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Functional Role of Lactoferrin in Intestinal Health and Inflammatory Bowel Disease

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Abstract

A chronic illness that causes inflammation in the digestive tract is called inflammatory bowel disease (IBD). It is brought on by the immune system of the body targeting healthy intestinal cells. Ulcerative colitis and Crohn's disease are two forms of IBD. Risk elements Age, environmental factors that impact the gut microbiome, and family history of IBD. Lactoferrin is frequently measured in stool samples as a marker for disease activity, with higher levels indicating increased inflammation in the colon. Lactoferrin functions as a potential anti-inflammatory agent in ulcerative colitis, primarily by binding to iron and limiting its availability to harmful bacteria, thereby reducing inflammation in the intestinal lining. We hope this information will provide a reference for future studies and lay a theoretical foundation for LF-based therapeutic interventions for IBD by understanding the particular effects of LF on intestine mucosal immune system.

Keywords: inflammatory bowel disease, Ulcerative colitis, Crohn's disease and Lactoferrin.

Introduction:

A chronic idiopathic inflammatory bowel disease (IBD) of the colon, ulcerative colitis (UC) results in a continuous, superficial mucosal inflammation that varies in severity from the rectum to the more proximal colon (Silverberg et al., 2005). The course of UC is marked by relapses and remissions. Tenesmus and bloody diarrhea with rectal urgency are the classic signs of ulcerative colitis. Even while the exact cause of UC is still up for debate, there is mounting evidence that it may have an autoimmune component (Halling et al., 2017; Das and Biancone, 2008). Extraintestinal manifestations (EIM), which involve several organs sharing characteristics with other autoimmune illnesses, are common in UC patients.

Risk factors:

Age and gender

The incidence of UC peaks in the second or third decades of life, and then again between the ages of 50 and 80. This gives UC a bimodal age distribution (Langholz, 1991). Although some research shows a male predominance in UC, no consistently significant difference in rates between men and women has been found (Loftus, 2004).

Smoking

Harries et al. were the first to report a link between smoking and UC (Harries et al., 1982). Active smoking had a significant negative correlation with active UC (OR 0.58, 95% CI 0.45–0.75), in contrast to CD (Mahid et al., 2006; Gajendran et al.., 2018). According to a prospective study, the risk of UC rose two to five years after quitting smoking and continued to rise for twenty years (Higuchi et al., 2012). Research has indicated that current smoking is linked to a gentler course of the disease, a later age of beginning, a lower requirement for immunosuppressive, and a lower need for surgery (Cosnes et al., 2004; Lakatos et al., 2007). However, it has not been discovered that replacing nicotine in UC lowers disease activity, indicating that tobacco use has an impact on UC that is separate from nicotine (Biedermann et al., 2014; Persson et al., 1993).

Microbiota

A number of epidemiological indicators suggest that IBD is associated with intestinal microbiota dysbiosis. A change in the makeup of commensal bacterial populations that results in a dysregulation of the immune system's reaction to bacterial antigens is known as dysbiosis. Compared to UC, CD has a larger disparity in microbial diversity. Compared to individuals with UC or their healthy twins, the mucosal transcriptional profile (which displays mucosal gene expression) from healthy siblings has a higher connection with bacterial gene expression, indicating a disturbed interaction between the mucosa and microbiota in IBD (Lepage et al., 2011). Additionally, UC has been linked to abnormalities in enteric virome and the growth of bacteriophages from the Caudovirales family, which are not related to bacterial dysbiosis (Norman et al., 2015).

Diet

An immune reaction to dietary antigens has been proposed as the cause of IBD development. A "Western" diet that includes processed meat, refined carbs, and other foods is linked to a higher risk of getting IBD. When compared to controls, cow's milk protein hypersensitivity during infancy has been proposed as a potential cause of UC (21% vs. 3%). An increased incidence of UC is also associated with higher dietary intakes of polyunsaturated fatty acids, animal fat, and total fat (Glassman et al., 1990; Geerling et al., 2000).

Clinical Symptoms:

Abdominal discomfort and bloody diarrhea are ulcerative colitis's primary signs. Other signs and symptoms include:

Frequent bowel movements, occasionally accompanied with blood, mucus, or pus; pain and cramping in the abdomen; Inadvertent weight loss; the sensation that one must have a bowel movement even when one's bowels are empty; Fever; Fatigue: Exhaustion; Skin conditions such as pyoderma gangrenosum or erythema nodosum; Ankylosing spondylitis or arthritis are examples of joint pain. The symptoms can vary in intensity. In moderate situations, for instance, you may have fewer than four bowel motions per day. You may have more than six bloody bowel motions each day in extreme circumstances (Gajendran et al., 2019).

