ADHERENT-INVASIVE ESCHERICHIA COLI STRAIN O83:H1 INDUCES INFLAMMATORY RESPONSE IN CROHN'S DISEASE

Gaetano Iaquinto, MD[1]; Giuseppe Mazzarella,MSc[2]; Vera Rotondi Aufiero, MSc[2]
[1]S. Rita Hospital, Atripalda, Italy, [2]National Council Research, Institute of Food Sciences, Avellino, Italy

INTRODUCTION

Several studies suggest that Adherent-Invasive Escherichia Coli (AIEC) colonize the ileal mucosa of Crohn's disease (CD) patients [1] . LF82 strain is able to adhere to and invade intestinal epithelial cells, and survive within macrophages, prompting an inflammatory response.
The aim of this study was to investigate, by using an organ culture model, the ability of AIEC strain O83:H1 to colonize intestinal epithelial cells of CD patients, inducing chronic inflammation.
The virulence factors of strain O83:H1 , that play a role in its invasive ability, are: 1) type 1 pili , inducing membrane extention; 2) flagella, confering bacteria motility and regulating type 1 pili expression;3) outer membrane vescicles, delivering bacterial effectors to host cells.

METHODS AND MATERIALS

Colonic biopsies from CD patients were used to set up an organ culture model to evaluate , by immunohistochemistry, the ability of AIEC strain 083:H1 to upregulate CEACAM 6 (CarcinoEmbryonic Antigen-related Cellular Adhesion Molecule 6), LAMP-1 (Lysosome Associated Membrane Protein 1), ICAM-1 (Intracellular Adhesion Molecule) and HLA-DR antigen expression, compared to a non-pathogenic AIEC strain (NP) . The staining of epithelial cells that expressed CEACAM6 and LAMP1, as well as the expression of ICAM1 on blood vessels, was evaluated in terms of staining intensity. The number of LAMP1 and HLA-DR lamina propria mononuclear cells (LPMNC) was evaluated within a total area of 1 mm^2 of lamina propria.
Moreover, RNA was extracted and, after a retrotranscription step, messenger RNA levels for IFN-γ, TNF-α and IL-8 were determined by real-time quantitative reverse transcription PCR (RT-qPCR).

RESULTS

Expression of CEACAM6 on intestinal epithelial cells and the expression of LAMP-1 on epithelial cells, as well as in the LPMNCs, were significantly increased in the biopsies cultured with the AIEC strain O83:H1, compared to the biopsies cultured with NP strain ($p < 0,05$) .
ICAM-1 and HLA-DR were significantly increased on blood vessels and on LPMNCs, respectively, in presence of AIEC strain O83:H1 as compared with NP strain ($p < 0,05$). (***Figure 1***).

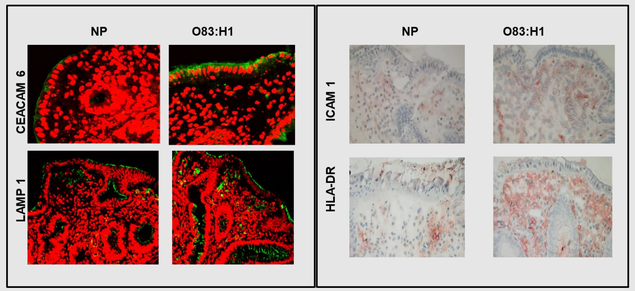

Figure 1. Increased expression of CEACAM6, LAMP-1, ICAM-1 and HLA-DR in the biopsies cultured with the AIEC strain O83:H1 compared to NP strain.

Moreover we observed an increased expression of IFN-γ, TNF-α and IL-8 mRNA trascripts in biopsies cultured with AIEC strain 083:H1 (Figure 2).

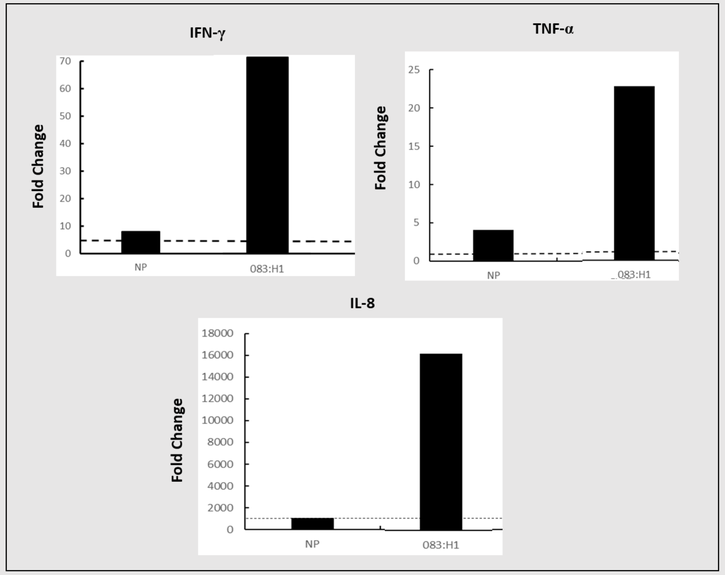

Figure 2. Increased expression of IFN-γ, TNF-α and IL-8, by RT-qPCR, in biopsies cultured with O83:H1 strain compared to NP strain ,

CONCLUSIONS

Our data suggest that AIEC strain O83:H1, like AIEC strain LF82, is able: 1) to increase CEACAM6 and LAMP1 expression on the surface of epithelial cells, 2) to increase HLA-DR and ICAM-1 expression in the lamina propria, 3) to increase inflammatory cytokines involved in active CD.

REFERENCES

[1] Darfeuille-Michaud, A., Neut, C., Barnich, N., Lederman, E., Di Martino, P., Desreumaux, P., Gambiez, L., Joly, B., Cortot, A., & Colombel, J. F. (1998). Presence of adherent Escherichia coli strains in ileal mucosa of patients with Crohn's disease. *Gastroenterology*, *115*(6), 1405–1413. https://doi.org/10.1016/s0016-5085(98)70019-8

CONTACT

<Gaetano Iaquinto>
<S. Rita Hospital, Atripalda, Italy>
Email: iaquintog@yahoo.it
Phone:
Website: