



Papel de las células T reguladoras en Inmunomodulación intestinal en la cirrosis antígenos bacterianos en un modelo experimental de daño hepático



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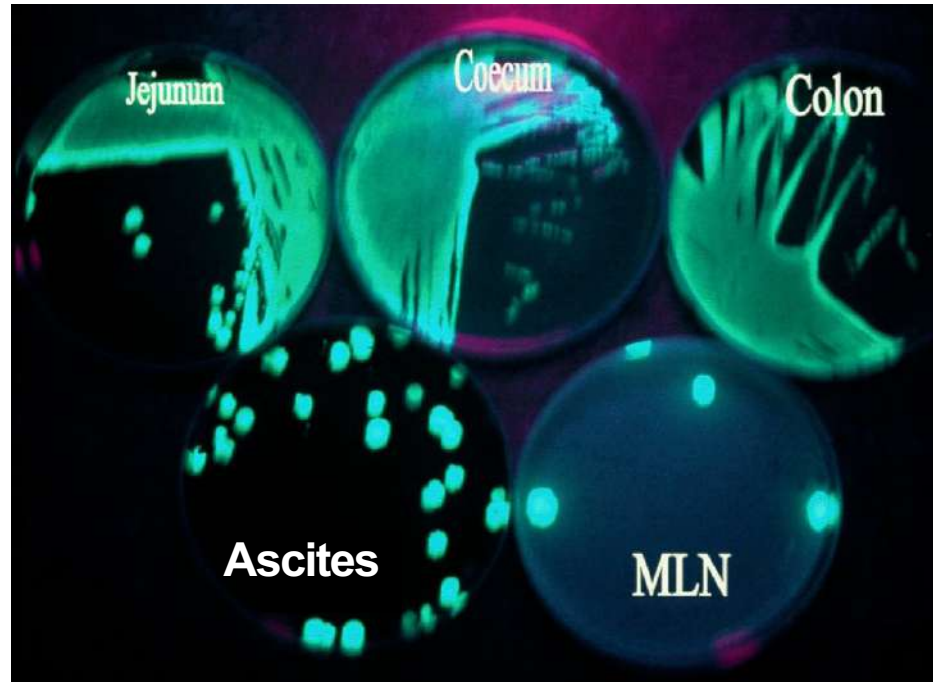
Dpto. Medicina Clínica – Universidad Miguel Hernández



Traslocación bacteriana

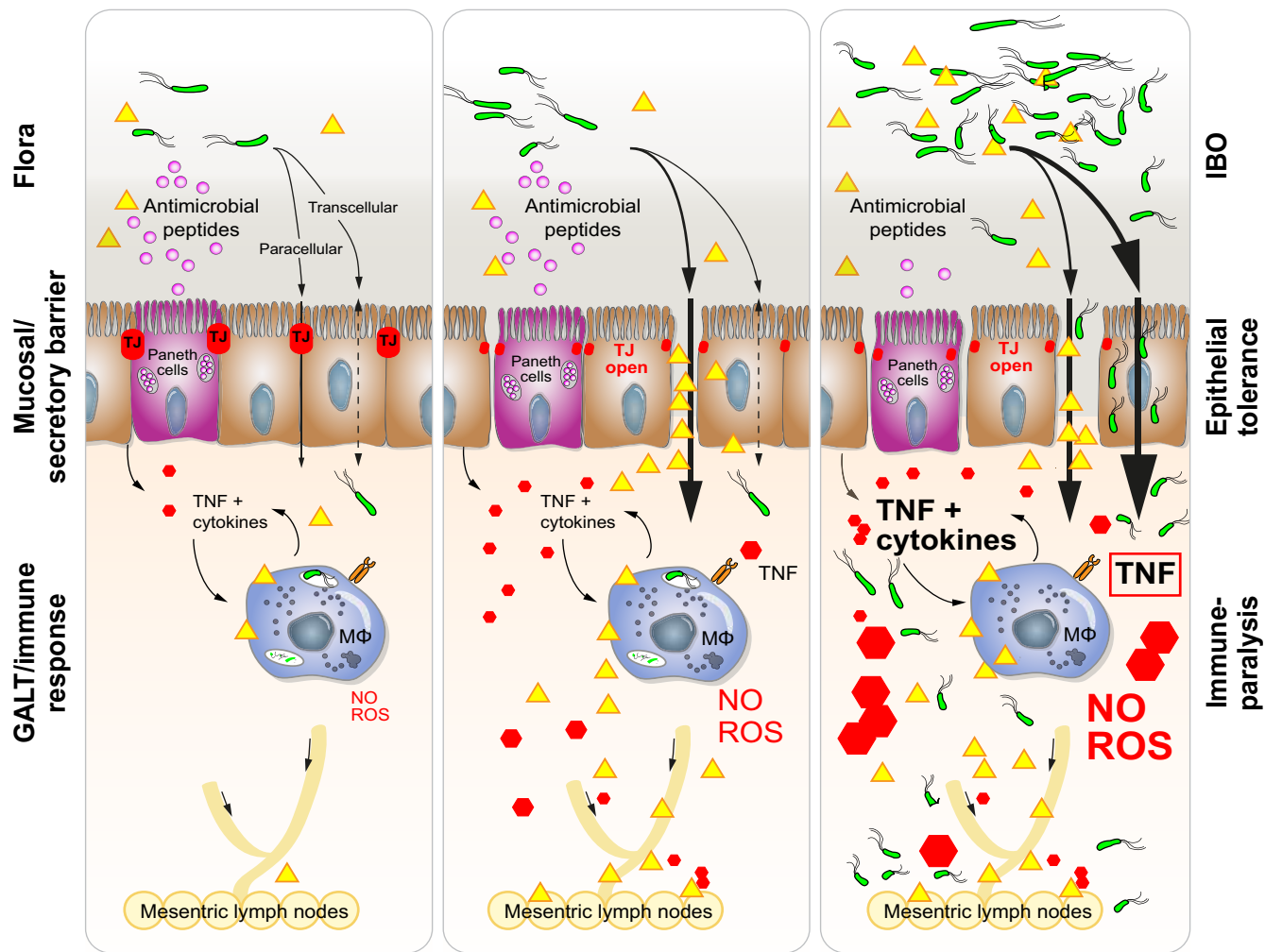
- Paso de bacterias desde la luz intestinal a los ganglios linfáticos mesentéricos y la sangre, alcanzando otros territorios. (Berg RD, Infect Immun 1979)
- Paso de bacterias o sus productos desde la luz intestinal a los GLMs y la sangre, alcanzando otros territorios. (Wiest R, Hepatology 2005)

Traslocación bacteriana

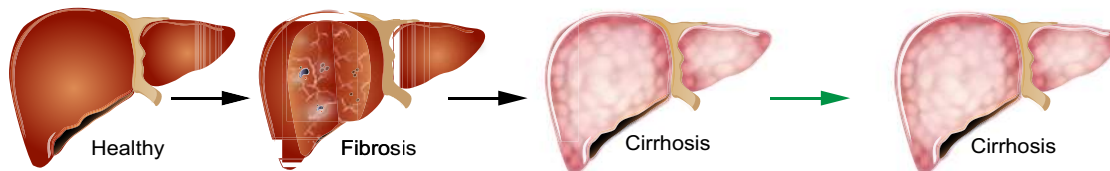


Green fluorescent protein (GFP)-marked *E. coli* in different compartments after oral gavage in an ascitic rat with cirrhosis.

(Teltschik et al. Hepatology 2012)



Stage of disease



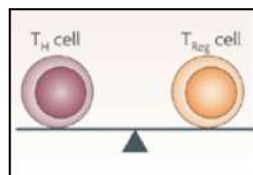
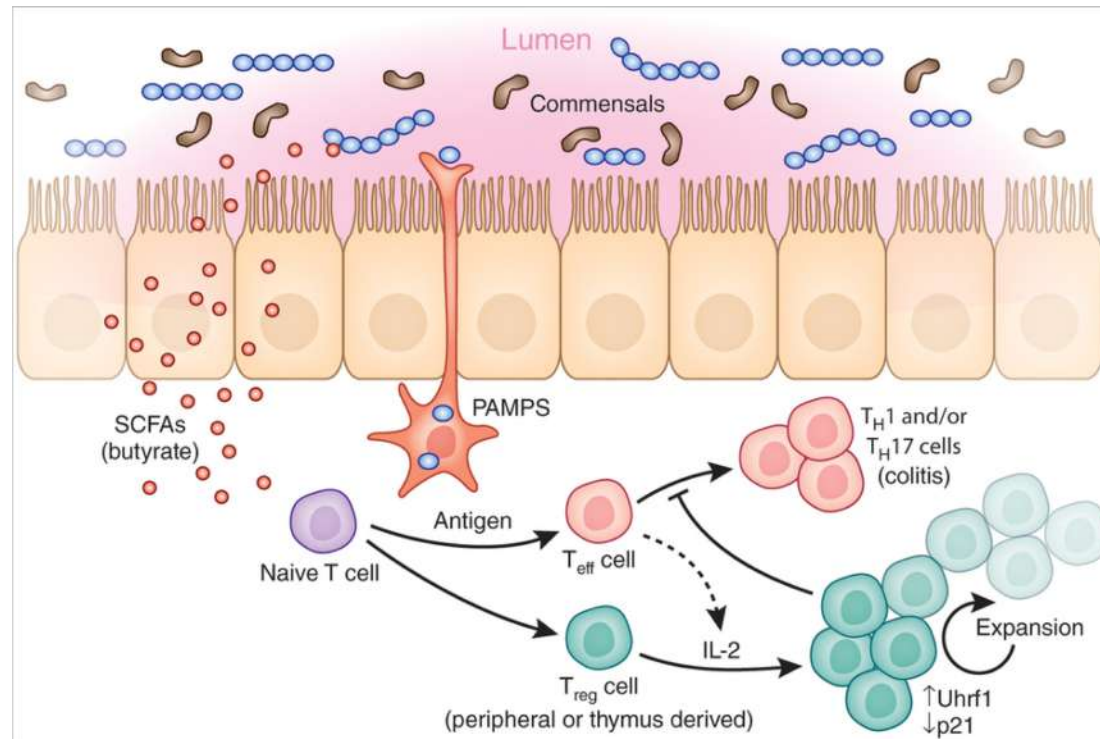
Compensated

Decompensated stadium

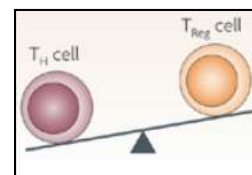
- Antimicrobial peptides
- Vital bacteria
- Microbial products
- TNF

(Wiest R, J Hepatol 2014)

