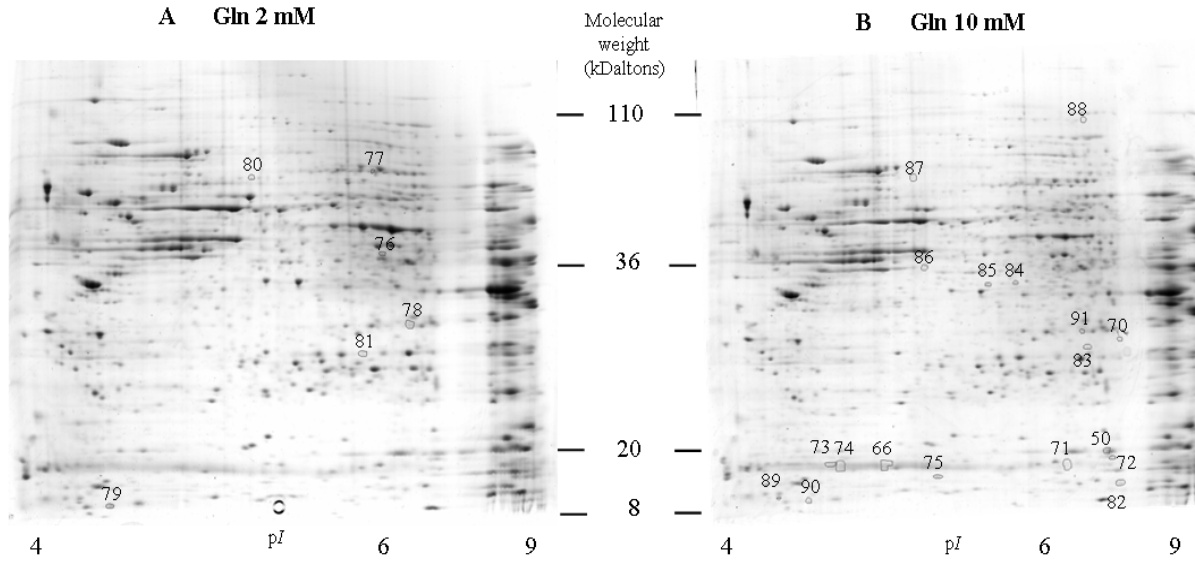


Xi et al, J Nutr Biochem 2012



Boukhattala et al, Amino Acids 2012

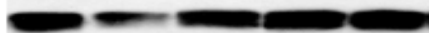
Basal conditions



A

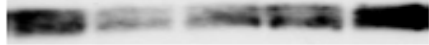
GLN (mM)	0	0	0.1	0.6	4
MSO (mM)	0	4	4	4	4

S



Claudin-1

I

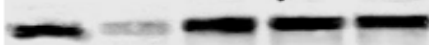


Claudin-1

B

GLN (mM)	0	0	0.1	0.6	4
MSO (mM)	0	4	4	4	4

S



Occludin

I



Occludin

C

GLN (mM)	0	0	0.1	0.6	4
MSO (mM)	0	4	4	4	4

S



ZO-1

I



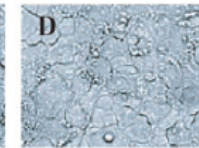
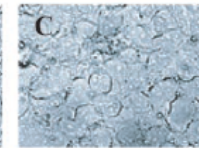
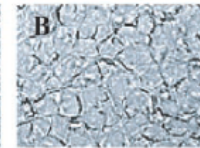
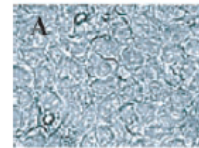
ZO-1

GLN 0mM

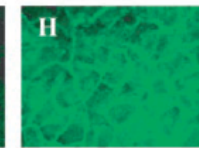
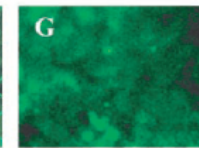
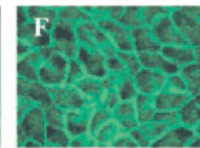
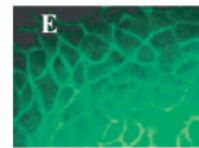
GLN 0.6mM

GLN 0/MSO 4mM

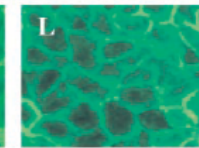
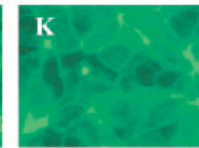
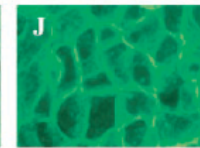
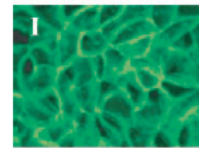
GLN 0.6/MSO 4mM



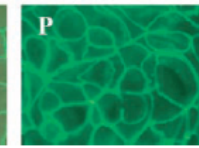
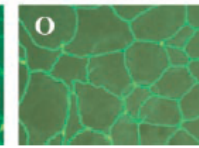
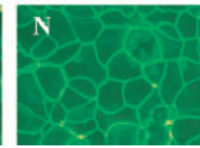
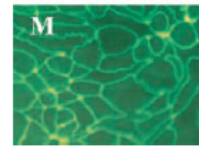
Caco-2



Claudin-1

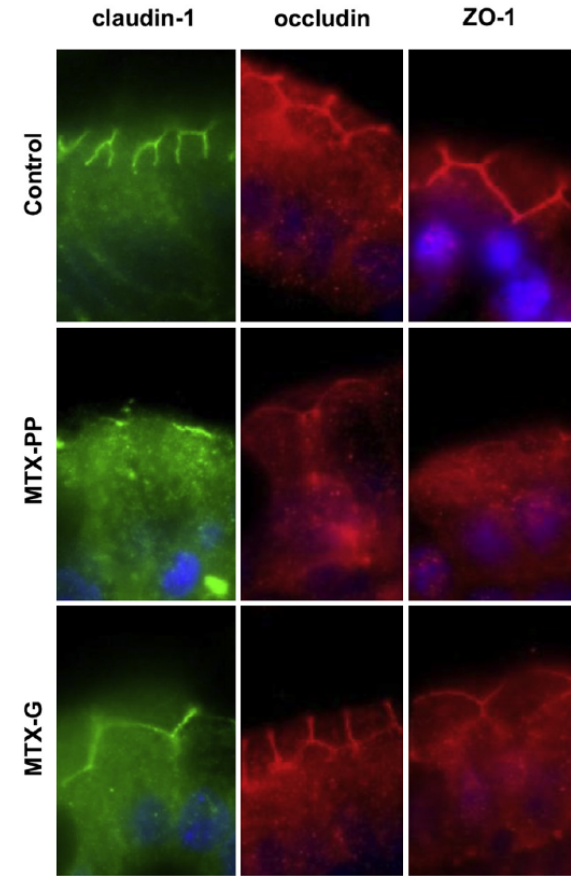
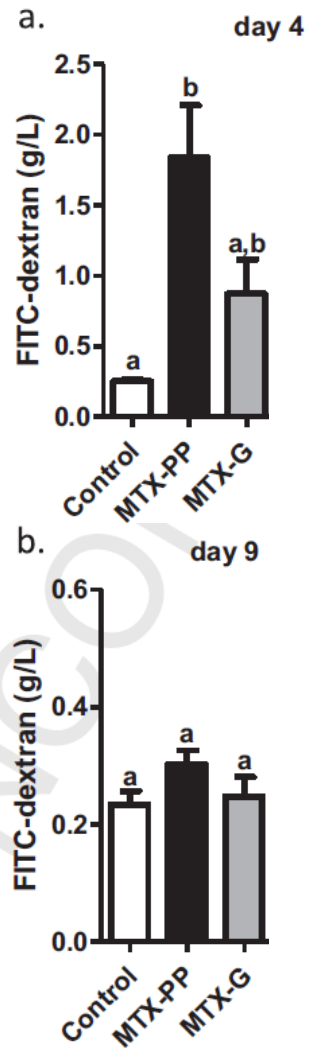
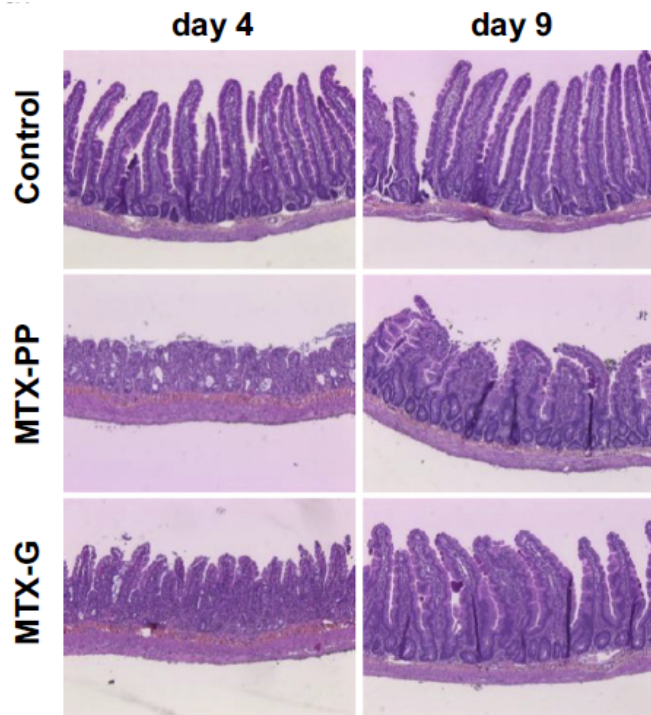


Occludin

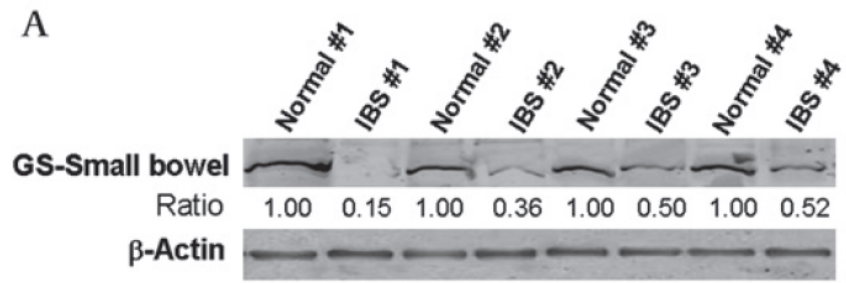
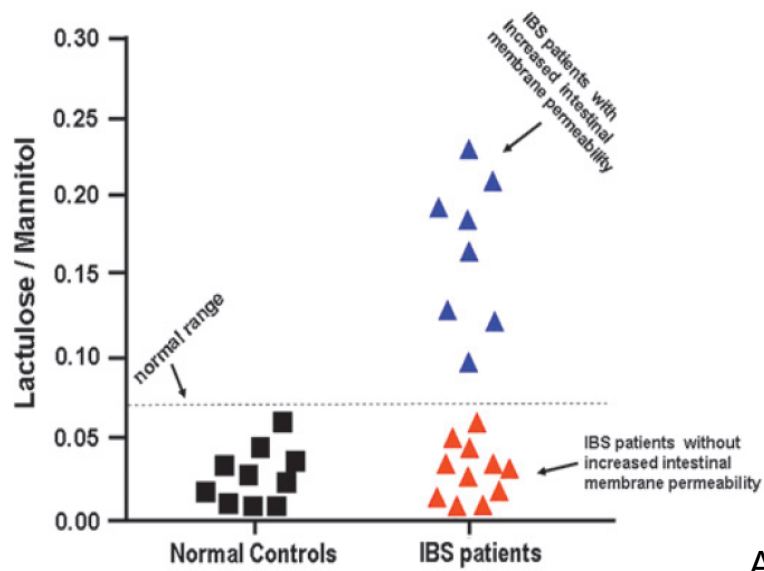


ZO-1

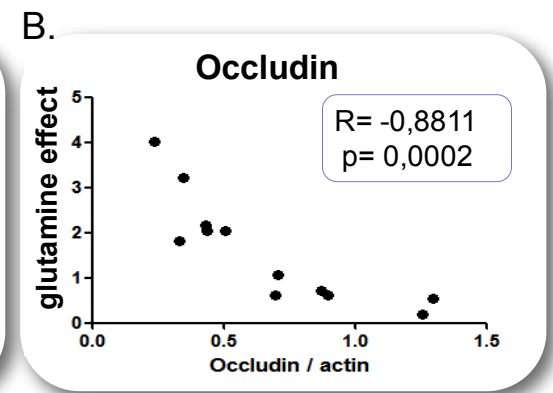
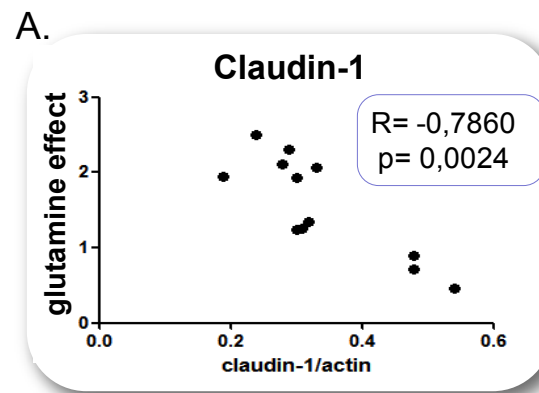
Li et al, 2004



Beutheu et al, Clin Nutr (In press)



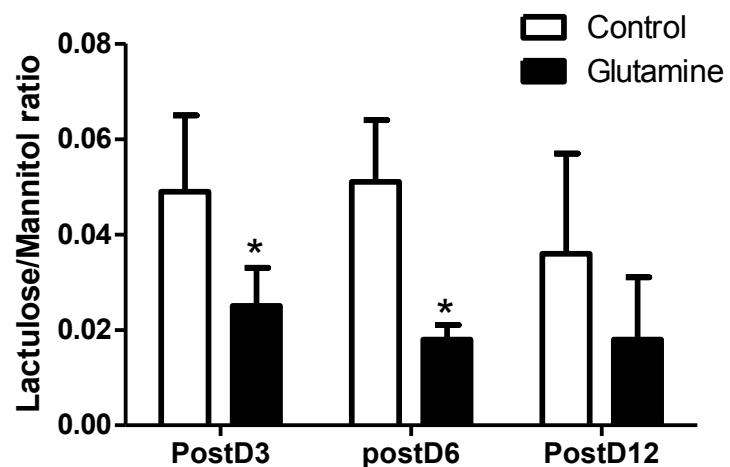
Zhou et al, 2009



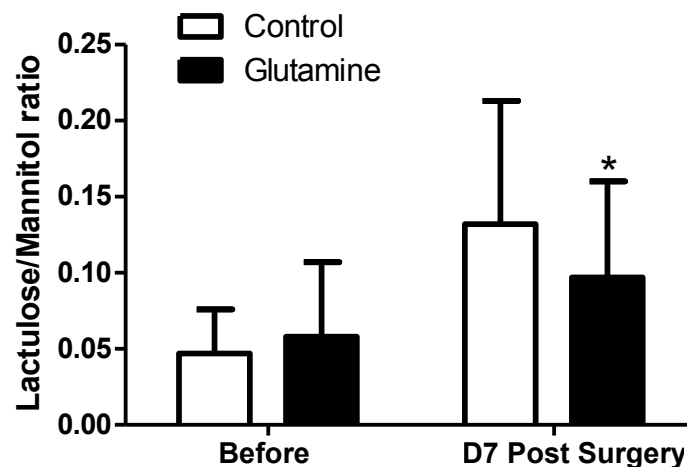
Bertrand et al, JFN2013 – P204

La glutamine diminue la translocation bactérienne chez des patients polytraumatisés sous nutrition parentérale exclusive.

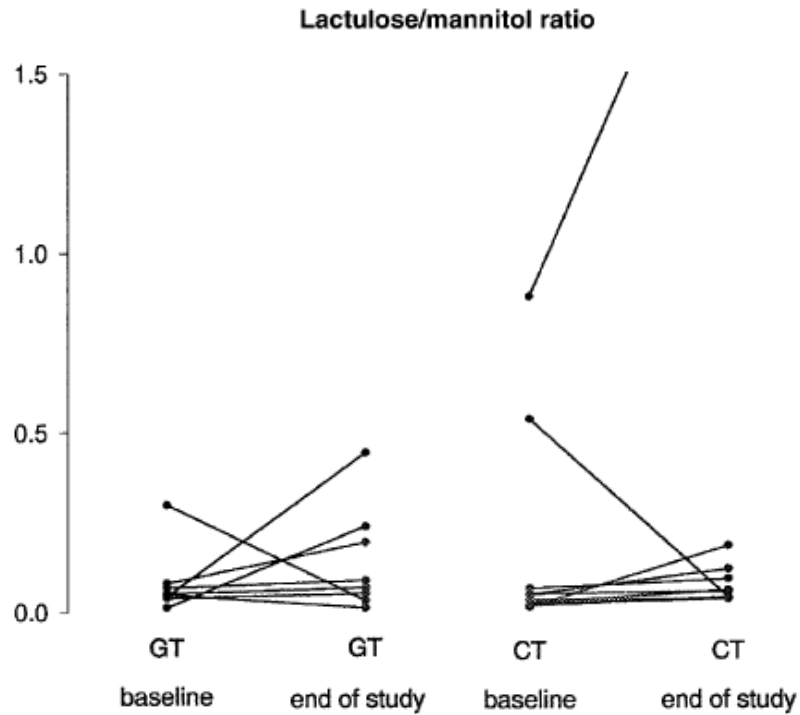
Van der Hulst et al, Lancet 1993



Zhou et al, 2003



Jiang et al, 1999



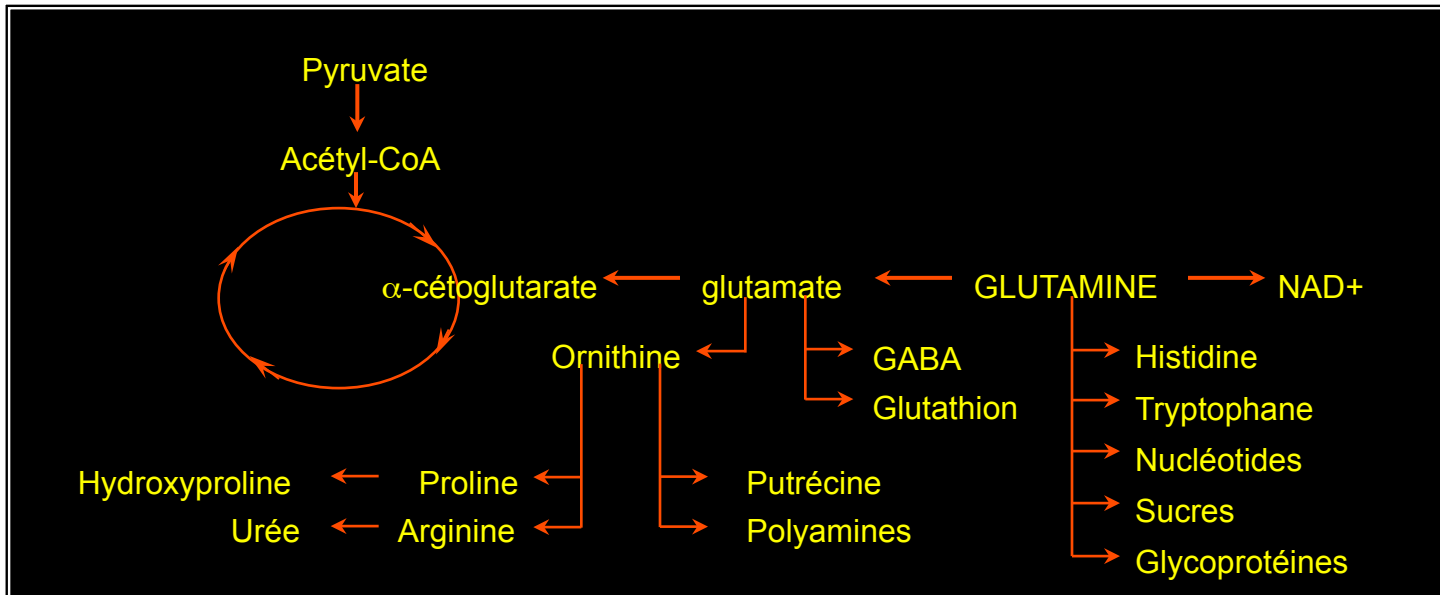
Intestinal permeability and systemic infections in critically ill patients: Effect of glutamine*

