

## Role of Associated Adherent-Invasive Escherichia Coli in Crohn's disease

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Several lines of evidence suggest that adherent-invasive Escherichia coli (AIEC) strains play an important role in Crohn's disease (CD). The objective of this study was to investigate the pathogenic role of two AIEC strains, LF82 and O83:H1, in CD patients. Organ cultures of colonic biopsies from patients were set up to assess the effects of LF82 and O83:H1 on the expression of CEACAM6, LAMP1, HLA-DR, ICAM1 by immunohistochemistry and of IL-8, IFN $\gamma$ , and TNF- $\alpha$  genes by RT-PCR. Moreover, on Caco2 cells, we analyzed the cell cycle, the expression of MGMT and DNMT1 genes, and DNA damage induced by LF82 and O83:H1, by FACS, RT-PCR, and DAPI staining, respectively. Epithelial and lamina propria mononuclear cells (LPMNC) expression of CEACAM6 and LAMP1 were higher in biopsies cultured in the presence of both O83:H1 and LF82 than in biopsies cultured with non-pathogenic E. coli. Both AIEC strains induced increased expression of ICAM-1 on blood vessels and HLA-DR on LPMNC. We observed higher levels of TNF- $\alpha$ , IFN- $\gamma$ , and IL-8 transcripts in biopsies cultured with both AIEC strains than in those cultured with NP. Both LF82 and O83:H1, block the cell cycle into S phase, inducing DNA damage, and modulate the expression of DNMT1 and MGMT genes. Our data suggest that LF82 and O83:H1 strains of E. coli are able to increase in CD colonic biopsies the expression of all the pro-inflammatory cytokines and all the mucosal immune markers investigated.