



Probiotics in Surgery

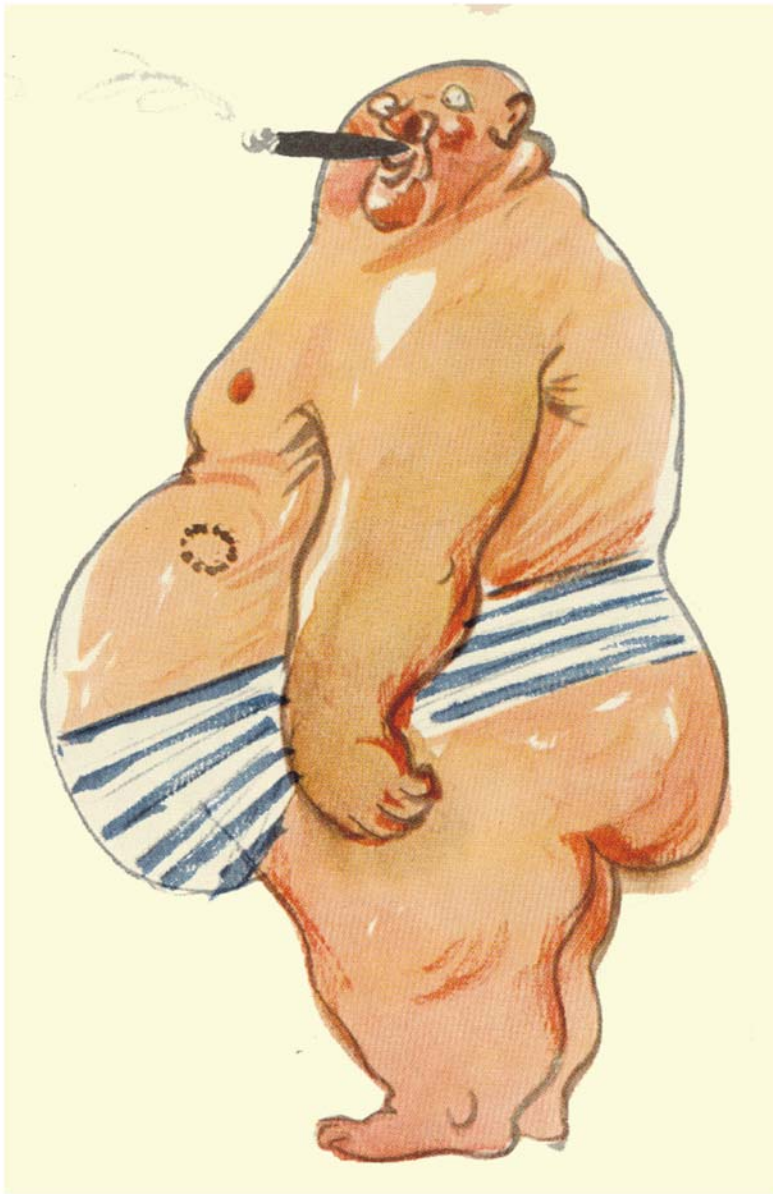
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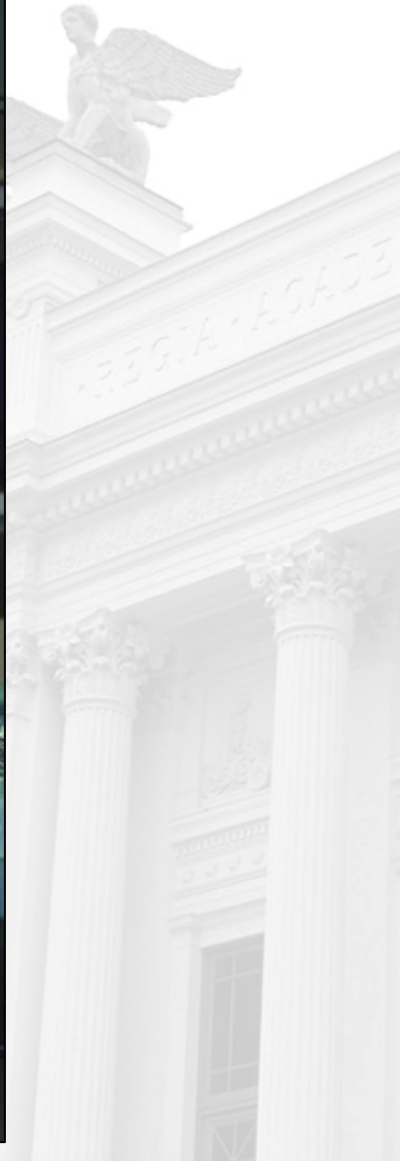


Malmö University Hospital

CRC



Homo bacteriens
More bacterial cells
than eukaryotic cells
 10^6 bact/cm²





Pulver till injektions- och infusionsvätska
Pulver till injektions- och infusionsvätska
Pulver till injektions- och infusionsvätska
TAZOCIN® 4g/100ml
lin. natr. respod. peracilin





Probiotics

- Living non-pathogenic micro-organisms which, when ingested, exert a positive influence on host health or physiology



Probiotics

- Lactobacilli
- Bifidobacteria
- Saccharomyces boulardii
- Non-pathogenic E.coli
- Enterococci