Daurea A. De-Souza, MD, PhD; Lewis J. Greene, PhD

Crit Care Med 2005 Vol. 33, No. 5

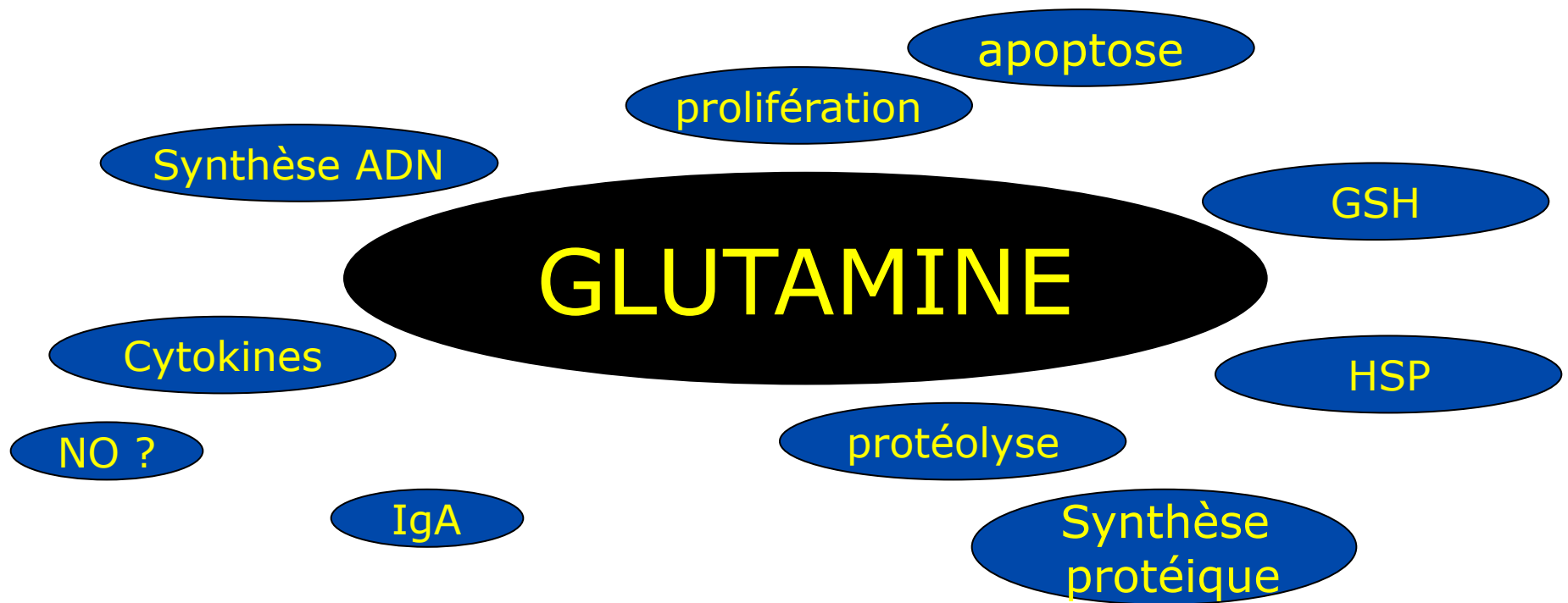
Conclusions: Glutamine administration improves the prognosis of critically ill patients presumably by maintaining the physiologic intestinal barrier and by reducing the frequency of infections. (Crit Care Med 2005; 33:1125–1135)

Hulsewe et al, 2004

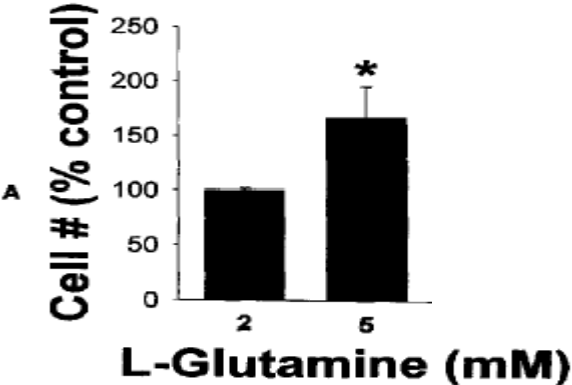


Versatilité de la glutamine : de nombreuses interactions métaboliques

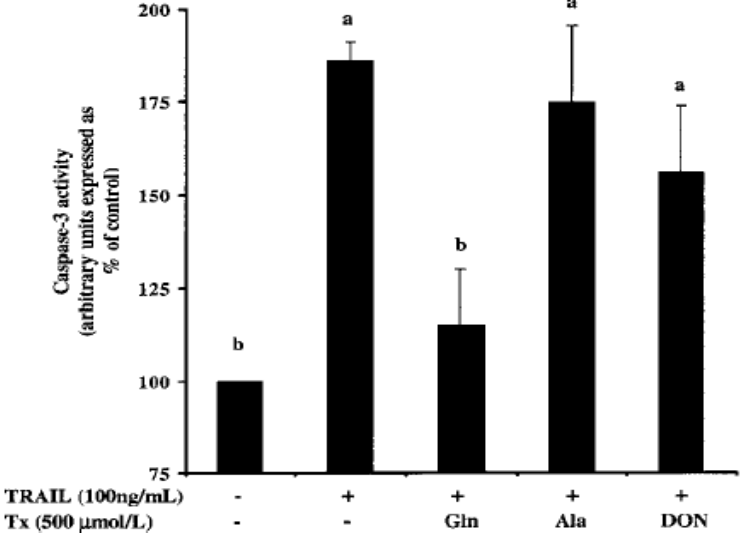
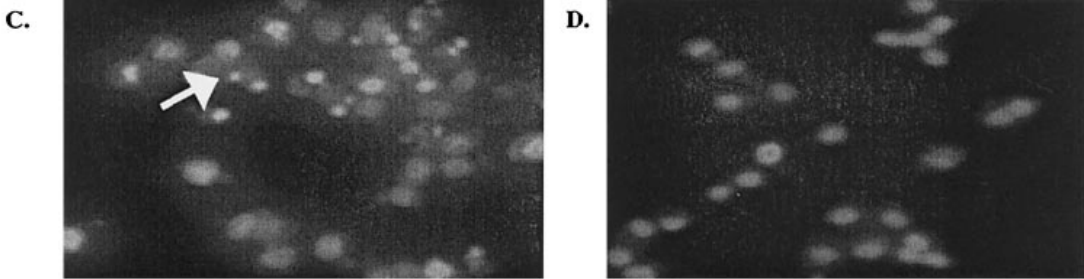
D 'après Neu J 2001



Prolifération/Apoptose

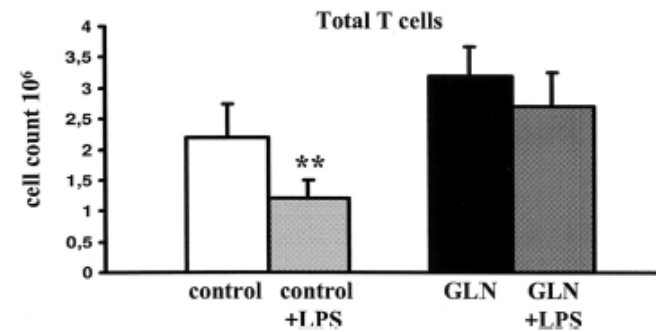
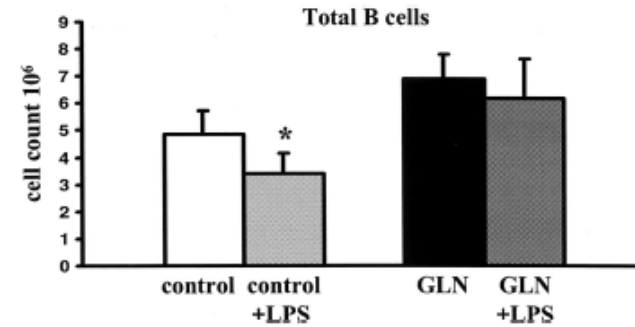
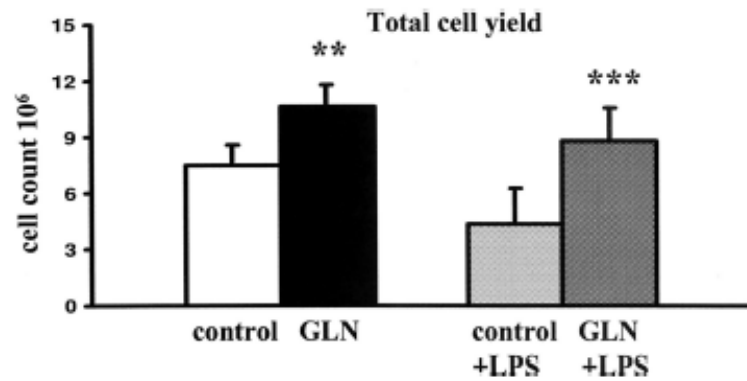


