

Novel cytokine peptide-based and virus-like particle vaccines for treatment of inflammatory bowel disease

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Background: In Crohn's disease, the tissue damage likely results from exaggerated Th1, IL-23/IL-17 pathway and IL-18 immune responses to antigens of the gut microflora. Blocking these cytokines with monoclonal antibodies (mAb) has been used in the treatment of the disease. However, the short half-life of the mAb and the development of antibodies to the infused mAb limit the use of this reagent.

Aims: To develop cytokine peptide-based and virus-like particle vaccines which induce long-lasting antibodies to the p40 subunit (shared by IL-12 & IL-23) or IL-18 or TGF β 1 and evaluate their effects in animal models.

Methods: The vaccine was constructed by inserting a small peptide, derived from the receptor binding site of the target cytokine, into a carrier, hepatitis B core antigen, via gene recombination methods. Recombinant vaccines were expressed using *E. coli* and purified appropriately. Chronic colitis was induced by weekly intrarectal administration of trinitrobenzene sulfonic acid eight times. At week 2, mice received three subcutaneous injections of vaccine or carrier or saline in a two-week interval.

Results: The vaccine that was presented as virus-like particles induced strong and long-lasting antibody responses against the target cytokine without the use of an adjuvant. Administration of a vaccine against the p40 subunit or IL-18 or TGF β 1 significantly down-regulated intestinal inflammation and fibrosis in mice with chronic colitis, as shown by the decrease in body weight loss, intestinal inflammation (H&E staining), amounts of soluble collagen and pro-inflammatory cytokines in colon tissue.

Conclusion: Cytokine vaccines may provide a potential therapeutic approach for the long-term treatment of inflammatory bowel disease.

Biography

Zhikang Peng received an M.D. in 1968 from Fudan University School of Medicine and then worked as a clinician. After training as a post-doctoral fellow in Johns Hopkins University and the University of Manitoba, in 1992 Dr. Peng became a faculty member in the University of Manitoba. Her current research interests are in the development of novel immunotherapies for treatment of inflammatory bowel disease and asthma. She is currently a Professor in the Dept. of Pediatrics and the Dept. of Immunology of the University of Manitoba and has published more than 70 papers in peer-reviewed journals.

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