Las células T reguladoras favorecen la homeostasis intestinal

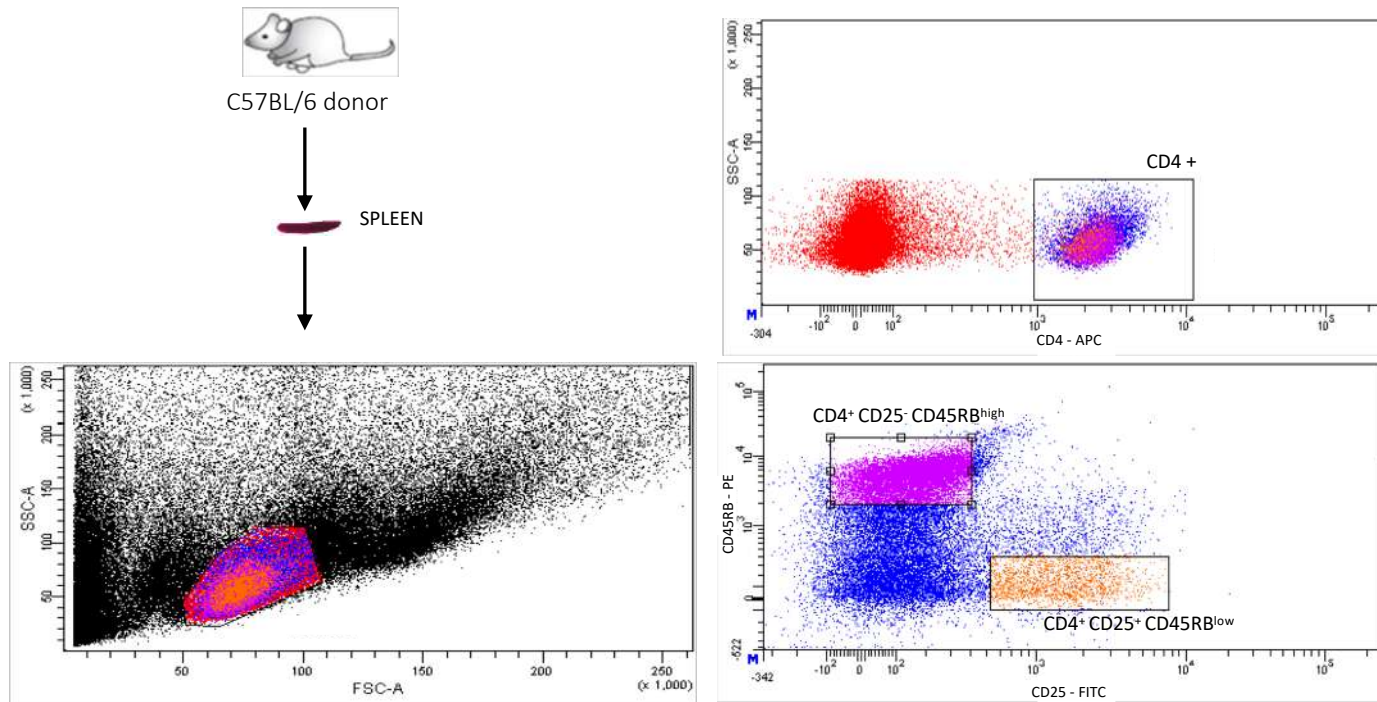


Eubiosis



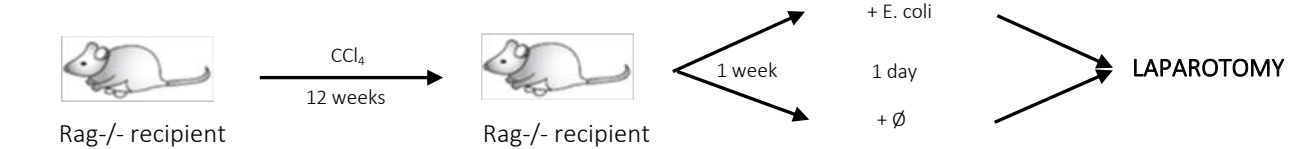
Disbiosis

Trasferencia de Tregs en ratones Rag-1^{-/-} con cirrosis inducida por CCl₄

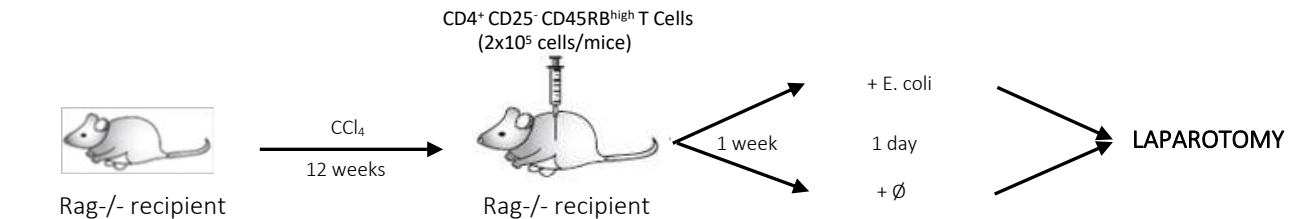


Trasferencia de Tregs en ratones Rag-1^{-/-} con cirrosis inducida por CCl₄