Murnin et al, 2000

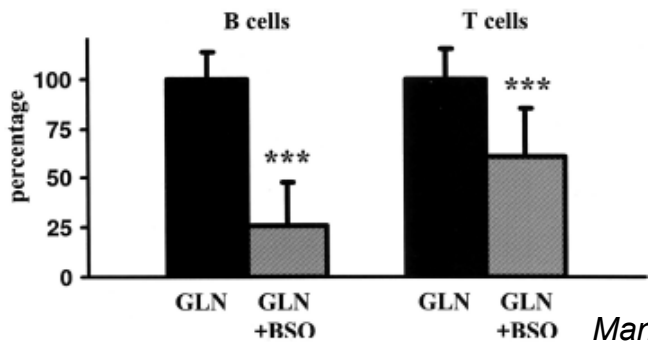
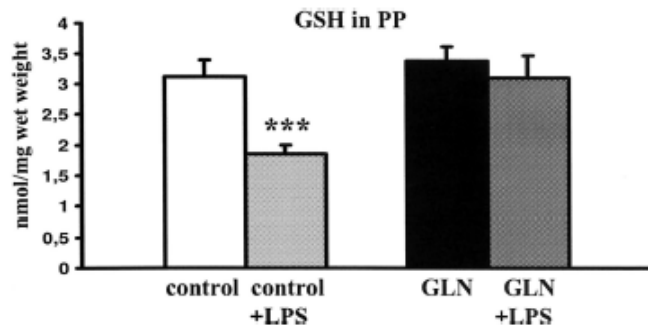
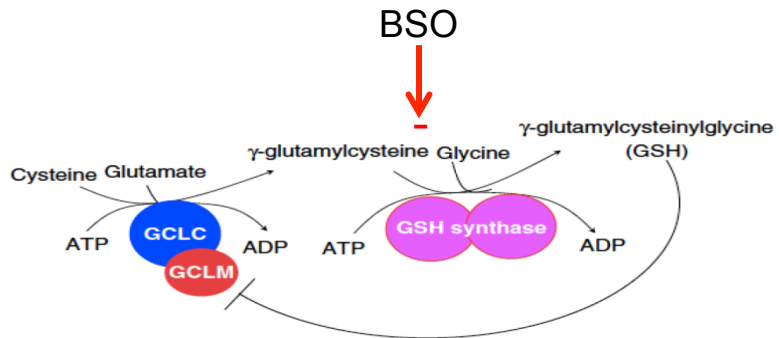


Evans et al, 2003.

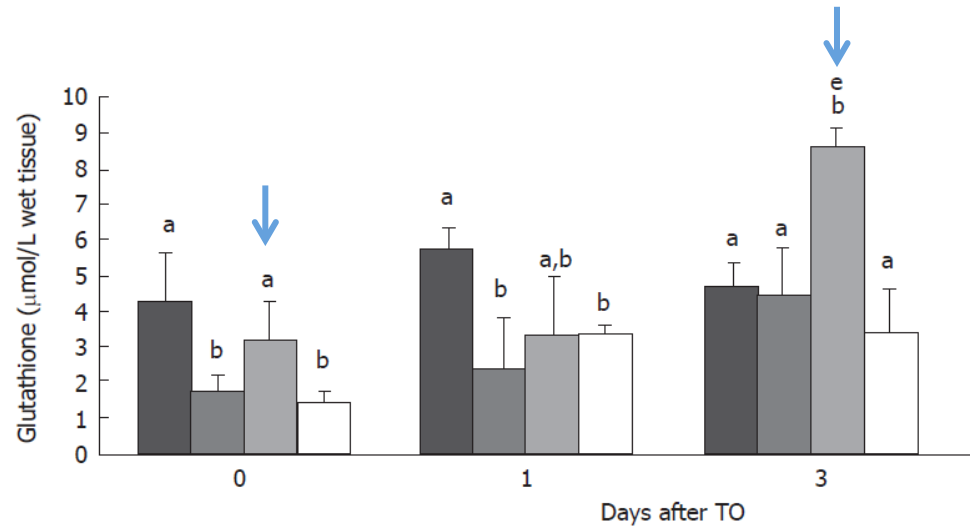
Réponse immunitaire



Manhart et al, 2001.



Manhart et al, 2001.

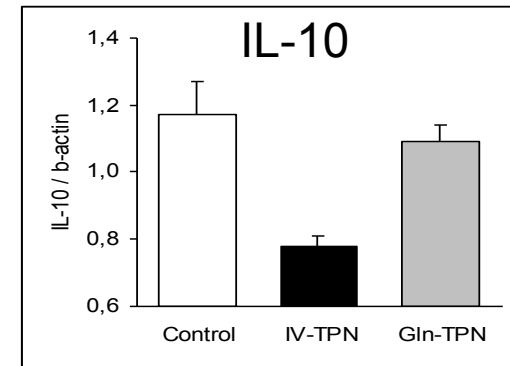
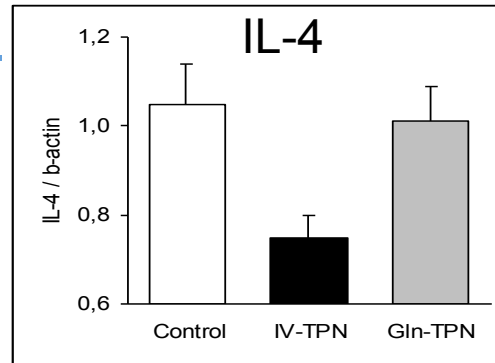


Belmonte et al, 2007.

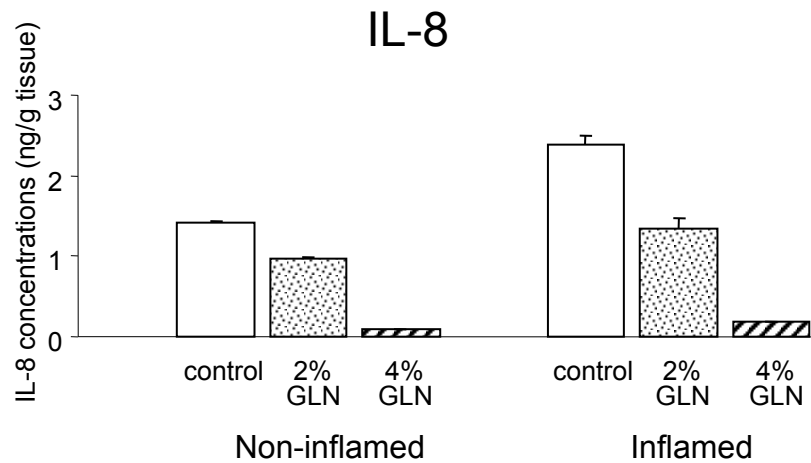
Pas d'effet de la glutamine sur le glutathion

LeBacquer et al, 2003

Réponse inflammatoire



Fukatsu et al, 2001



Ameho et al, 1997

↓ Chimiokines (I-TAC, IP-10)

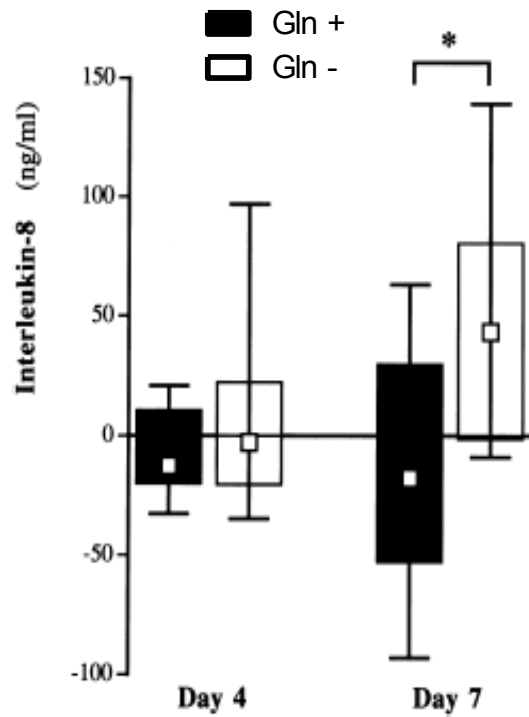
Marion et al, Clin Nutr 2004

↓ cytokines pro-inflammatoires
IL-6, TNF α

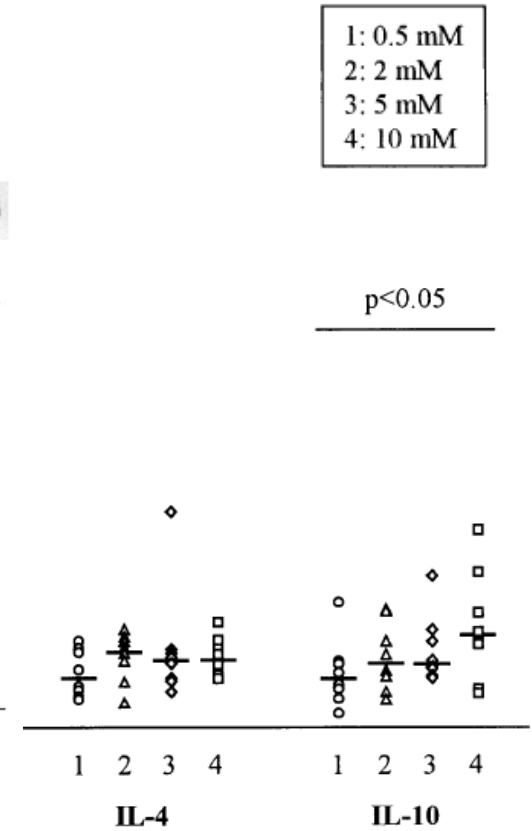
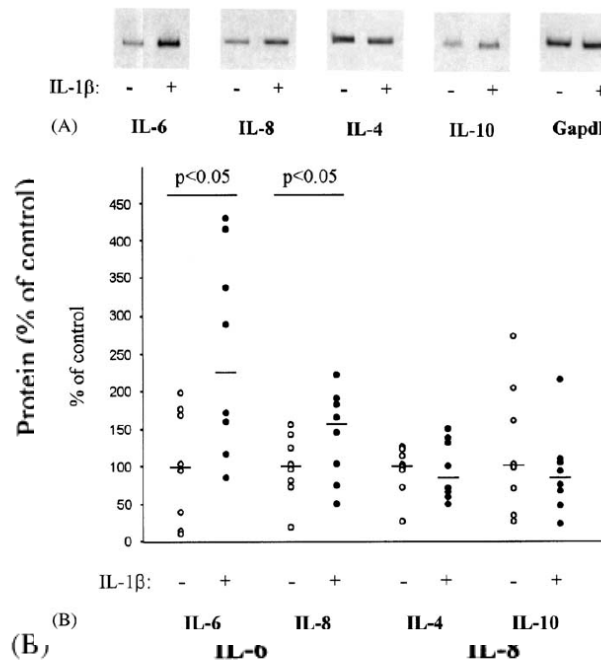
Aosasa et al, JPEN 2003