Gut microbiota

**Saccharolytic
fermentation**

SCFA

**Proteolytic
fermentation**

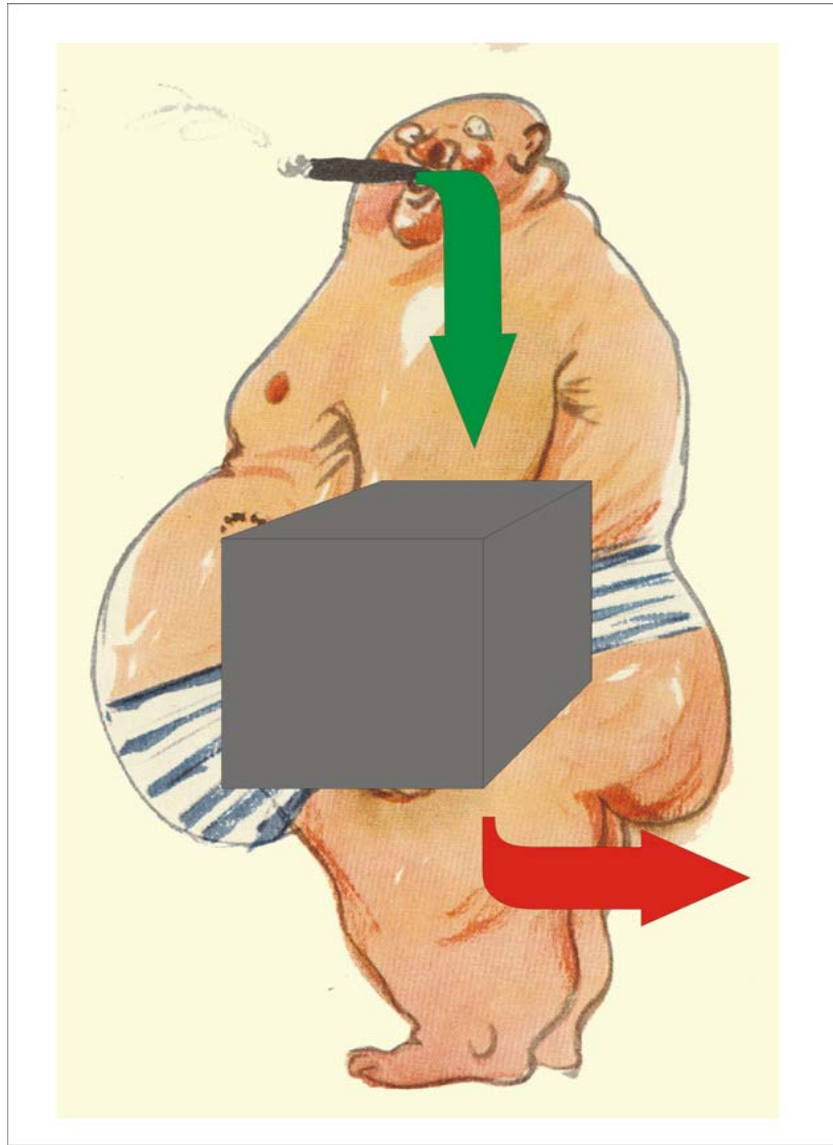
**Phenolic
compounds**



Mechanisms of action

- Bacterial antagonism
- Improvement of barrier function
- Altered inflammatory response and immunoregulation







Bacterial antagonism

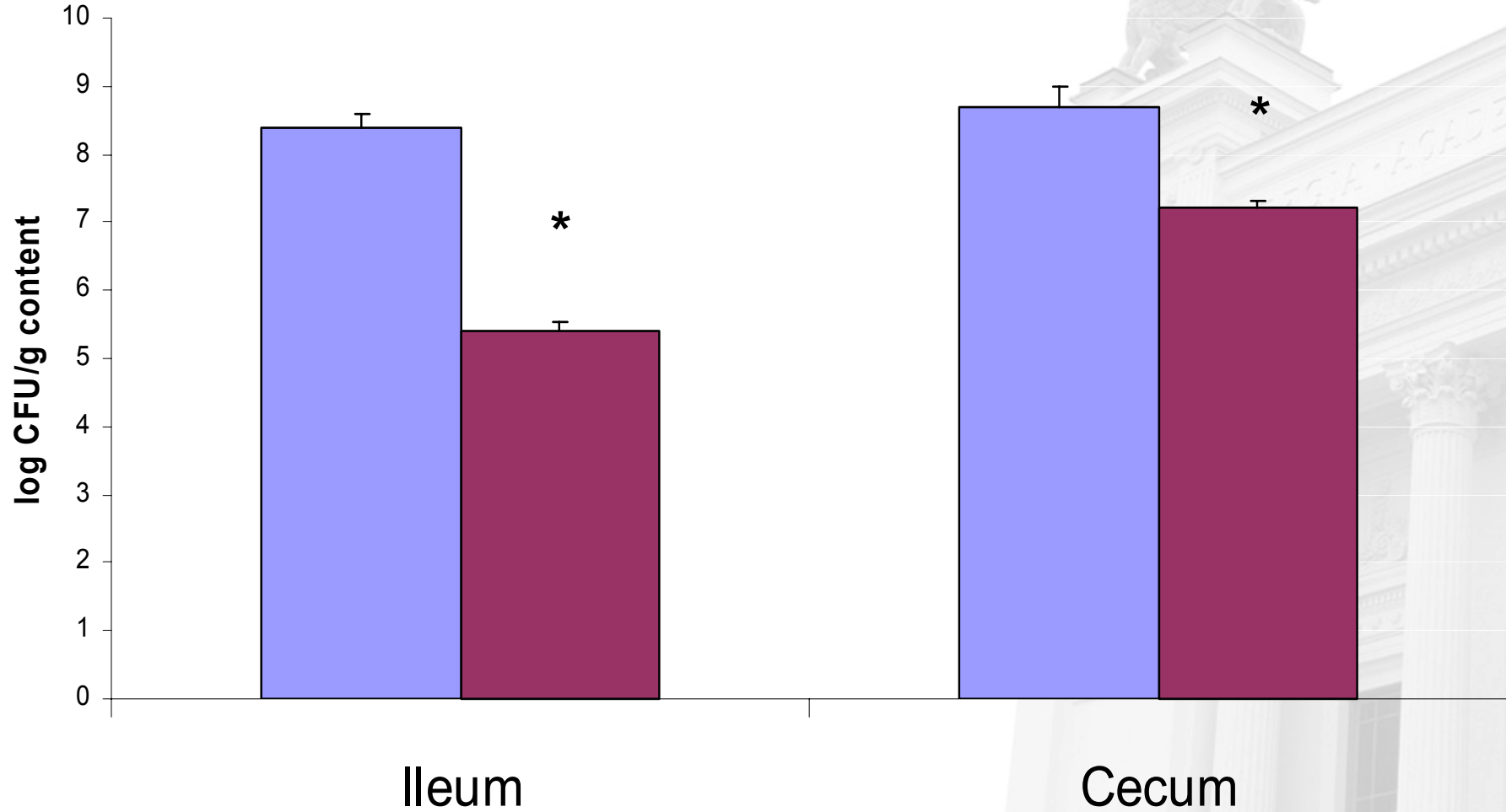
- Counteract disturbances of normal flora
- Reduce the risk of colonization by pathogenic bacteria