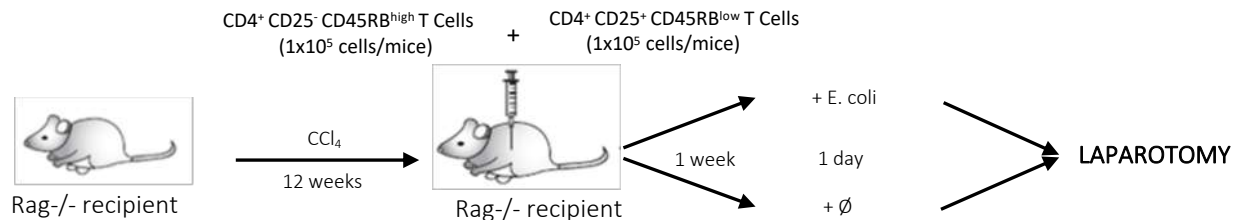
No Transfer



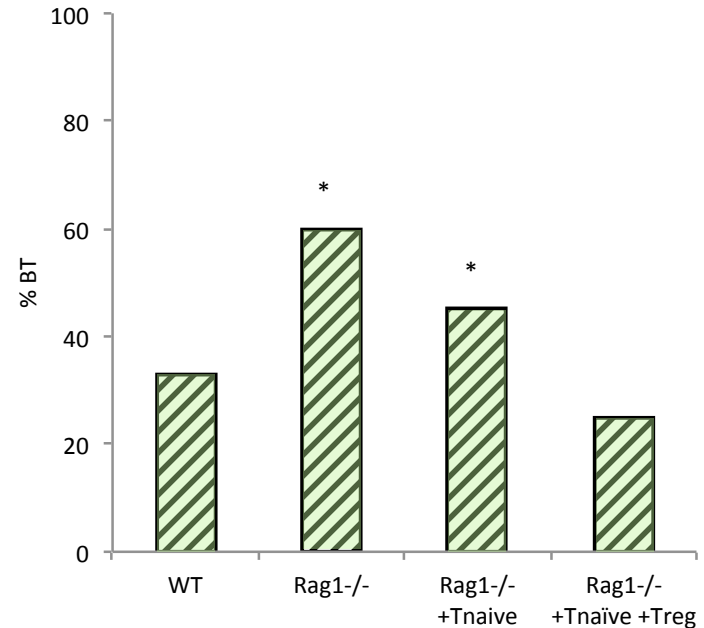
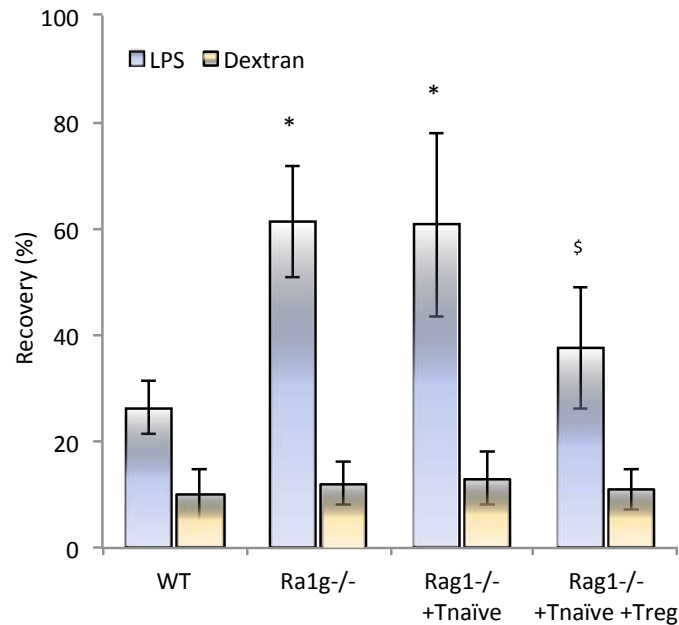
Transfer



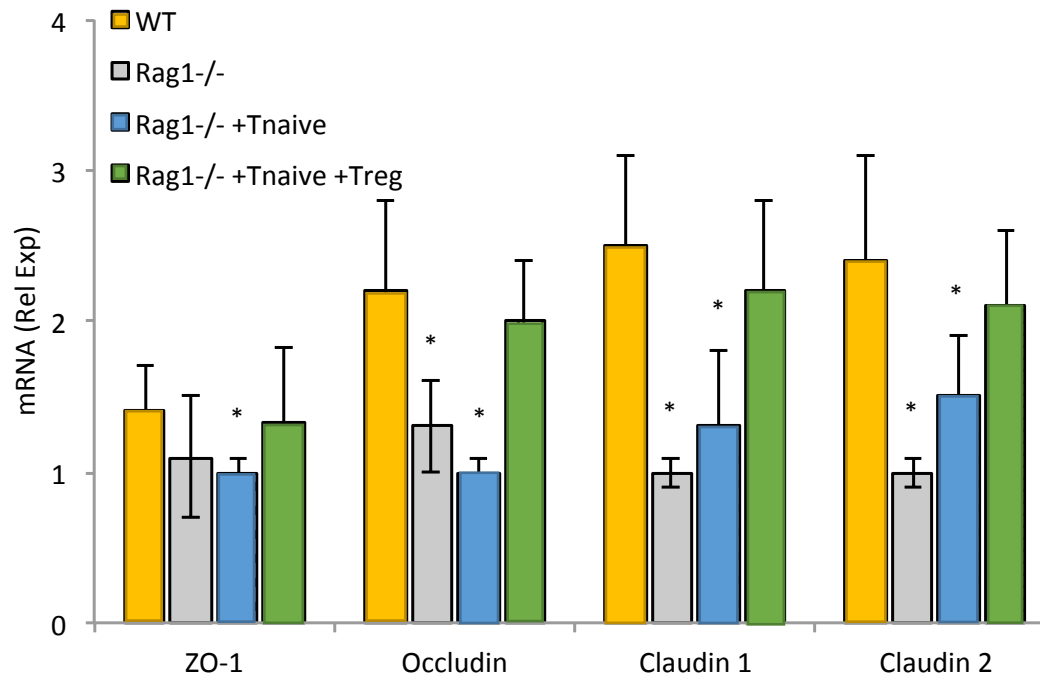
Co-Transfer



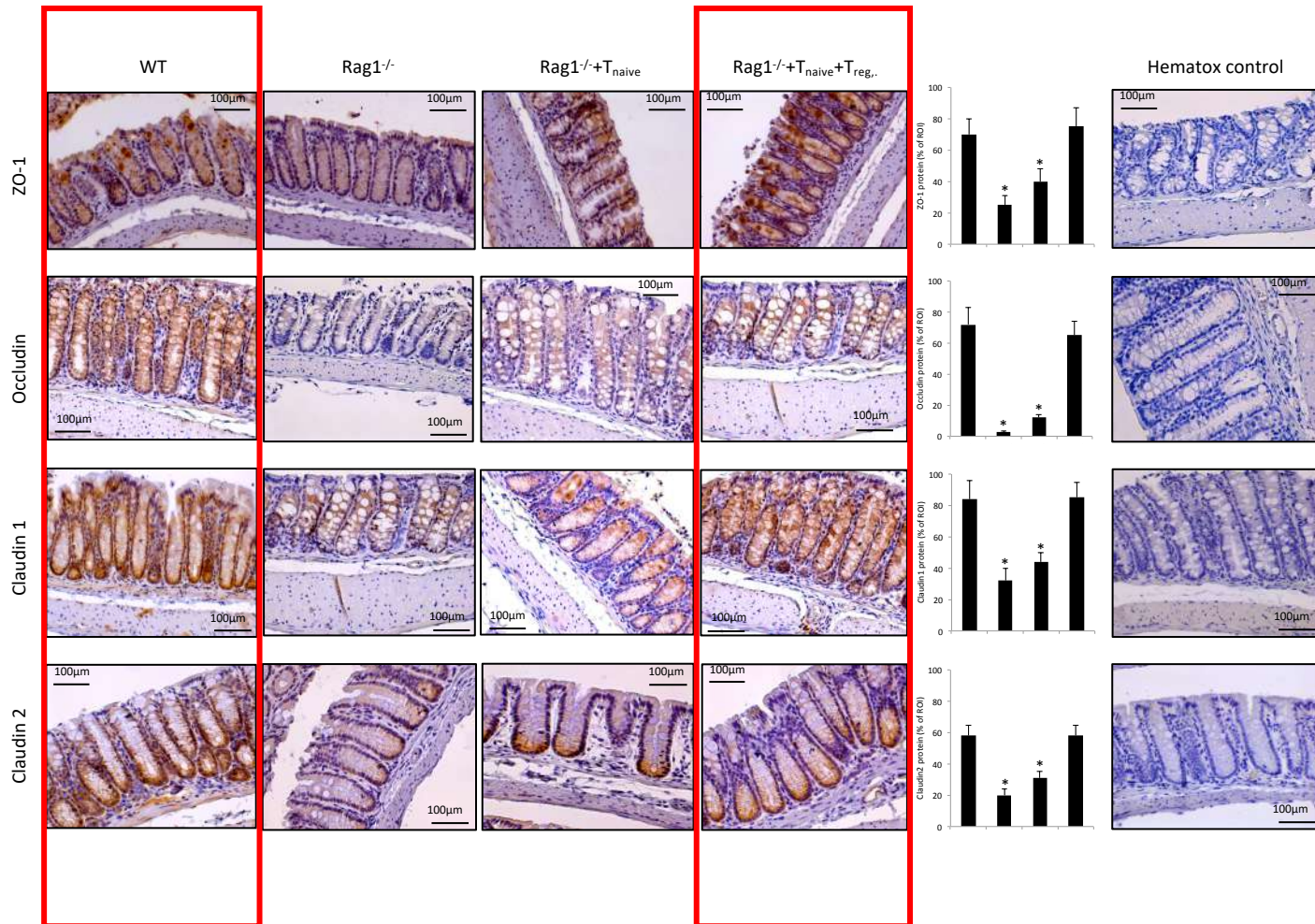
Permeabilidad intestinal frente a endotoxina bacteriana