↑ cytokine anti-inflammatoire
IL-10

Aosasa et al, JPEN 2003



DeBeaux et al, 1998



Coëffier et al, 2003

Heat shock proteins

Induction ou stimulation de l'expression des HSP par la glutamine
(HSP70, HSP27, HSP32)

in vitro ⇒ différents lignées cellulaires
(*Ehrenfield et al 1995, Wischmeyer et al 1997, Chow et al 1998*)

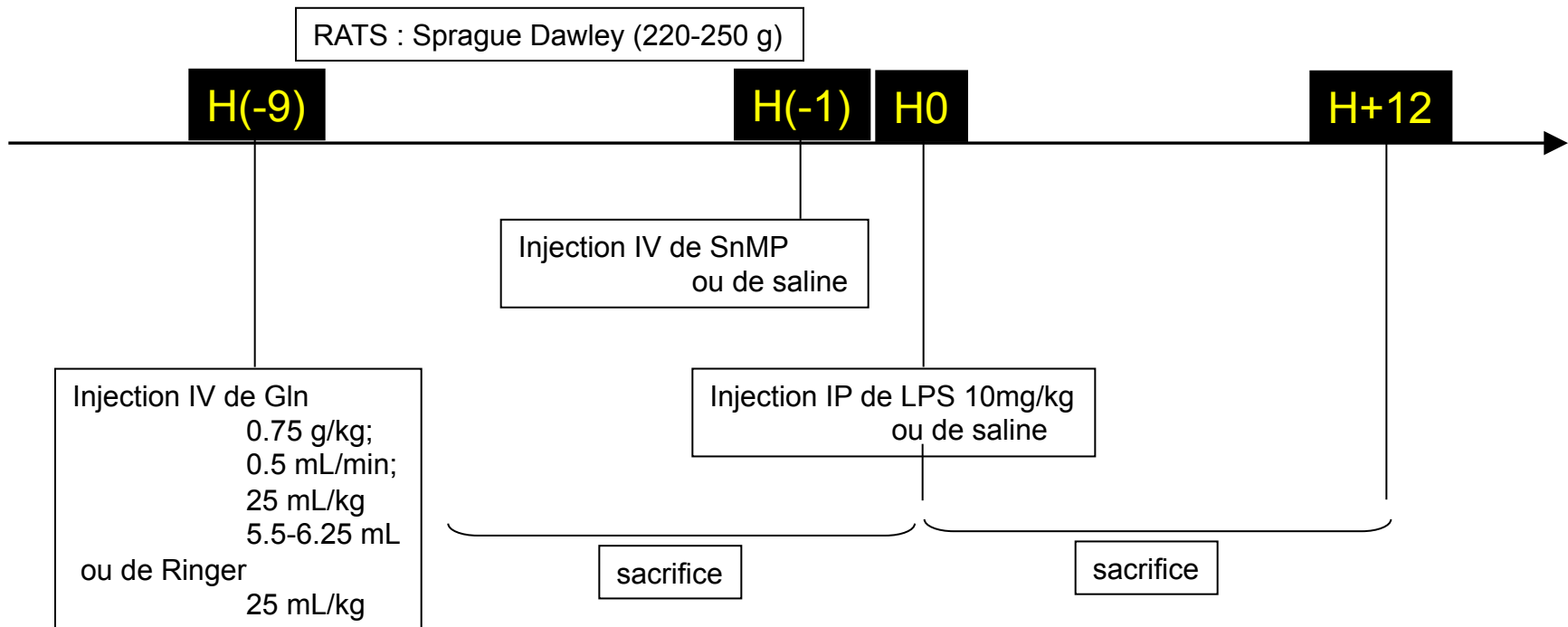
in vivo (rat) ⇒ différents tissus (cœur, poumons, intestin)
(*Wischmeyer et al 2001*)

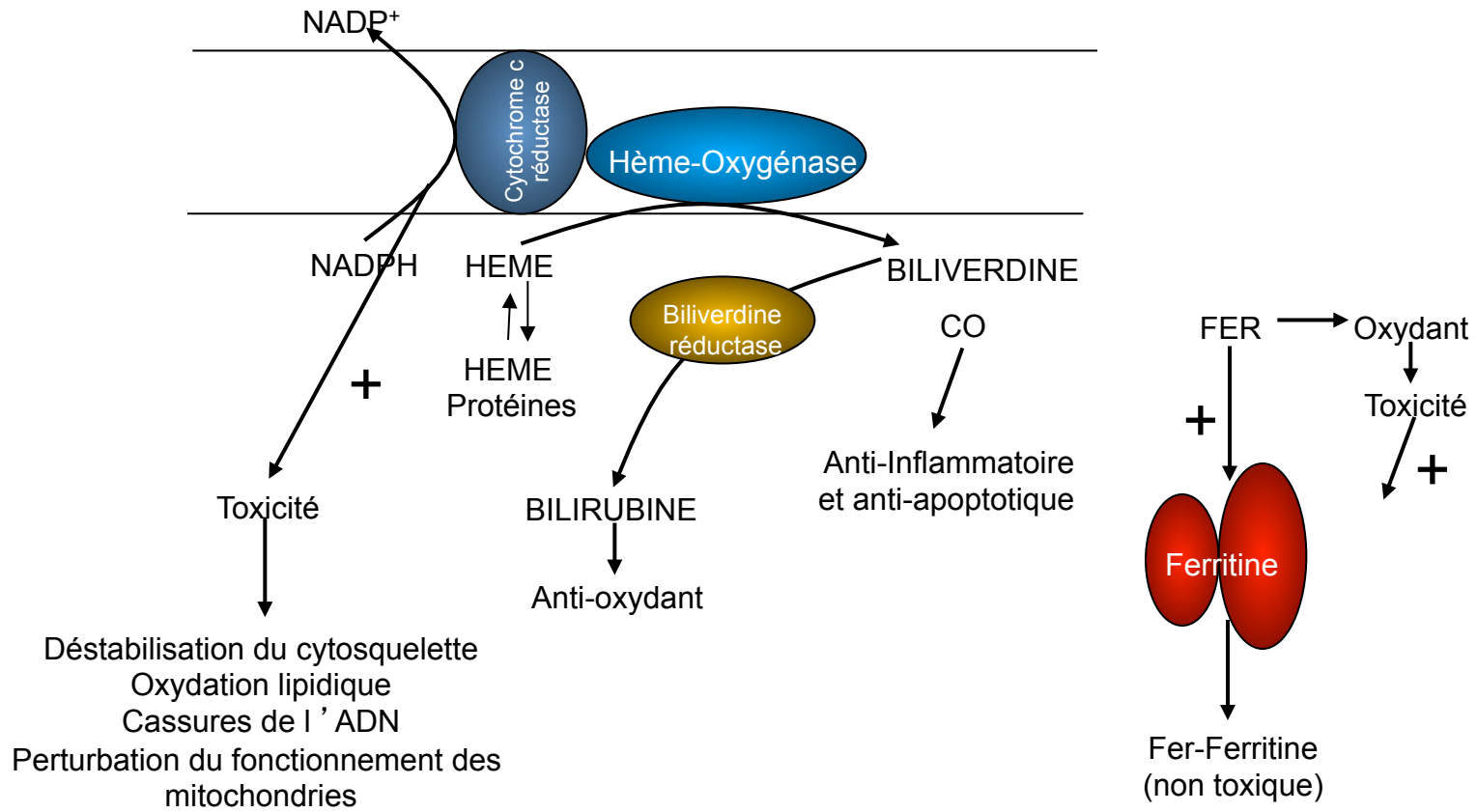
Effet protecteur de la glutamine sur l'intestin ⇔ à une induction de HO-1 chez le rat
(*Tamaki et al 1999*)
(*Uheara et al, 2005*)

The lower intestinal tract-specific induction of heme oxygenase-1 by glutamine protects against endotoxemic intestinal injury*

Kenji Uehara, MD; Toru Takahashi, MD; Hiromi Fujii, MD; Hiroko Shimizu, MD; Emiko Omori, MSc; Masaki Matsumi, MD; Masataka Yokoyama, MD; Kiyoshi Morita, MD; Reiko Akagi, PhD; Shigeru Sassa, MD, PhD

Crit Care Med 2005 Vol. 33, No. 2





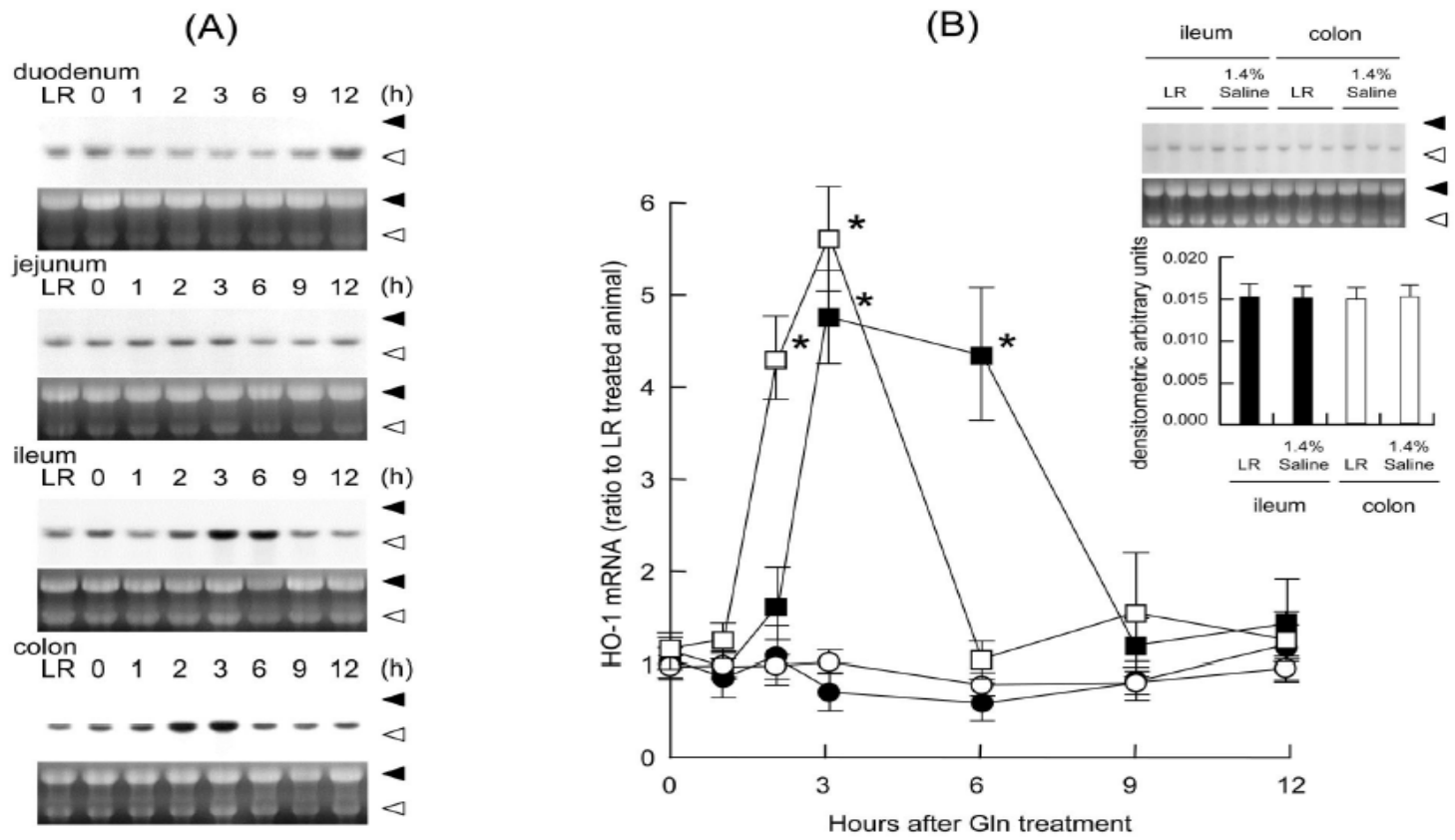


Figure 1. Effect of glutamine (*Gln*) administration on heme oxygenase (*HO*)-1 gene expression in various regions of the intestine.

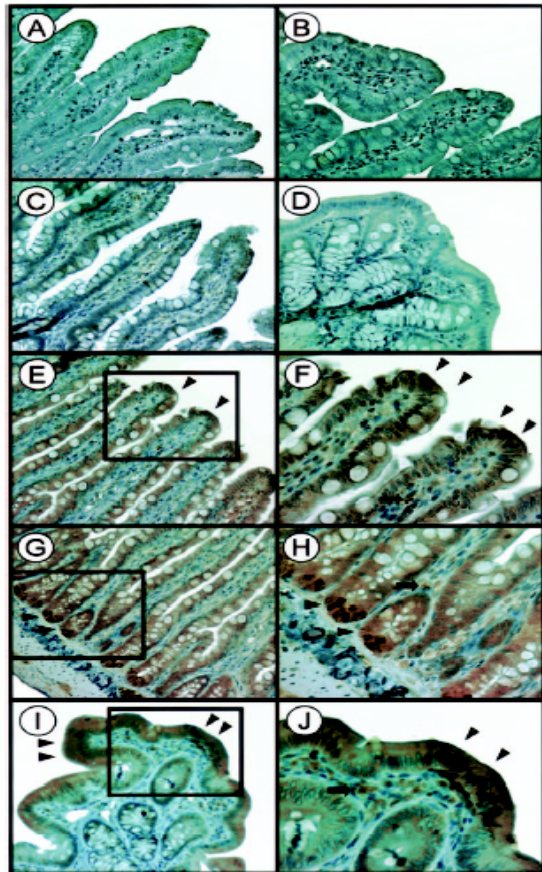
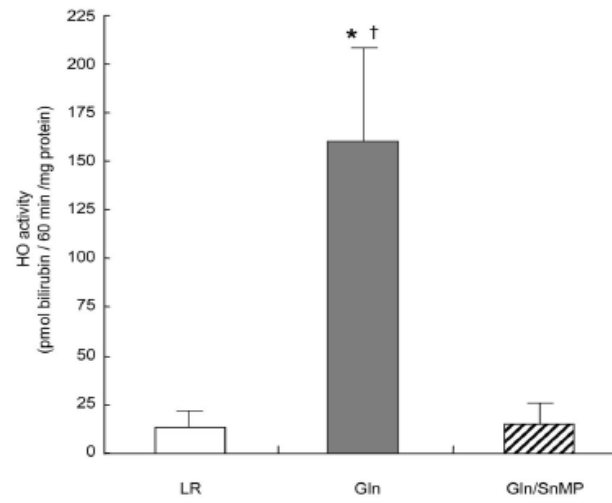


Figure 2. Immunohistochemistry of heme oxygenase (HO)-1



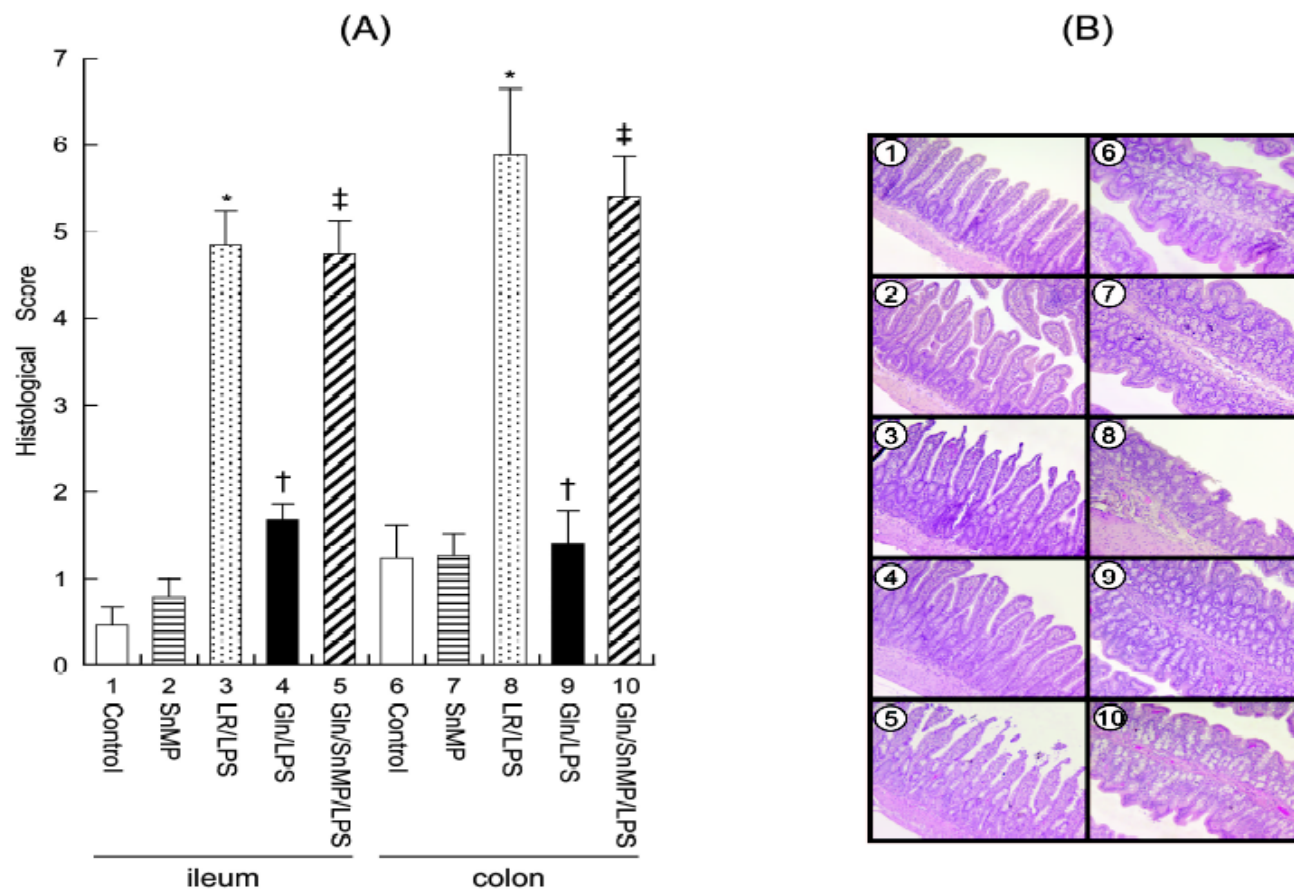


Figure 4. Effect of glutamine (*Gln*) pretreatment on histologic damage in the lower intestine of lipopolysaccharide (*LPS*) rats.