Ileum and cecum *Enterobacteriaceae* count



■ MTX Control ■ Lb. 299





Bacterial antagonism

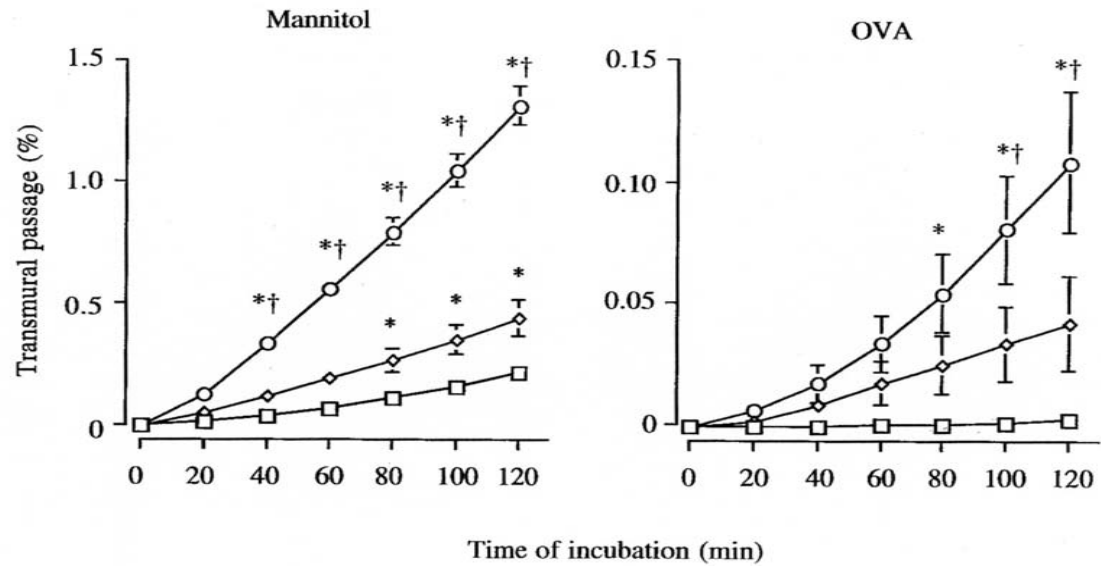
- Production of antimicrobial substances such as organic acids, bacteriocins and peptides
- Interference with adhesion of gastrointestinal pathogens or with toxin production



Strengthening of barrier function

- Inflammatory bowel disease
- Multiple organ failure
- Intestinal obstruction
- Obstructive jaundice
- etc

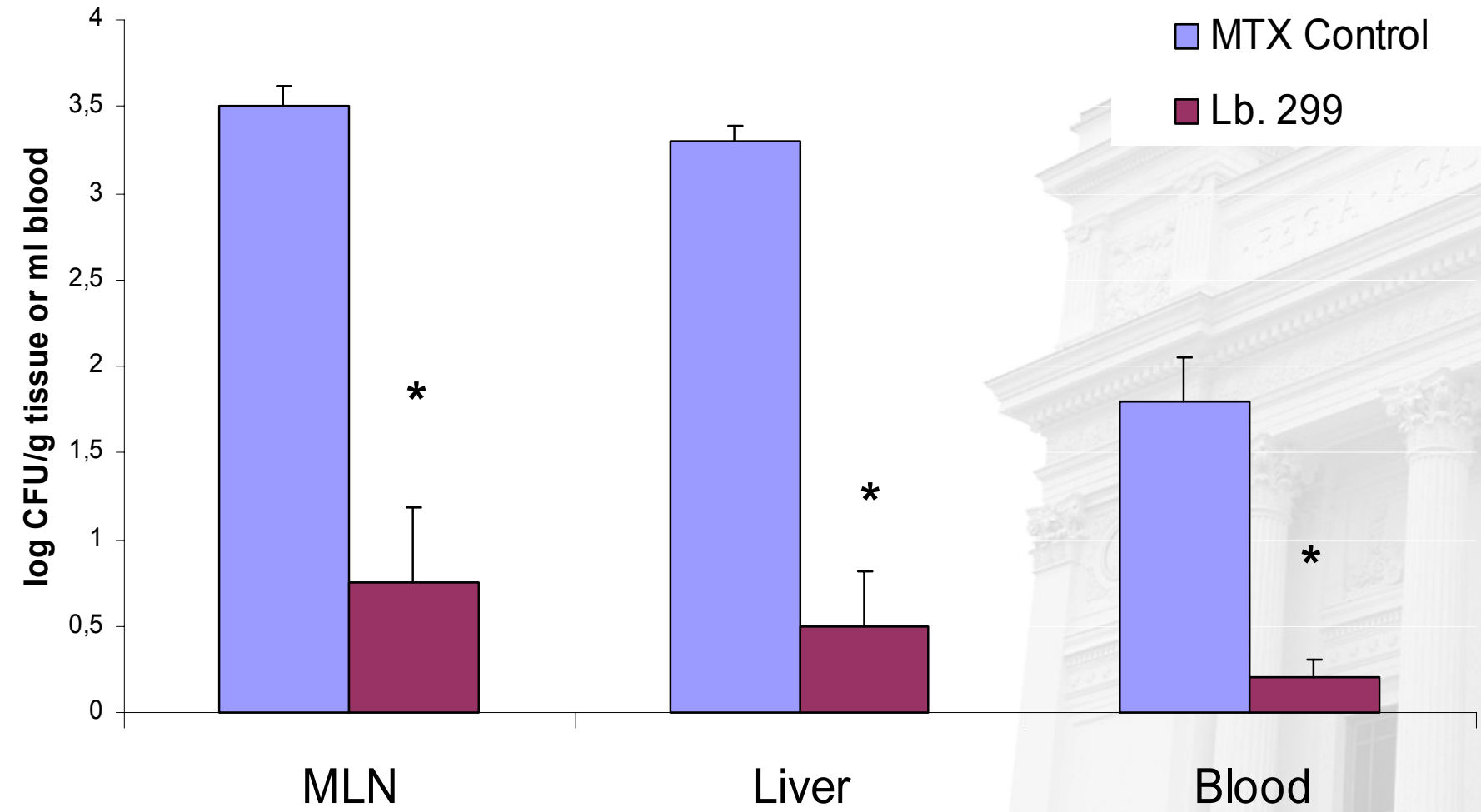




Scand J Gastroenterol, 1998; 33: 749-53



Bacterial translocation to MLNs, Liver and Blood



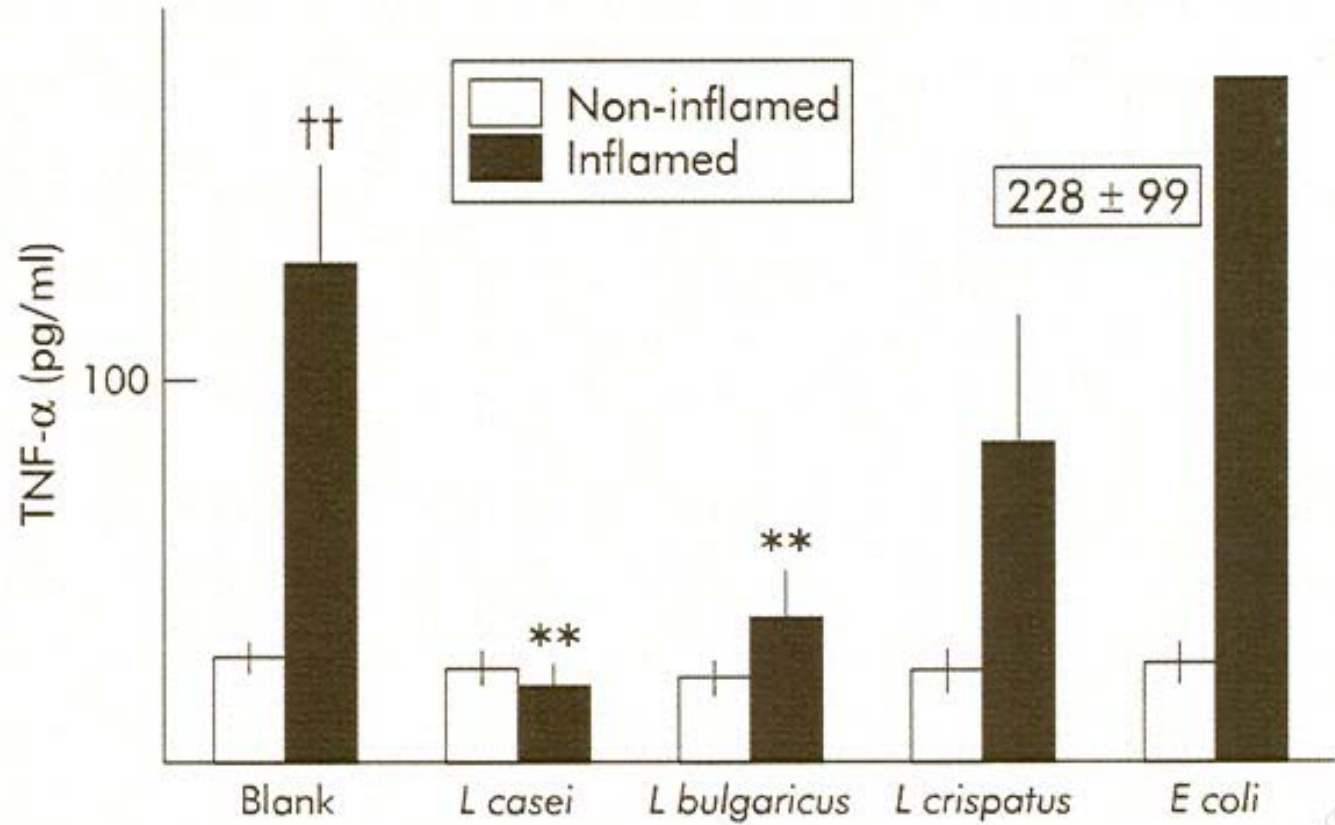


Immune stimulation





Colonic mucosa



Gut 2002;51:659-664



Clinical studies

- Alteration of gut microecology
 - Liver transplantation
 - Acute pancreatitis
 - Prophylaxis in major surgery
 - Intensive care therapy





ANNALS OF SURGERY
Vol. 218, No. 2, 111-119
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WHAT'S NEW IN GENERAL SURGERY

The Gastrointestinal Tract

The "Undrained Abscess" of Multiple Organ Failure

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Incidence, type of Infections, and clinical outcome in the study groups

	Group 1 (SBD)	Group 2 (<i>Lactobacillus</i>)	Group 3 (heat-killed)	P value
Patients with infections (n)	15 (48%)	4 (13%)	11 (34%)	0.017
Total number of infection (n)	23	4	17	
Type of Infection (n)				
Cholangitis	10	2	8	
Pneumonia	6	1	4	
Sepsis	3	0	0	
Urinary tract infection	0	0	3	
Wound infection	1	0	0	
Others	3	1	2	
Isolated Bacteria (n)				
Enterococci	8	1	8	
<i>Escherichia coli</i>	2	0	1	
Staphylococci	6	1	3	
<i>Klebsiella</i>	0	0	1	
None	7	2	5	
ICU stay (days)	15.7±12	11.7±7	13.5±12	NS
Hospital Stay (days)	39±0.5	35±2.4	36±2.7	NS
Cumulative length of antibiotic therapy (days)	12±17	7±7	12±18	NS



Infective complications of acute pancreatitis



	Control group (n=23)	Lb. 299 group (n=22)
Systemic inflammatory response syndrome	6	11
Multiple organ failure	2	2
Positive aspiration culture	7	1 *
Positive blood culture	4	1
Pancreatic abscess	3	0
Infected necrosis	4	1
Chest infection	2	2
Antibiotic therapy	9	4
Septic complications requiring operation	7	1 *
Death	2	1

* $P < 0.05$ versus control



Postoperative infections



	Control (n=30)	Active (n=30)	Inactive (n=30)
Patients with infection	9 (30%)	3 (10%) *	3 (10%) *
Kind of Infection			
Pneumonia	6	2	1
Sepsis	1	0	1
Peritonitis	1	0	0
Urinary tract infection	0	1	0
Wound infection	1	0	0
Ear infection	0	0	1