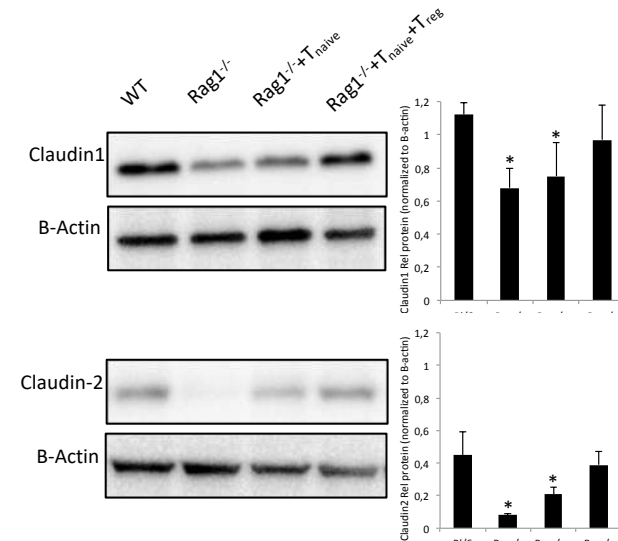
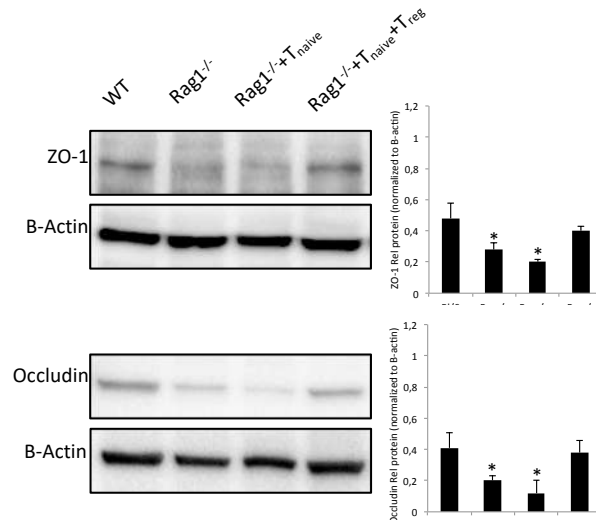
Expresión de genes implicados en la integridad de la barrera



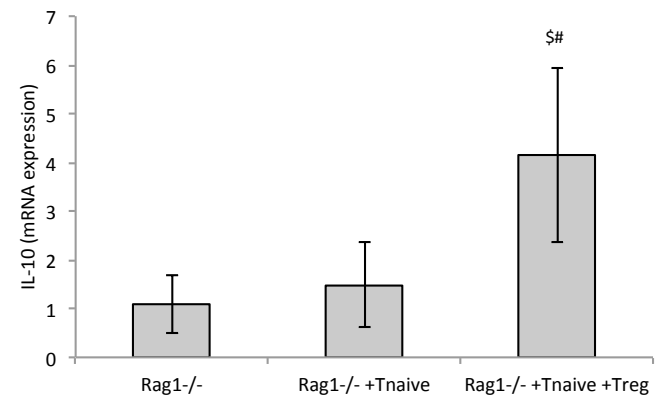
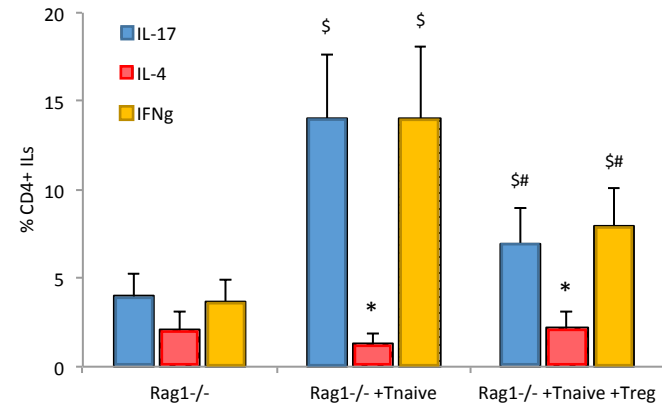
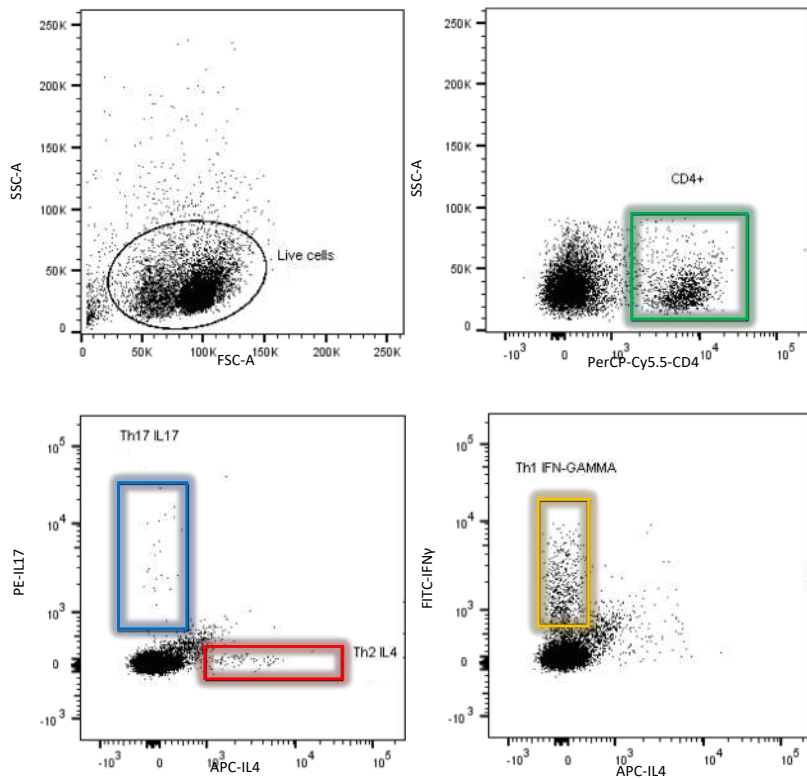
Distribución de proteínas implicadas en la integridad de la barrera



