

IFN-gamma. The above distinction regarding Th1 response and Th2 response is not an absolute one, as CD and UC also include Th17-type immune responses. Gut biopsies from both CD and UC patients show increased expression of IL-17A, increased Th17 cells, and increases in the subset of Th17 cells that is “Th1/Th17 cells,” which express both interferon-gamma (IFN-gamma) and IL-17. In CD, gut cells express high levels of IL-12, and high levels of IL-18, a cytokine that enhances Th1-type immune response. The gut in CD is infiltrated with Th17 cells, which express IL-17A, IL-17F, IL-21, IL-22, and IL-26 (35).

In lesions of CD, CD4<sup>+</sup> T cells express large amounts of the Th1-type cytokine, IFN-gamma. In contrast, in UC, the lesions result from the Th2-type cytokines. Both diseases involve IL-17-producing T cells. These diseases result in gastrointestinal pain, and require diet therapy and the services of a dietician.

A number of self-antigens have been identified as targets in IBD, but the extent to which immune response against these antigens is responsible for the pathology of IBD is not clear. The self-antigens in UC include

lyso-sulfatide glycoprotein (36), colonic tropomyosin (hTm5) (37), goblet cell glycoproteins (38), and the antigen of “perinuclear antineutrophil cytoplasmic antibodies” (39). The self-antigens in CD include goblet cell glycoproteins (40), prohibitin, calreticulin, apolipoprotein A–I, and protein disulfide isomerase (41). The primary defect in IBD seems not to be related to these self-antigens, but instead is a result of an abnormal gut epithelial barrier, which allows for invasion of gut bacteria past the layer of epithelial cells of the large intestines, and overactive immune response and chronic inflammation (42).

## II. DETAILED MECHANISM OF ACTION OF MULTIPLE SCLEROSIS

### a. Introduction

Multiple sclerosis is a disorder of the central nervous system (CNS) characterized by chronic inflammation, myelin loss, and progressive neurological dysfunction (43). Symptoms that occur most commonly in multiple sclerosis include tremor, optic neuritis or double vision,

<sup>35</sup>Zorzi F, et al. Distinct profiles of effector cytokines mark the different phases of Crohn’s disease. *PLoS One* 2013;8:e54562.

<sup>36</sup>Fuss IH, et al. NKT cells reactive to sulfatide self-antigen populate the mucosa of ulcerative colitis. *Gut* 2014;63:1728–36.

<sup>37</sup>Das KM, Bajpai M. Tropomyosins in human disease: ulcerative colitis. *Adv. Exp. Med. Biol.* 2008;644:158–67.

<sup>38</sup>Wen Z, Fiocchi C. Inflammatory bowel disease: autoimmune or immune-mediated pathogenesis. *Clin. Dev. Immunol.* 2004;11:195–204.

<sup>39</sup>Wen Z, Fiocchi C. Inflammatory bowel disease: autoimmune or immune-mediated pathogenesis. *Clin. Dev. Immunol.* 2004;11:195–204.

<sup>40</sup>Wen Z, Fiocchi C. Inflammatory bowel disease: autoimmune or immune-mediated pathogenesis. *Clin. Dev. Immunol.* 2004;11:195–204.

<sup>41</sup>Zhou Z, et al. Immunoproteomic to identify antigens in the intestinal mucosa of Crohn’s disease patients. *PLoS One* 2013;8:81662.

<sup>42</sup>Corridoni D, et al. Probiotic bacteria regulate intestinal epithelial permeability in experimental ileitis by a TNF-dependent mechanism. *PLoS One* 2012;7:e42067.

<sup>43</sup>Nicot AB. Gender and sex hormones in multiple sclerosis pathology and therapy. *Front. Biosci.* 2009;14:4477–515.