Administration of lb before colonic resection

Lb plantarum 299V 7 days before operation and until discharge

80 patients were randomized to active therapy or placebo

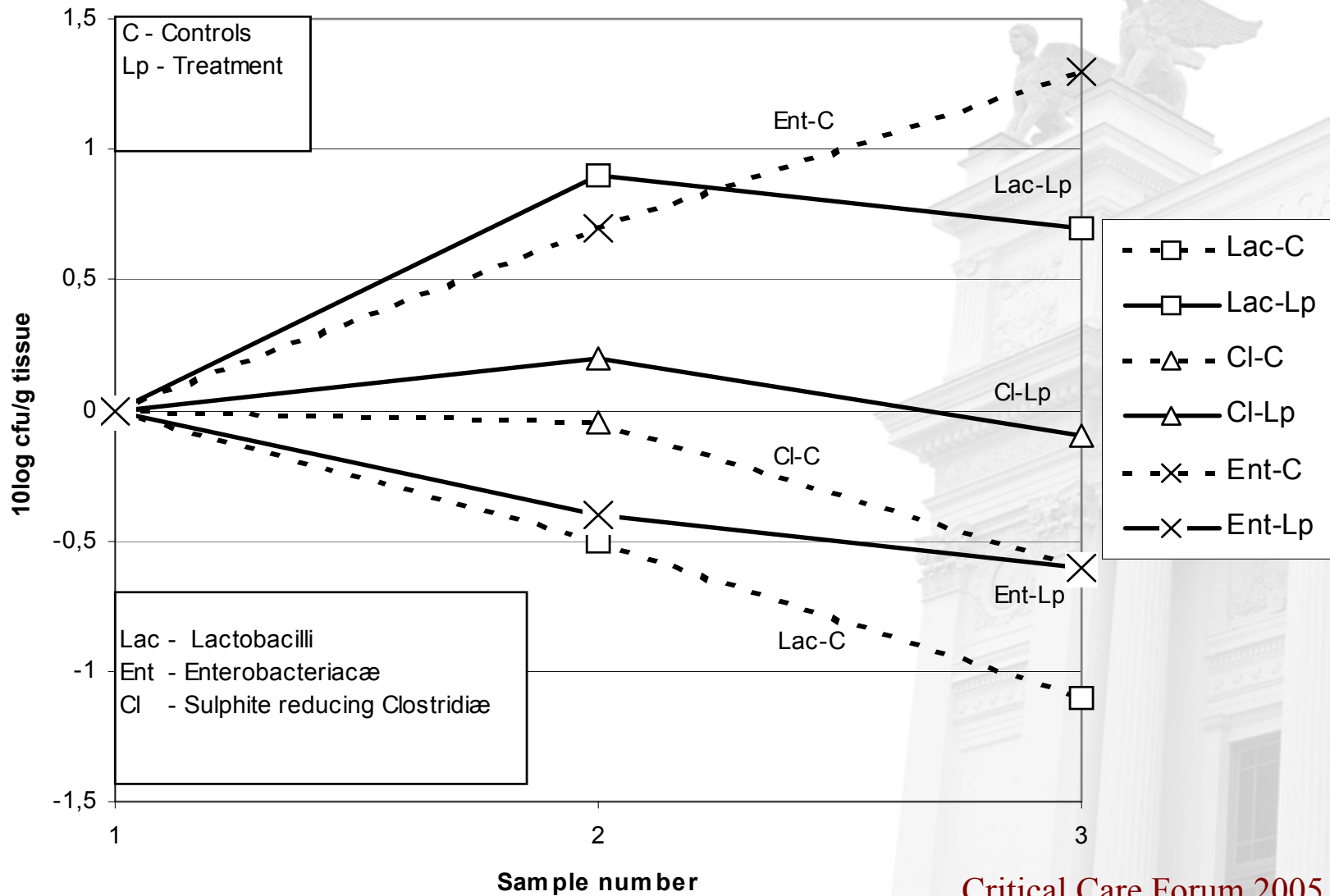


Infectious complications

	Lb plantarum (n=32)	Placebo (n=32)
Minor	5	9
Major	3	7



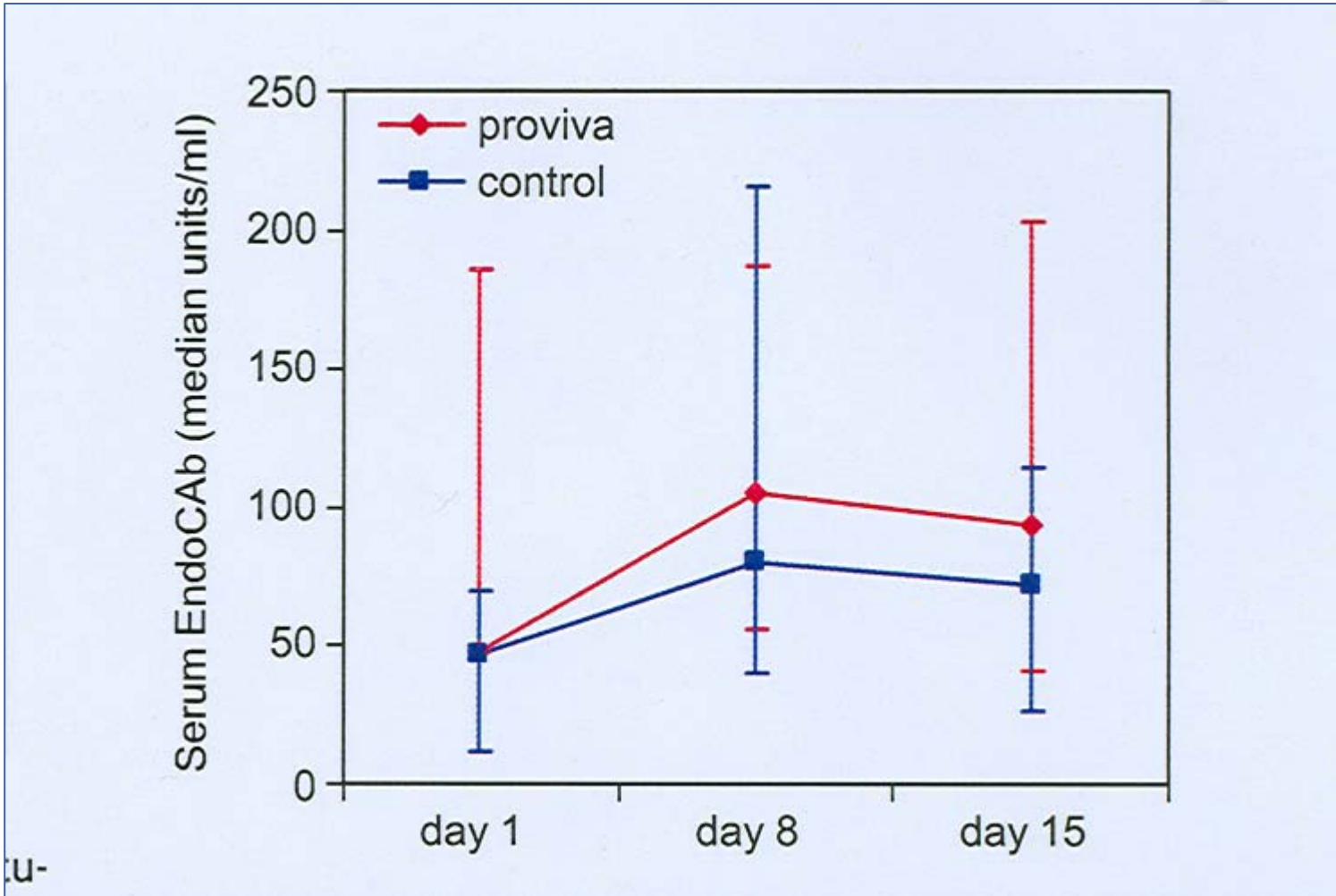
Changes of bacterial counts from rectal biopsies (means) Comparisons to initial sample