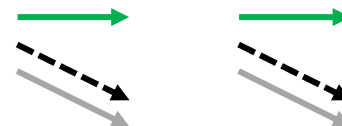
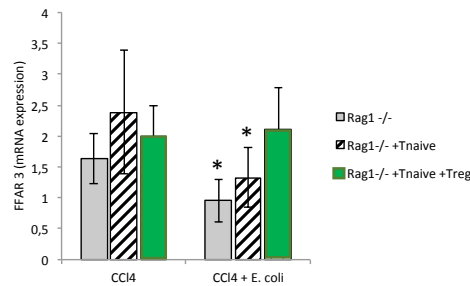
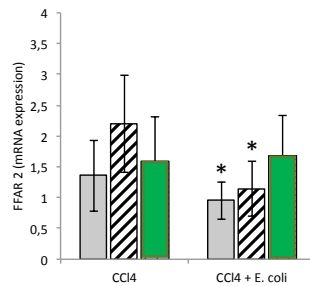
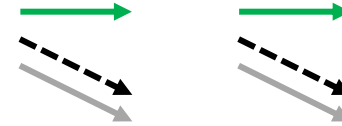
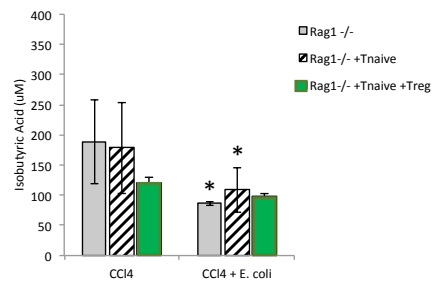
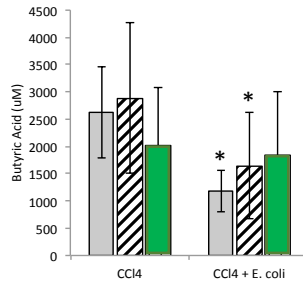
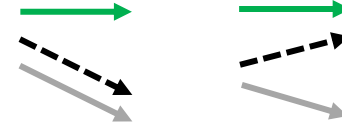
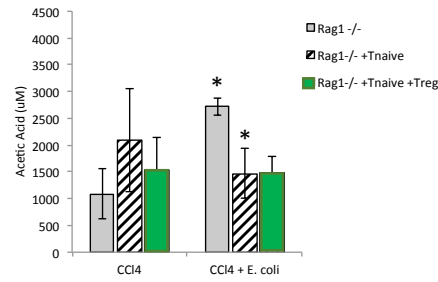
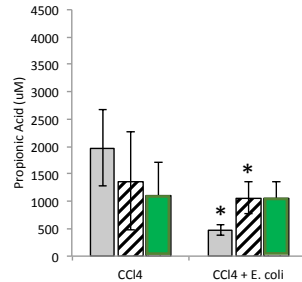
Expresión de proteínas implicadas en la integridad de la barrera



Diferenciación de la respuesta T y expresión de citocinas



Niveles de SCFAs y receptores en pared intestinal

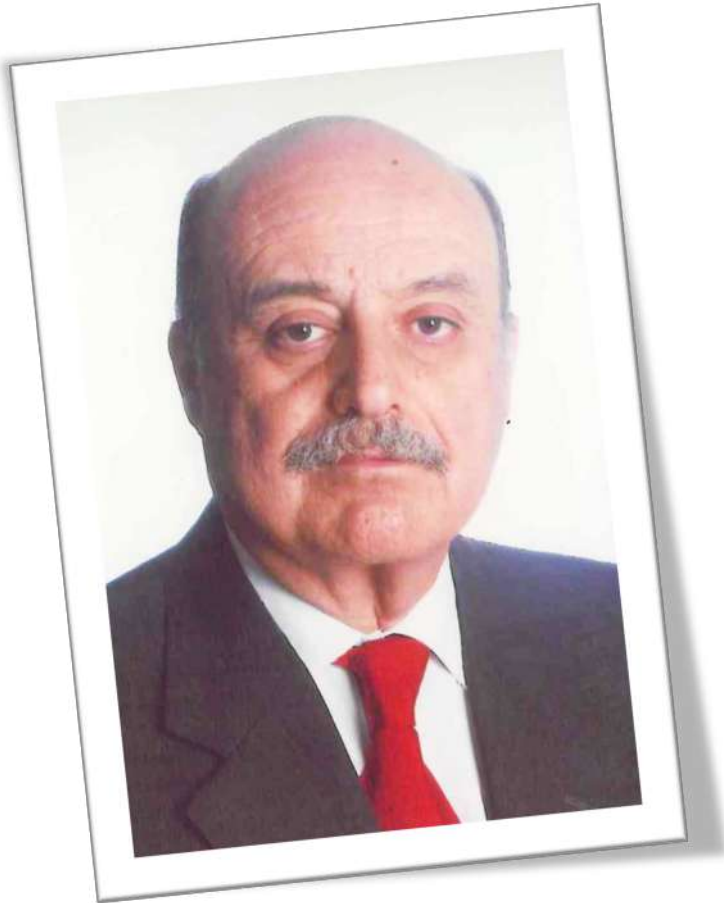


Conclusiones

- Las células T reguladoras contribuyen a:
 - reducir la permeabilidad intestinal
 - mejorar la integridad de la barrera
 - limitar los episodios de TB
 - restringen la pérdida de SCFAs y sus receptores
- La estimulación de las Treg permite controlar la progression inflamatoria en la cirrosis

MIGUEL PÉREZ-MATEO

Miguel Pérez-Mateo



- Apoyo desde el comienzo
- Presidente del Tribunal de Tesis
- IP de múltiples proyectos
- Evaluador de Agencias Nacionales de Investigación
- Profesor de Universidad

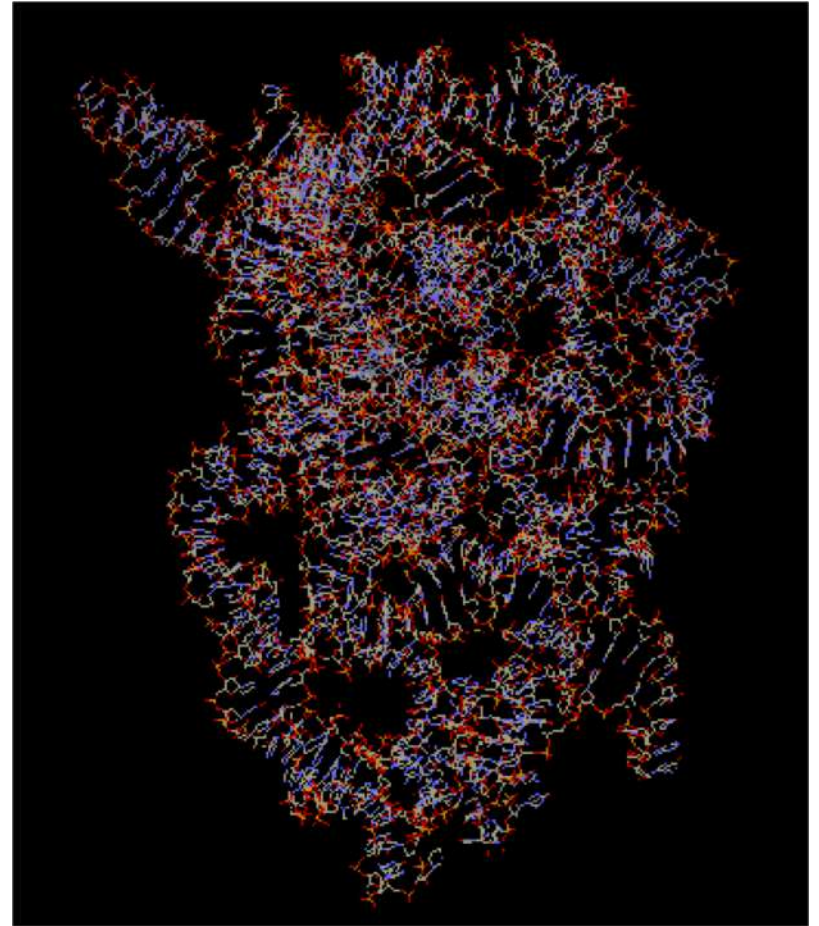
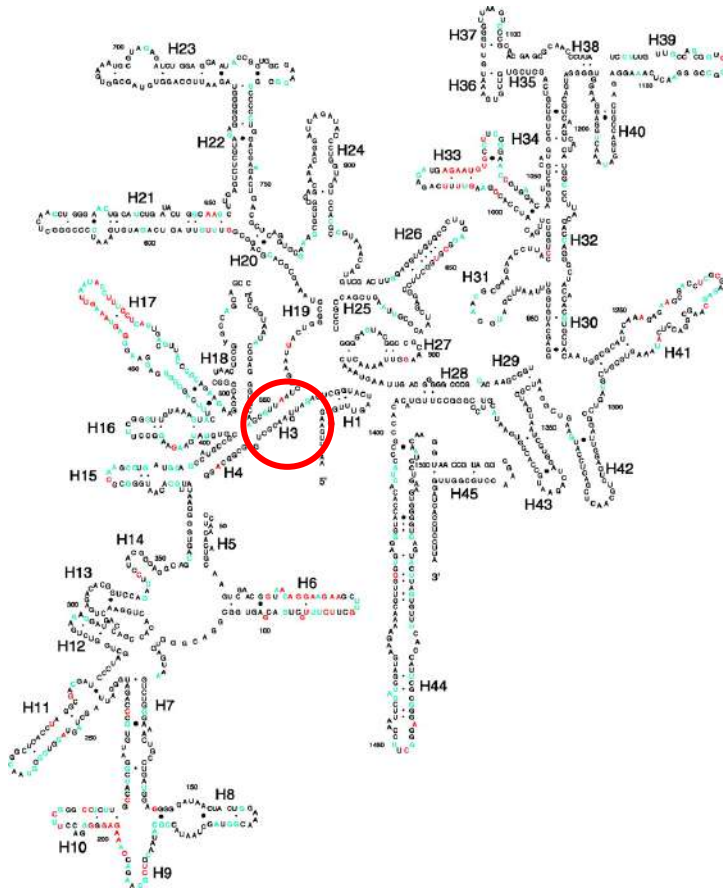
Miguel Pérez-Mateo

- Apoyo desde el comienzo (protección)
- Apoyo en la etapa Rubén 2.0 (amistad)
- 1×10^6 consejos
- Tiempo juntos fuera del Hospital



Detección de DNA bacteriano

Gen 16SrRNA de procariontas



Muchas pruebas... y a cruzar los dedos !!

