Title

Identification of candidate bacterial pathogens in ulcerative colitis using a disease-specific marker antibody

Journal

GASTROENTEROLOGY, 114(4)

ISSN

0016-5085

Authors

Cohavy, O

Tayebali, AB

Phu, PK

et al.

Publication Date

1998

Abstract Deadline: Must be RECEIVED by PRISM by December 9, 1997

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J. ABSTRACT BOX

IDENTIFICATION OF CANDIDATE BACTERIAL PATHOGENS IN ULCERATIVE COLITIS USING A DISEASE-SPECIFIC MARKER ANTIBODY

O. Cohavy, A.B. Tayebali, P.K. Phu, M.P. Eggena, D. Bruckner, G. Harth, M. Horwitz, S. Targan, J. Braun.

Departments of Pathology and Medicine, UCLA School of Medicine, Cedars-Sinai Medical Center Los Angeles, CA 90095

Ulcerative colitis is associated in most patients with a unique marker antibody, UC-pANCA. Previously, representative monoclonal antibodies identified an epitope present in the C-terminal basic random-coil domain of histone H1. This study addresses the hypothesis that pANCA reacts with a microbial antigen(s), and detects histone H1 through molecular mimicry. BLAST analysis of the peptide databases revealed H1 epitope homologues in ORFs of the *M. tuberculosis* genome. Western analysis of extracts from six Mycobacterial species directly demonstrated reactivity to a single conserved 32 kDa. protein. Peptide sequencing confirmed its identity as a novel 214 amino acid ORF with 48% similarity to human H1. The second approach involved direct culture of colonic flora under a large range of selective conditions. Three organisms were isolated by sequential cloning, and monitored for antigen expression by Western analysis. 16S rRNA typing identified two members of the *E. coli* family, and one most similar to *Bacteroides cecae*. Peptide analysis revealed at least three protein antigens, distinct in structure from the Mycobacterial antigen. Our findings indicate that the ulcerative colitis marker antibody detects a structural domain recurrent among colonic microbiota, and crossreactive with a DNA-binding domain of histone H1. These organisms deserve further evaluation for their role in the tissue-specific inflammatory response of this disease. Supported by NIH DK46763.

K. DISCLOSURE INFORMATION

Signature Offer Cohavy Print Name OFFER COHAVY

Phone: (310) 825 1590 FAX: (310) 825 5674

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