Ecology in intensive care patients

Positive cultures	Lactobacilli n=22	Placebo n=23
Faecal Cl dif	1	5
Blood	2	3
BAL and trachea	9	26



Clinical Nutrition 2005; 24: 211-219



but

What bacteria should we use?

One or several bacteria?

Live or dead?

Combination with prebiotics

We must address safety issues







FACULTY OF MEDICINE

State of health and intraoperative data in the study groups^a

	Group 1 (SBD, n=32)	Group 2 (<i>Lactobacillus</i> , n=31)	Group 3 (heat-killed, n=32)
Male/Female	19/13	15/16	15/17
Age (y)	47±2	50±2	50±2
Child-Pugh classification (n)			
A	4	1	5
B	15	15	19
C	9	15	6
No cirrhosis (HCC, ALF)	3/1	-	1/1
Smokers (n)	6	8	11
Mean operating time (min)	304±13	306±12	299±13
Intraoperative transfusions (units)			
Red blood cells	4.9±0.5	6.5±0.7	4.8±0.6
Fresh-frozen plasma	8.8±0.8	9.8±0.9	7.6±0.8

^a There were no significant differences among groups.

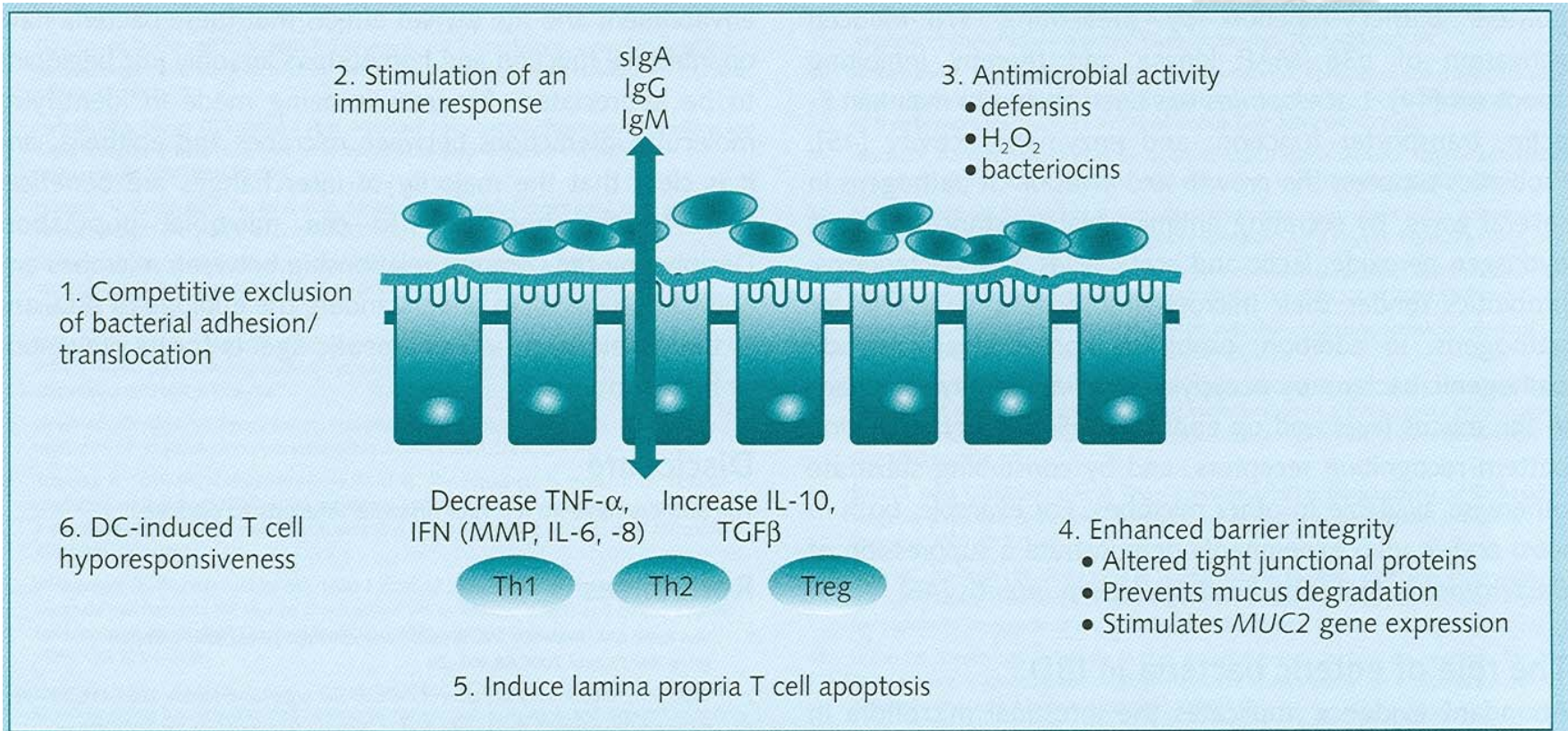
HCC: hepatocellular carcinoma; ALF: acute liver failure





Mechanisms implicated in the barrier effect:

- competition for attachment sites
- competition for nutrient availability
- growth inhibition by production of antimicrobial substances
- influence on mucosal barrier
 - mucus production
 - epithelial growth
- influence on immune function





Duration of antibiotic therapy



	Control (n=30)	Active (n=30)	Inactive (n=30)
Length of hospital stay (days)	16±5.5	14±4	15±7.4
Duration of antibiotic therapy (days)	8±6.5	4±3.7 *	7±5.2
First day of bowel movement (day)	5	4	4
Patients with other complications	9(30%)	4(13%)	5(17%)

* Compared vs control and inactive groups



Clinical studies

Gionchetti P, Rizzello F, Helwig U et al: Prophylaxis of pouchitis onset with probiotic therapy: a double-blind, placebo-controlled trial. *Gastroenterology* 2003;124:1202-1209.

