Expert Review of Clinical Immunology

ISSN: 1744-666X (Print) 1744-8409 (Online) Journal homepage: informahealthcare.com/journals/ierm20

Inflammatory bowel disease

Stephen B Hanauer & Daan W Hommes

To cite this article: Stephen B Hanauer & Daan W Hommes (2010) Inflammatory bowel disease, Expert Review of Clinical Immunology, 6:4, 499-500, DOI: 10.1586/eci.10.52

To link to this article: https://doi.org/10.1586/eci.10.52

Published online: 10 Jan 2014.

Submit your article to this journal

Article views: 502

View related articles

Full Terms & Conditions of access and use can be found at
https://informahealthcare.com/action/journalInformation?journalCode=ierm20

For reprint orders, please contact reprints@expert-reviews.com

Inflammatory bowel disease

Expert Rev. Clin. Immunol. 6(4), 499–500 (2010)

Stephen B Hanauer

Author for correspondence:
Chief, Section of Gastroenterology, Hepatology and Nutrition, University of Chicago, 5841 S. Maryland Avenue, MC 4076, Chicago, IL 60637, USA
Tel.: +1 773 834 7308
Fax: +1 773 702 2182
shanauer@uchicago.edu

Daan W Hommes

Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands
Tel.: +31 071 526 5217
d.w.hommes@lumc.nl

"This special focus issue of *Expert Review of Clinical Immunology* provides an overview of the current concepts and controversies regarding the pathogenesis, current and future therapeutic approaches, and the course of inflammatory bowel disease."

Ulcerative colitis and Crohn's disease remain idiopathic inflammatory bowel diseases (IBDs) with an expanding worldwide incidence and prevalence owing to the influence of Western lifestyles (e.g., diet and hygiene) that continue to pervade Second- and Third-world environs [1–3]. Etiopathogenic clues include predisposing genetic factors, environmental 'triggers' and immunologic dysregulation, none of which have been completely defined or collated to explain the heterogeneity and diversity of clinical presentations and prognoses. This special focus issue of *Expert Review of Clinical Immunology* provides an overview of the current concepts and controversies regarding the pathogenesis, current and future therapeutic approaches, and the course of IBD.

Theories of immune dysregulation are polarized between potential genetic contributions to defects in innate immunity (*NOD2*/*CARD15* mutations, defective autophagy and altered defensins, as reviewed by Anthony Segal [4]) and the potential role of the gut microbiome (including atypical mycobacteria as explored by Jean-Daniel Lalande and Marcel Behr [5]) to ongoing foci on T cells and cytokine signaling (addressed by Femke van Wijk and Hilde Cheroutre [6], and Francesco Pallone and colleagues [7]).

Epidemiologic observations and hypothetical interactions between the gut microflora and mucosal immune system are consistent with nutritional approaches to IBD that can alter microbial species, populations and metabolism of nutrients (e.g., prebiotics, as discussed by Andrew Day and colleagues [8] and Lynnette Ferguson [9]). Such nutritional and dietary interventions remain effective under rigid clinical trial settings and are popular integrative/alternative approaches within the lay community but have yet to attain an acceptable evidence-based status for the majority of adult patients.

Instead, the strongest evidence for therapeutic efficacy derives from immunomodulatory approaches, including aminosalicylates in ulcerative colitis, and corticosteroids, thiopurines and anti-TNF therapies in both Crohn's disease and ulcerative colitis (see the articles by Athos Bousvaros [10], Brijen Shah and Lloyd Mayer [11], and Ellen Zimmermann and colleagues [12]). Therapeutic approaches for the induction and maintenance of clinical remissions with these agents have been highly efficacious; however, to date, less than half of patients with symptoms and signs that are refractory to conventional (nonbiological) strategies are maintained in steroid-free remissions. Hence, there is a need to optimize adherence (reviewed by Sunanda Kane and Steven Bernick [13]) in ulcerative colitis, monitor disease activity and predict relapse (discussed by Giacomo Carlo Sturniolo and colleagues [14]) and to develop novel therapeutic approaches (explored by Alan C Moss and colleagues [15]). Initial clinical trials have demonstrated efficacy and led to the approval of natalizumab in the USA for the treatment of Crohn's disease refractory to anti-TNF agents and it appears that a more selective anti-adhesion target that is devoid of the risk of progressive multifocal leukoencephalopathy will be necessary to gain patient acceptance of these novel mechanistic approaches

EXPERT REVIEWS

 10.1586/ECI.10.52 © 2010 Expert Reviews Ltd ISSN 1744-666X

(discussed by Stephen J Bickston and Kishor Muniyappa [16], and Silvio Danese and colleagues [17]). Meanwhile, stem cell transplantation remains an 'ultimate' means of impacting both the innate and adaptive arms of the immune system. Whether autologous hematopoetic stem cell transplants necessitating bone marrow ablation or mesenchymal stem cell transplantations or infusions that do not require intense chemotherapeutic lymphoablation will be efficacious will be determined by evidence from awaited controlled trials (reviewed by Julián Panés and colleagues [18]). The ultimate risks of immune-directed approaches include opportunistic infections and neoplasia. The infectious risks have been well clarified from clinical trials and post-marketing studies. By contrast, neoplasia, and lymphoma in particular, has been a major concern impacting the long-term management of patients receiving immunomodulatory therapy with conventional and biologic approaches. The complexity of attributing the lymphoma risk to anti-TNF therapies has been confounded by the frequent coadministration of combination therapies (described by James Lewis and Meenakshi Bewtra [19]).

