recently reported that S1P, a lipid mediator, contributes to the regulation of migration of pathogenic CD4 T and mast cells from the systemic immune compartment into the large intestine and inhibition of S1P-mediated pathway results in the inhibition of development of allergic diarrhea (205).

Celiac Disease

Celiac disease is another related disorder of mucosal immunity, which is characterized by small-intestinal mucosal injury in response to the dietary ingestion of gluten (29). Gluten is a proline- and glutamine-rich protein that is found in wheat, rye, and barley. Pathologic features of celiac disease include increased numbers of IELs and less extensive villous atrophy and crypt hypertrophy (29). IELs from patients with celiac disease preferentially include NK-like cells, which recognize stress-induced MICA molecules expressed on IECs (29). This process has been considered to be mediated by IL-15. IL-15 induces increased expression of MICA and subsequent interaction between MICA and its receptor, NKG2D, and up-regulates gluten-specific CTL activity in the small intestine (206). Gluten-free diet currently is the only accepted therapy for celiac disease, and various immunological approaches such as blocking IL-15 and treatment with IL-10 have been examined (29). However, in terms of quality of life, it is doubtful that this treatment will be effective with so many potential side effects. Thus, it is essential to identify the gluten-specific pathogenic immunocompetent cell population for the development of novel strategies to selectively delete the specific pathogenic populations.

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