- | | |
|--------------------------|--------------------------|
| 1. Control MW | 6. Control MW |
| 2. <i>E.coli</i> | 7. <i>P. aureuginosa</i> |
| 3. <i>S. agalactiae</i> | 8. <i>P. mirabilis</i> |
| 4. <i>S. epidermidis</i> | 9. <i>Salmonella</i> |
| 5. <i>K. pneumoniae</i> | 10. <i>C. difficile</i> |

- | | |
|---------------------|----------------------|
| 1. Control MW | 7. Control MW |
| 2. Suero paciente 1 | 8. Suero paciente 3 |
| 3. LA paciente 1 | 9. LA paciente 3 |
| 4. Suero paciente 2 | 10. Control negativo |
| 5. LA paciente 2 | 11. Control negativo |
| 6. <i>E.coli</i> | 12. Reactivos |









Calle 1. Con
Calle 2

vetes
Patients **Non**
José Such, Rubén Francis, Carlos Muñoz, Javier Sola-Vera,
Francisco Rodríguez-Valera, Sonia Pascual, José M. Palazón, and Miguel Pérez-Macías

[illegible]

Rubén Francés,¹ Susana Benlloch,² Pedro Zapater,³ José M. Juan A. Casellas,² Francisco Uceda,² José M Palazón,² F

Spontaneous bacterial peritonitis (SBP) is an infection developing in patients with ascites, in the absence of any intraabdominal or extraabdominal identifiable clinically treatable source of infection.¹ It is considered the final consequence of repeated episodes of bacterial translocation (BT) from the intestinal lumen to the peritoneal cavity. The actual translocation (BT) from the intestinal lumen to the peritoneal cavity is the result of the actual arrival of bacteria in the ascitic fluid of the patient. The ascitic fluid is the result of the predisposition to develop a SBP episode. The ascitic fluid is the result of its intrinsic bactericidal properties.²⁻⁴

Abbreviations: JNP, spontaneous bacterial peritonitis; AF, ascitic fluid; S, serum; PCR, polymerase chain reaction; UH, Unidad Hospitalaria; Sec, Secretaría de Salud; Udel, Universidad del Estado; UdelV, Universidad del Valle; UdelG, Universidad del Guayaquil; UdelB, Universidad del Bío-Bío; UdelA, Universidad de Antioquia; UdelC, Universidad de Cundinamarca; UdelE, Universidad de El Salvador; UdelF, Universidad de Friburgo; UdelH, Universidad de Huelva; UdelI, Universidad de Iquique; UdelJ, Universidad de Jujuy; UdelK, Universidad de Kaliningrad; UdelL, Universidad de La Plata; UdelM, Universidad de Mendoza; UdelN, Universidad de Neuquén; UdelO, Universidad de Oporto; UdelP, Universidad de Palermo; UdelQ, Universidad de Quito; UdelR, Universidad de Rosario; UdelS, Universidad de Santiago de Chile; UdelT, Universidad de Tucumán; UdelU, Universidad de Ulsan; UdelV, Universidad de Valparaíso; UdelW, Universidad de Wollongong; UdelX, Universidad de Xiamen; UdelY, Universidad de Yantai; UdelZ, Universidad de Zhengzhou.

Background and aims: Translocation of intestinal bacteria to ascitic fluid is not a new phenomenon. However, the development of episodes of spontaneous bacterial peritonitis in ascites has been reported. The detection of bacterial DNA in blood and peritoneal fluids has been what we consider as molecular evidence of bacterial translocation. The aim of this study was to determine the immunogenic role of bacterial DNA in ascitic fluid and to evaluate its capacity to activate the immune response in mice.

bacterial infection with chronic inflammation. The first step in the development of bacterial infections is the invasion of the host by bacteria. Bacteria can enter the host through the skin, mucous membranes, or the respiratory tract. Once inside the host, bacteria can multiply and cause damage to the host's tissues. The host's immune system responds to the infection by sending white blood cells to the site of infection. These cells can kill the bacteria and remove the damaged tissue. However, if the infection is not cleared, it can lead to a chronic infection. Chronic infections are characterized by a persistent inflammatory response. This response can lead to the formation of granulomas, which are clusters of immune cells that surround and contain the bacteria. Granulomas can cause tissue damage and scarring. In some cases, chronic infections can lead to the development of cancer. For example, chronic infection with the bacterium *Helicobacter pylori* is a major risk factor for the development of gastric cancer.

[illegible]

Shoreline bacterial peritonitis (SBP) is a life-threatening complication of peritoneal dialysis (PD) that has been defined as the presence of a polymicrobial infection in the absence of any

the findings in this study. The results of the current study suggest that the pattern of BactDMS

Independent Prognostic Factor in Noninfected Patients with Cirrhosis

with *hscDNA* in a passive fluid and serum samples. In a prospective, multicenter study, *hscDNA* and actin (first or second) were administered for eradication of large-bowel adenomas. Survival rates of patients were identified *hscDNA* corresponding to the case of death was statistically significant. *hscDNA* negative serum samples were identified *hscDNA* corresponding to the case of death was statistically significant. *hscDNA* negative serum samples were identified *hscDNA* corresponding to the case of death was statistically significant.

...non-chronic
...of 48
...e respectively)
...DNA (MELD) score less
...Spontaneous
...at admission,
...episodes is an
...non-chronic
...id protein.

AGRADECIMIENTOS

Grupo Vithas



Real Academia



Dr. Caturla



Dr. Lluís



Servicio de Medicina Digestiva



Grupo CIBERehd - HGUVA - UMH



Família Francés Gutiérrez



Gracias Miguel