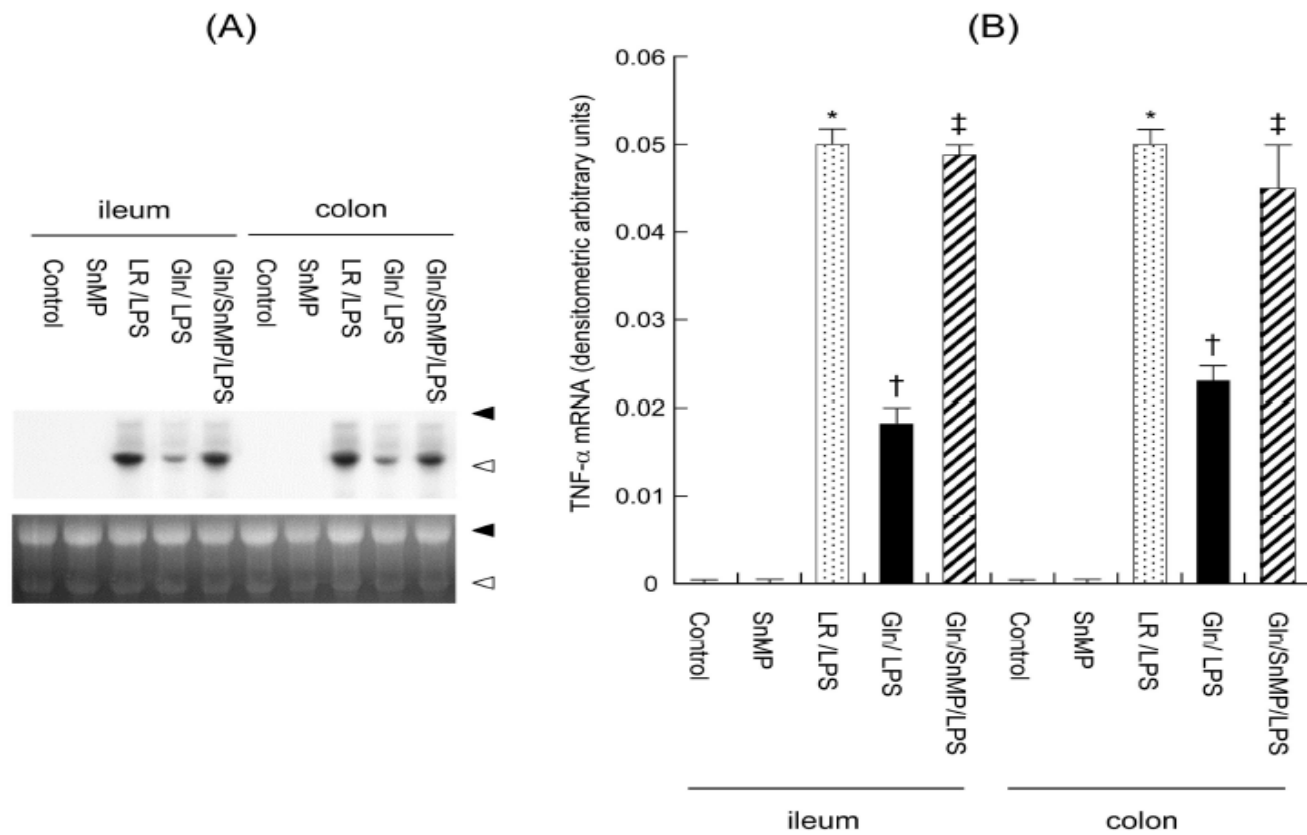


Figure 5. Effect of glutamine (*Gln*) pretreatment on tumor necrosis factor (TNF)- α gene expression in the lower intestine of lipopolysaccharide (*LPS*) rats.

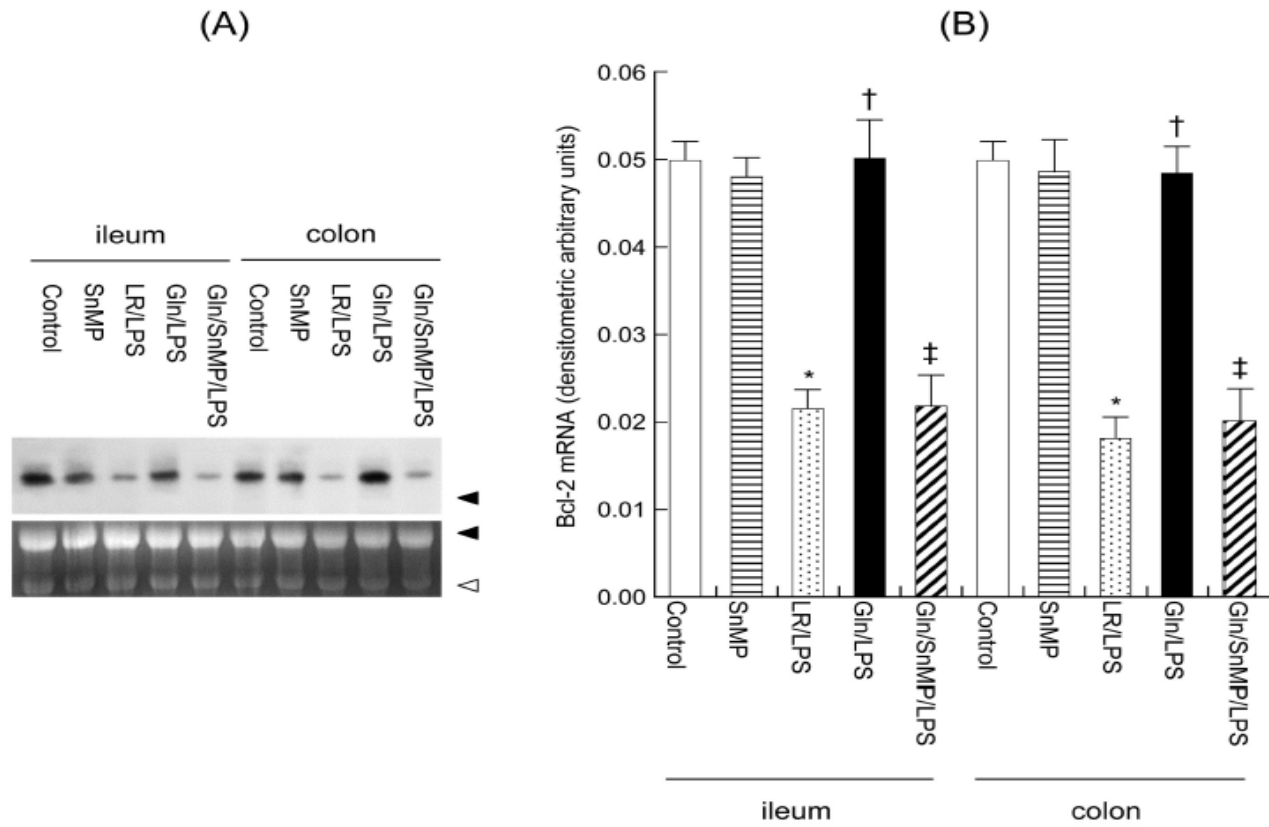


Figure 6. Effect of glutamine (*Gln*) pretreatment on Bcl-2 gene expression in the lower intestine of lipopolysaccharide (*LPS*) rats.

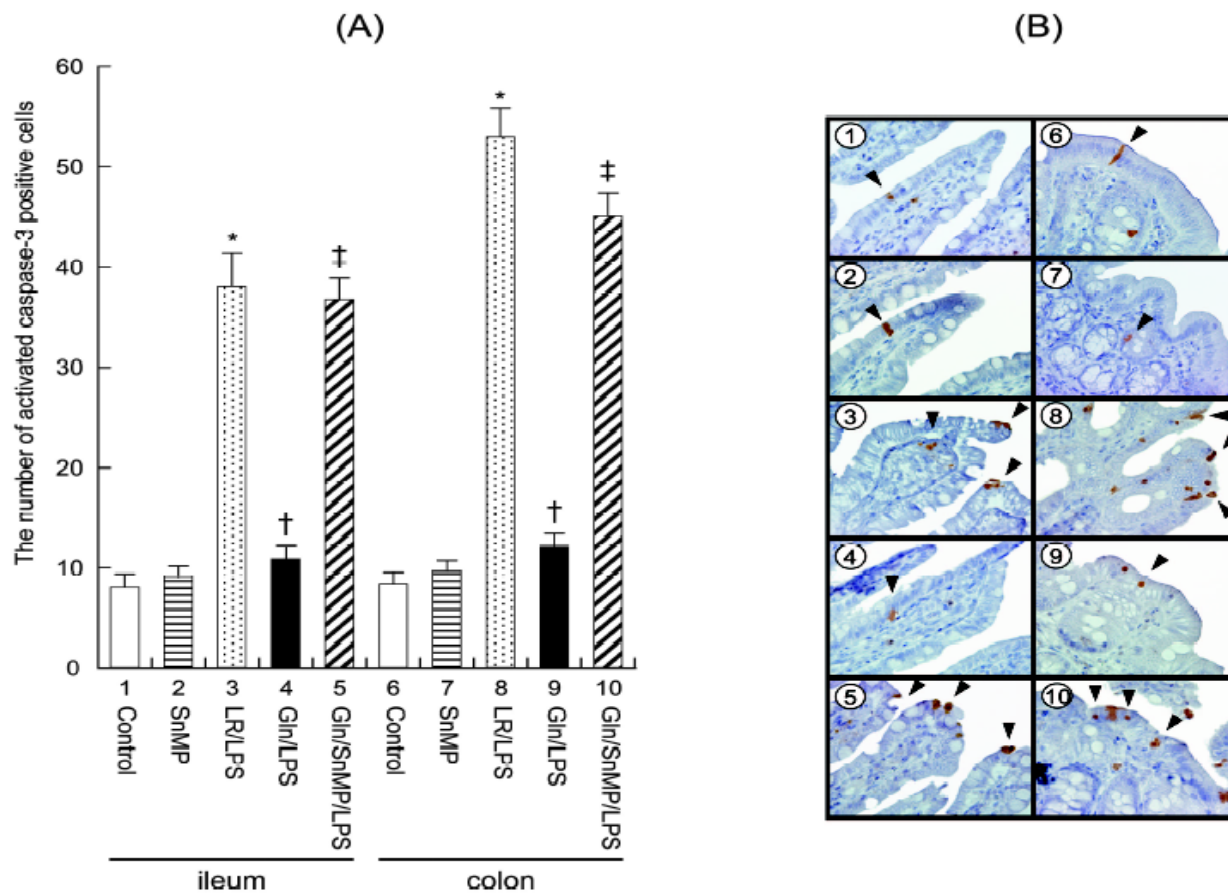


Figure 7. Effect of glutamine (*Gln*) pretreatment on expression of activated caspase-3 in the lower intestine of lipopolysaccharide (*LPS*) rats.