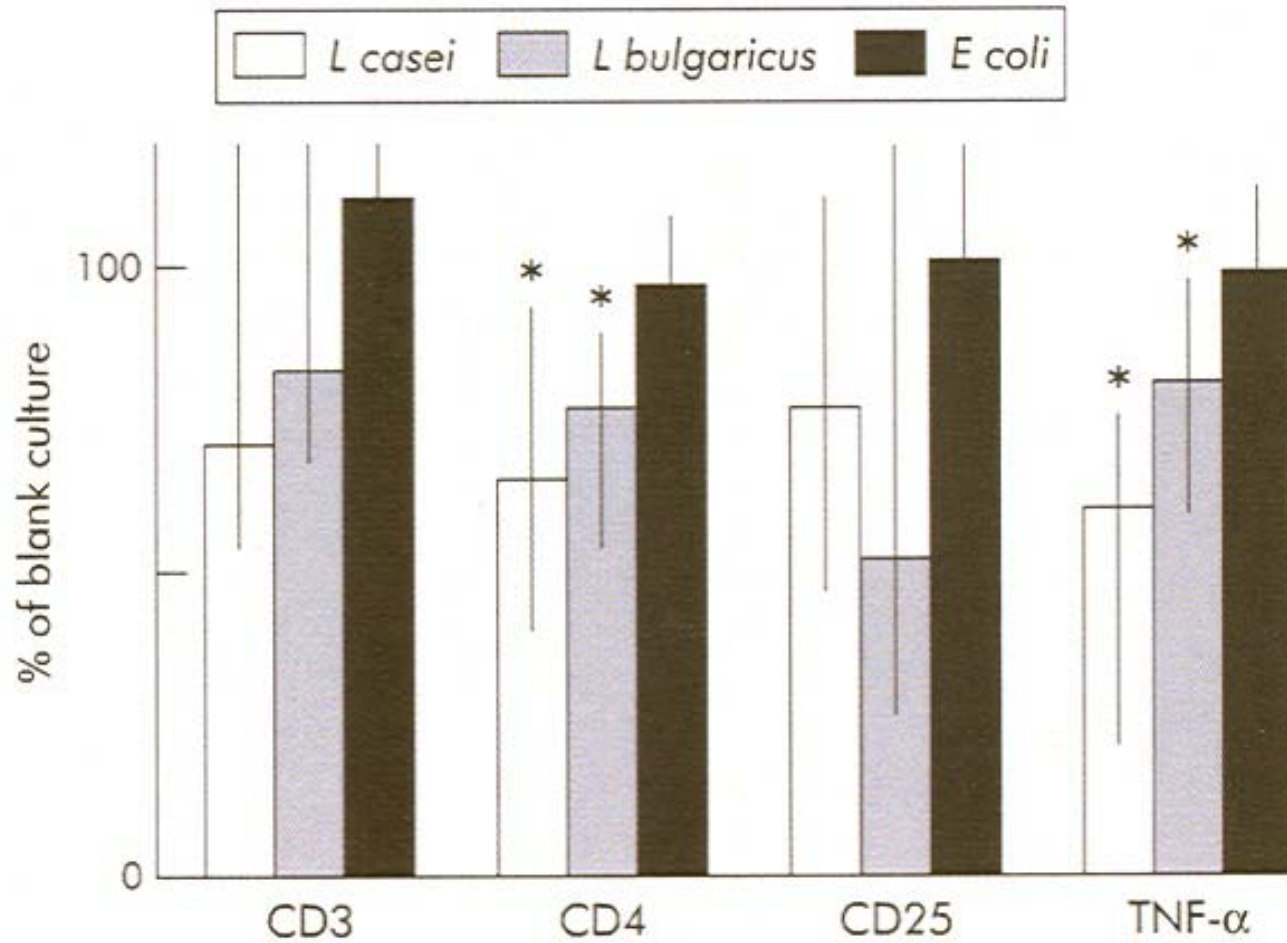
Kruis W, Frick P, Pokrotnieka J et al: Maintaining remission of ulcerative colitis with the probiotic Escherichia coli Nissle 1917 is as effective as with standard mesalazine. *Gut* 2004;53:1617-1623.

Kato K, Mizuno S, Omesaki U et al: Randomized placebo-controlled trial assessing the effect of bifidobacteria-fermented milk on active ulcerative colitis. *Aliment Pharmacol Ther*; 2004;20:1133-1147.

Guandalinis: Use of Lactobacillus GG in pediatric Crohn's disease. *Dig Liver Dis* 2002; 34(Suppl 2):S63-S68.