Finally, the bidirectional impact of pregnancy on IBD and IBD on pregnancy provides clues to both the etiopathogenesis (i.e., why do some women go into clinical remissions during pregnancy?) along with the ultimate safety of individual and combined therapeutic approaches (reviewed by Uma Mahadevan and Lola Kwan [20]). The inherent ability of women to downregulate immune responses may, ultimately, lead to the identification of an endogenous mediator that could be utilized for therapeutic benefits. In the meantime, we continue to move ahead with basic and clinical investigations into the complex interactions between human genetics, the luminal environment and immune dysregulation that lead to the syndromes we now describe as ulcerative colitis and Crohn's disease.

Financial & competing interests disclosure

Stephen B Hanauer works as a consultant for Alevan, Amgen, Astellas Pharma Global, AstraZeneca, GSK, McNeil PPC, Millenium Pharmaceuticals, Novartis, Novo Nordisk and Takeda. He also works as a consultant and in clinical research for Abbott Labs, Bristol Myers Squibb, Centocor, Chemocentryx, Elan, Ferring, Genentech, Pfizer, Prometheus, Salix, Shire, Therakos, UCB Pharma and Warner-Chilcott. Daan W Hommes works as a consultant for Abbott Labs, Centocor, MSD and UCB, and recieves research grants from Abbott Labs, Centocor, MSD, UCB, Ferring, Giuliani Pharma and FALK. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

1 Saro C, Sicilia B. Inflammatory bowel diseases: a disease (s) of modern times? Is incidence still increasing? *World J. Gastroenterol.* 14(36), 5491–5498 (2008).

2 Koloski NA, Bret L, Radford-Smith G. Hygiene hypothesis in inflammatory bowel disease: a critical review of the literature. *World J. Gastroenterol.* 14(2), 165–173 (2008).

3 Sood A, Midha V. Epidemiology of inflammatory bowel disease in Asia. *Indian J. Gastroenterol.* 26(6), 285–289 (2007).

4 Hayee B, Rahman FZ, Sewell G, Smith AM, Segal AW. Crohn's disease as an immunodeficiency. *Expert Rev. Clin. Immunol.* 6(4), 585–596 (2010).

5 Behr M, Lalande J-D. Mycobacteria in Crohn's disease: how innate immune deficiency may result in chronic inflammation. *Expert Rev. Clin. Immunol.* 6(4), 633–641 (2010).

6 Van Wijk F, Cheroutre H. Mucosal T cells in gut homeostasis and inflammation. *Expert Rev. Clin. Immunol.* 6(4), 559–566 (2010).

7 Pallone F, Fina D, Caruso R, Monteleone G. The role of IL-21 in inflammatory bowel disease. *Expert Rev. Clin. Immunol.* 6(4), 537–541 (2010).

8 Otley AR, Russell RK, Day AS. Nutritional therapy for the treatment of pediatric Crohn's disease. *Expert Rev. Clin. Immunol.* 6(4), 667–676 (2010).

9 Ferguson LR. Nutrigenomics and inflammatory bowel diseases. *Expert Rev. Clin. Immunol.* 6(4), 573–583 (2010).

10 Bousvaros A. Use of immunomodulators and biologic therapies in children with inflammatory bowel disease. *Expert Rev. Clin. Immunol.* 6(4), 659–666 (2010).

11 Shah B, Mayer L. Current status of monoclonal antibody therapy for the treatment of inflammatory bowel disease. *Expert Rev. Clin. Immunol.* 6(4), 607–620 (2010).

12 Dahan A, Amidon GL, Zimmermann EM. Drug targeting strategies for the treatment of inflammatory bowel disease: a mechanistic update. *Expert Rev. Clin. Immunol.* 6(4), 543–550 (2010).

13 Bernick SJ, Kane S. Insight into the widespread problem of nonadherence to therapy in ulcerative colitis patients. *Expert Rev. Clin. Immunol.* 6(4), 677–682 (2010).

14 Caccaro R, D'Incà R, Sturniolo GC. Clinical utility of calprotectin and lactoferrin as markers of inflammation in patients with inflammatory bowel disease. *Expert Rev. Clin. Immunol.* 6(4), 551–558 (2010).

15 Lawlor G, Ahmed A, Moss AC. Once-daily mesalamine granules for ulcerative colitis. *Expert Rev. Clin. Immunol.* 6(4), 521–526 (2010).

16 Bickston SJ, Muniyappa K. Natalizumab for the treatment of Crohn's disease. *Expert Rev. Clin. Immunol.* 6(4), 513–519 (2010).

17 Fiorino G, Correale C, Fries W, Repici A, Malesci A, Danese S. Leukocyte traffic control: a novel therapeutic strategy for inflammatory bowel disease. *Expert Rev. Clin. Immunol.* 6(4), 607–620 (2010).

18 Panés J, Ordás I, Ricart E. Stem cell treatment for Crohn's disease. *Expert Rev. Clin. Immunol.* 6(4), 597–605 (2010).

19 Bewtra M, Lewis JD. Update on the risk of lymphoma following immunosuppressive therapy for inflammatory bowel disease. *Expert Rev. Clin. Immunol.* 6(4), 621–631 (2010).

20 Kwan LY, Mahadevan U. Inflammatory bowel disease and pregnancy: an update. *Expert Rev. Clin. Immunol.* 6(4), 643–657 (2010).