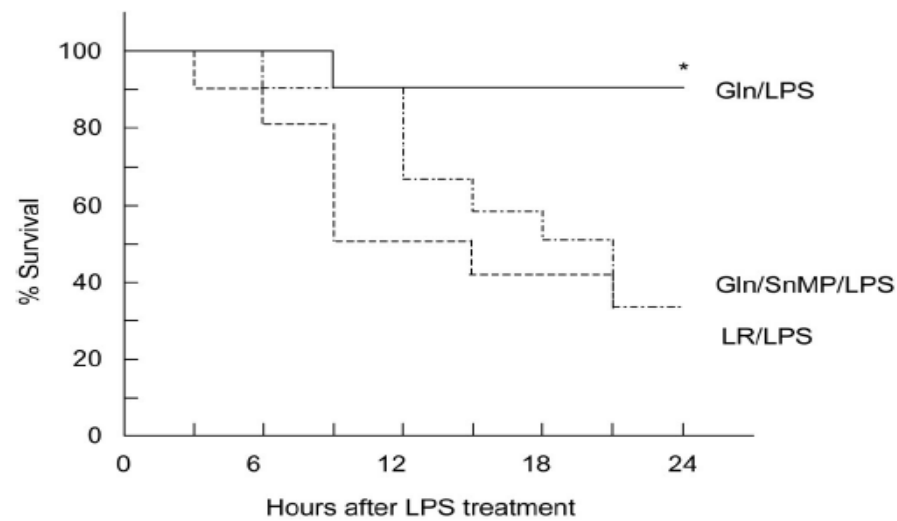


Figure 8. Effect of glutamine (*Gln*) pretreatment on survival of rats after lipopolysaccharide (*LPS*) administration. Rats were administered with *Gln* or lactated Ringer's solution (*LR*) intravenously 9 hrs before intraperitoneal injection of *LPS* (20 mg/kg). Tin mesoporphyrin (*SnMP*; 1 μ mol/kg) was administered to rats intravenously 1 hr before *LPS* treatment, and their survival was examined. *LR/LPS* (dashed line); *LPS* with *LR* pretreatment; *Gln/LPS* (solid line), *LPS* with *Gln* pretreatment; *Gln/SnMP/LPS* (dashed and dotted line), *LPS* with *Gln* pretreatment followed by *SnMP* administration. Results are from 12 independent experiments ($n = 12$ for each group). Shown is the Kaplan-Meier plot of survival in rats after *LPS* treatment. * $p < .05$ vs. *LR/LPS* or *Gln/SnMP/LPS*.

10 volontaires sains



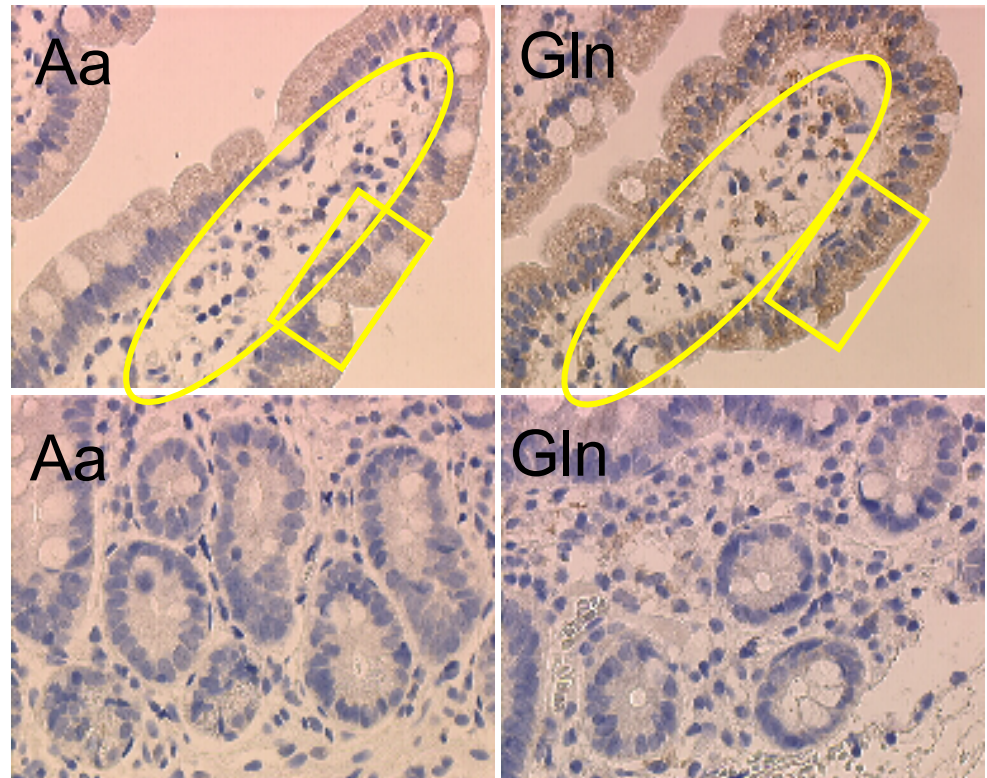
15 jours



Perfusion entérale
x 6 heures

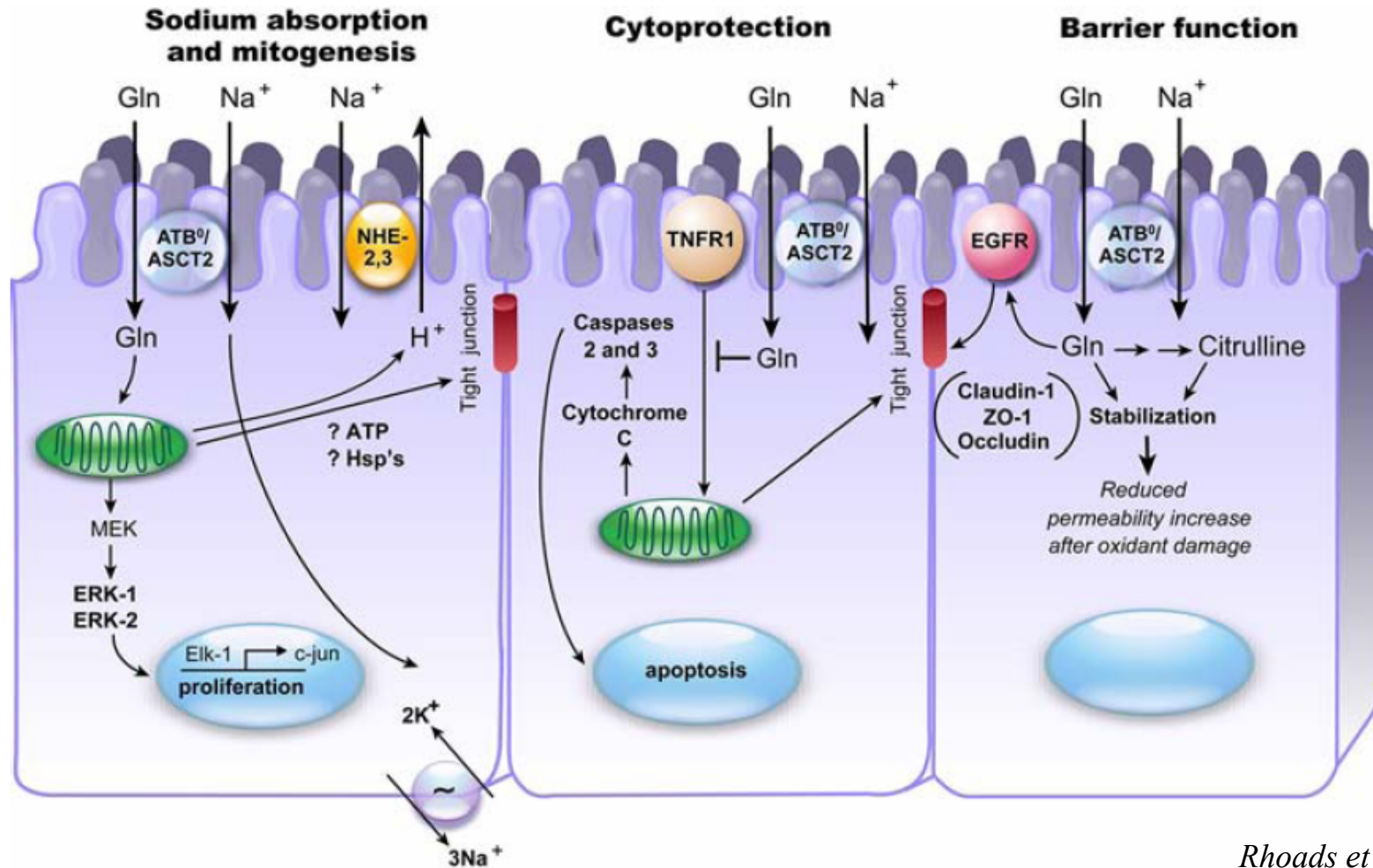
Mélange de 7
acides aminés
(AA)

Glutamine
0.8mmol/kg/h



→ Augmentation du taux des ARNm de HO-1

Coëffier et al, 2002



Rhoads et al, 2009