VISUALIZATION OF TRANSEPITHELIAL PASSAGE OF THE IMMUNOGENIC 33-RESIDUE PEPTIDE FROM ALPHA2-GLIADIN IN GLUTEN-SENSITIVE RHEUS MACAQUES.


Divisions of *Microbiology, **Comparative Pathology and ***Veterinary Medicine, Tulane National Primate Research Center, Covington, Louisiana
****Department of Chemistry, Stanford University, Stanford, California
*****Department of Microbiology and Immunology, Tulane University School of Medicine, New Orleans, Louisiana.

Abstract

BACKGROUND & AIMS: Based on clinical, histopathological and serological similarities to human celiac disease (CD), we recently established the rhesus macaque model of gluten sensitivity. In this study, we visualized the entry and transepithelial transport of a proteolytically resistant, immunotoxic, 33-residue peptide from alpha2-gliadin in the distal duodenum of gluten-sensitive macaques in remission or with active disease.

METHODS: Six rhesus macaques (Macaca mulatta) were selected for study from a pool of 500 animals, including two healthy controls and four gluten-sensitive animals with elevated anti-gliadin antibodies (AGA) and/or anti-tissue transglutaminase 2 (TG2) antibodies as well as a history of chronic diarrhea of non-infectious origin. Pediatric endoscope-guided pinch biopsies were collected from each animal's distal duodenum following administration of gluten-containing diet (GD) and again after serological and clinical remission were achieved by administration of a gluten-free diet (GFD).

RESULTS: Duodenal biopsies from control animals showed normal villous architecture regardless of dietary gluten content, whereas gluten-sensitive animals administered a GD exhibited a variable range of histopathological changes ranging from mild lymphocytic infiltration to villous atrophy, typical of human CD. Immunofluorescent microscopic analysis of duodenal biopsies revealed IgG+ and IgA+ plasma-like cells producing antibodies that colocalized with TG2 in gluten-sensitive macaques but not in controls. Following instillation in vivo, the Cy-3-labeled 33-residue gluten peptide was colocalized with the brush border protein villin in all animals. In one gluten-sensitive macaque with substantial enteropathy and a "leaky" duodenum, the peptide was observed to penetrate beneath the epithelium into the lamina propria.

CONCLUSIONS: The rhesus macaque model of gluten sensitivity not only resembles the histopathology of CD but it also may provide a model for studying intestinal permeability in states of epithelial integrity and disrepair.

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