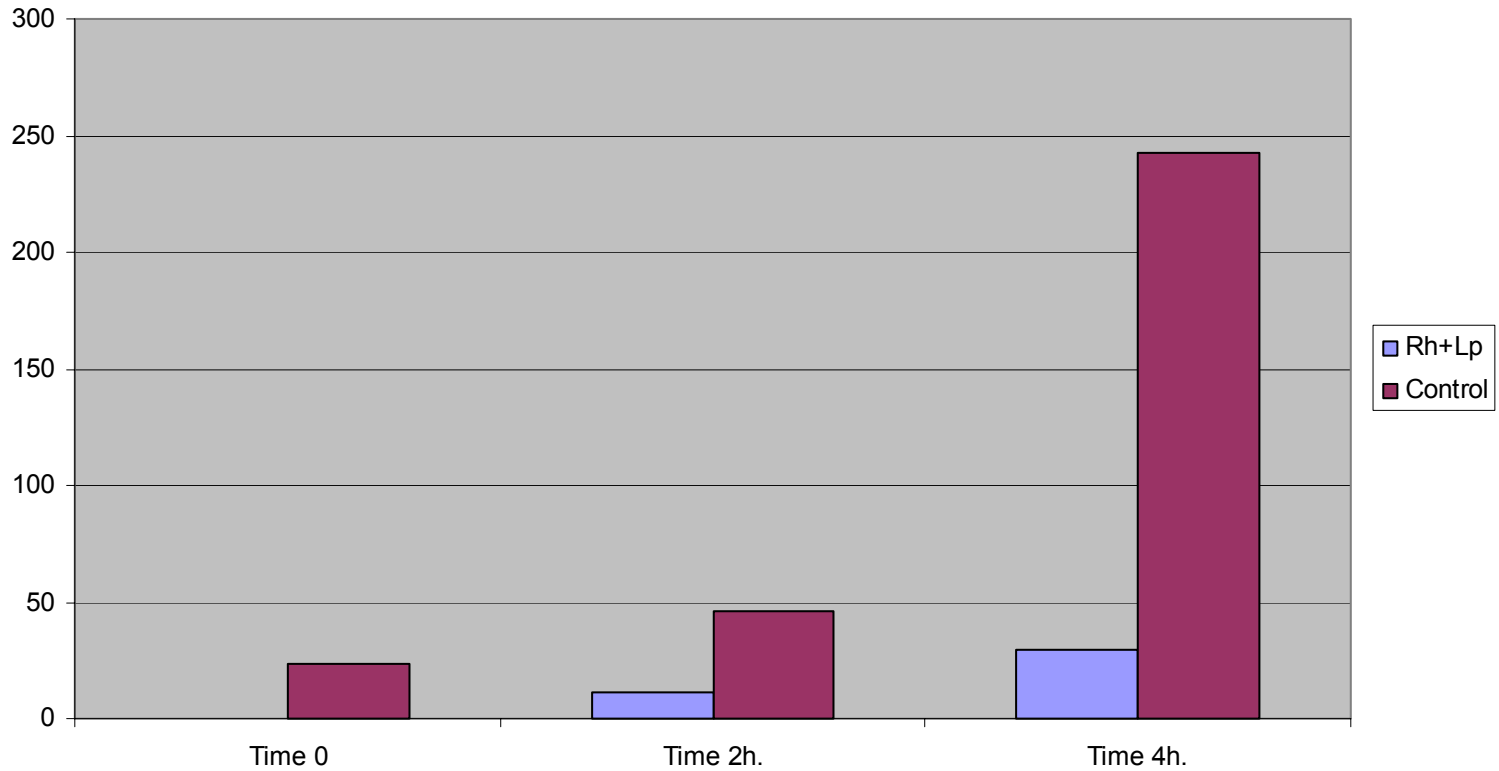
Intraepithelial lymphocytes

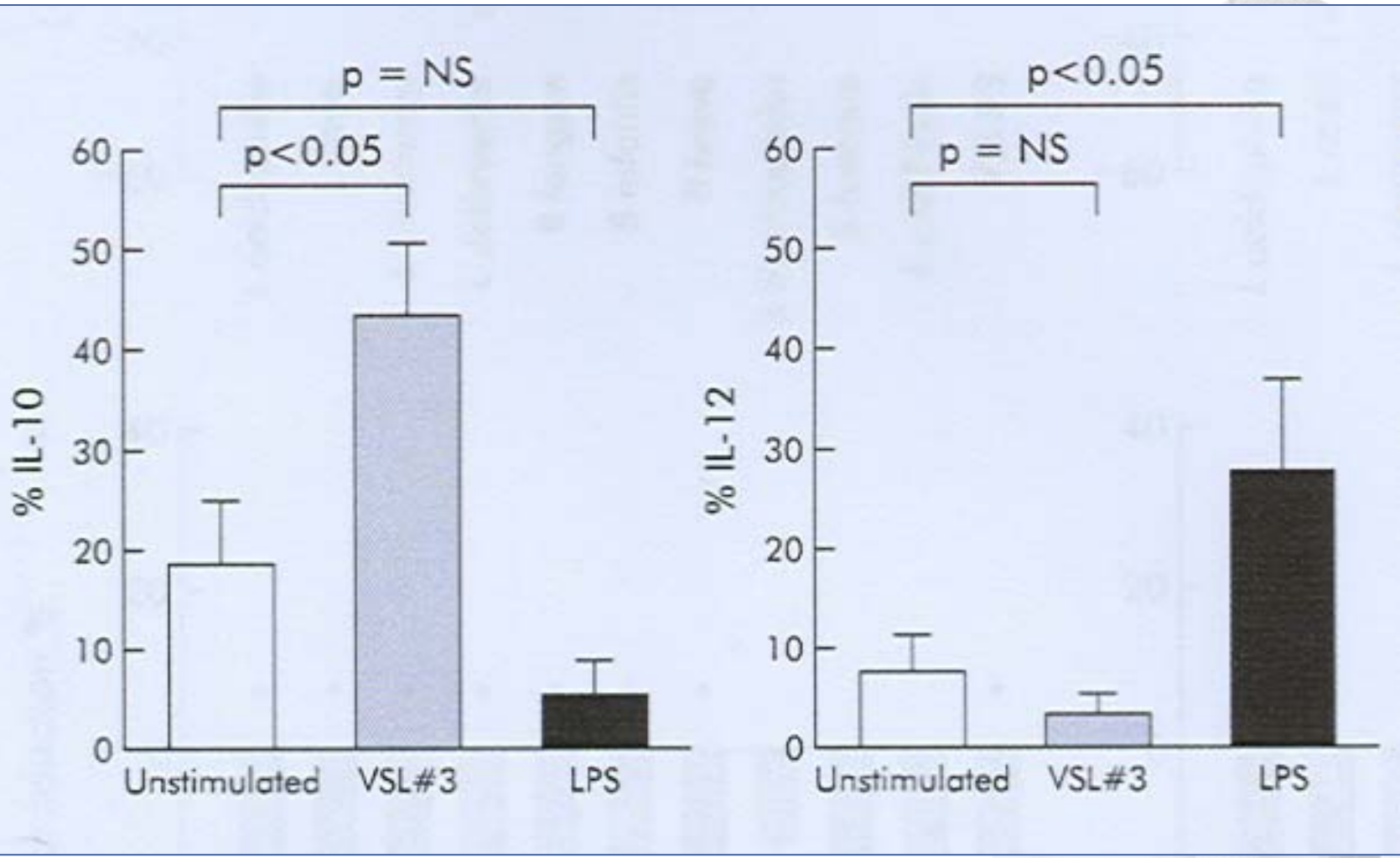


Gut 2002;51:659-664



MIP-2 in TNF-alfa medium 10ng/ml in the Group treated with Rh+Lp versus Control Group





Gut 2004;53:1602-1609



Probiotics– mechanisms of action

1. Bacterial antagonism –suppression of other bacteria or virus
2. Production of short-chain fatty acids (SCFA)
3. Mucus production
4. Strengthening of barrier function
5. Immune stimulation