Lactoferrin:

First discovered as a red protein in whey in 1939, lactoferrin (LF) (Sorensen and Sorensen 1940). It was separated and refined from both human and cow's milk in 1960 (Groves 1960; Johanson 1960). The isolated protein could reversibly bind ferric (Fe^{+3}) ions and shared structural similarities with serum transferrin, with >60% sequence identity (Baker 1994; Johanson 1960). Since serum transferrin, melanotransferrin, and ovotransferrin are also members of the transferrin family, LF is also included in this group (Lambert, Perri, and Meehan 2005).

Milk, saliva, and seminal fluid are among the biological fluids that contain LF (Cheng et al. 2008). Additionally, it can be found in certain polymorphonuclear leukocyte granules and mucosal surfaces. Human and bovine milk are the most prevalent sources of LF. The amount of LF in milk varies greatly between species and with lactation stages. Compared to mature breast milk, which contains 2–3 g/L of LF, human colostrum contains more than 5 g/L. While bovine milk only contains 0.03–0.49 g/L of LF, bovine colostrum has an approximate 0.8 g/L concentration. Breastfed infants are thought to be protected against bacterial infection and inflammation by the greater concentration of LF in colostrum (Artym and Zimecki 2005).

causing inflammatory processes may also be inhibited by LF.

A glycoprotein found in breast milk called lactoferrin (LF) aids in the development and maturation of an infant's intestines. LF also guards against infections and aids in the immune system's development. Intestinal epithelial cell growth is stimulated by LF. Intestinal epithelial cell

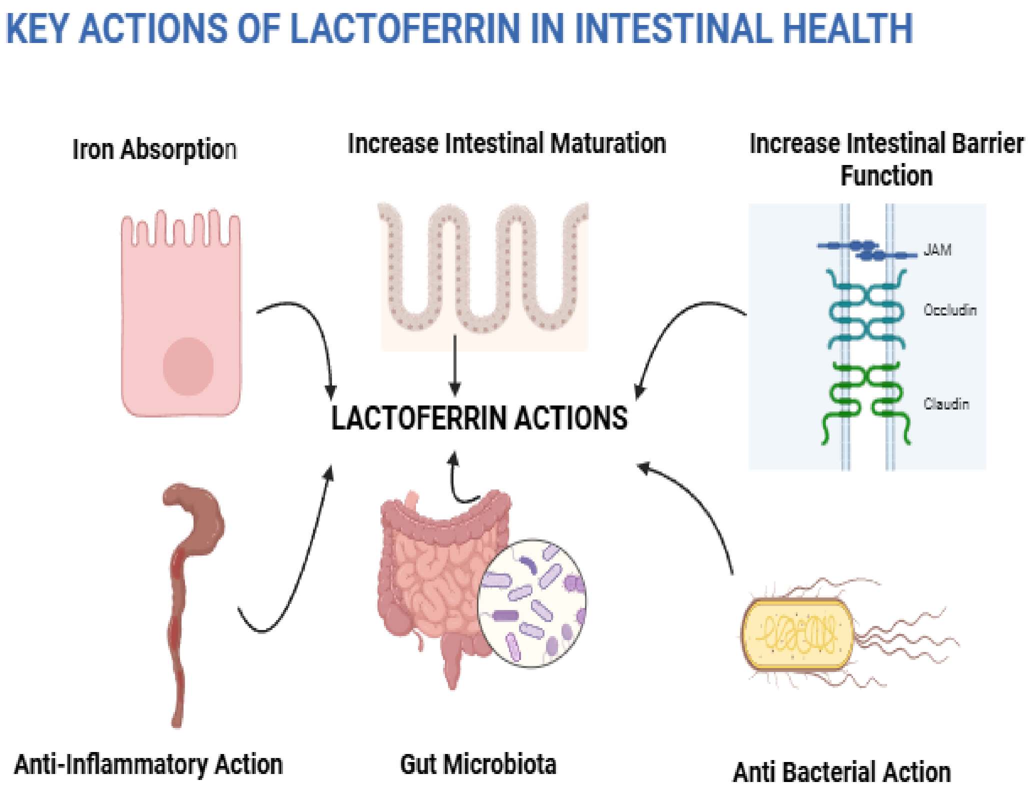

Figure No 1: Key Action of Lactoferrin in Intestinal Health

The human body absorbs iron more readily when LF is present (Paesano et al. 2010). It prevents the production of many poisonous chemicals, scavenges dangerous free radicals, and regulates cell development (Baveye et al. 1999). For these reasons, LF is included in a wide range of commercial items, such as toothpaste, cosmetics, fermented milk, therapeutic drinks, and powdered newborn formula (Tomita et al. 2009). Research interest has grown as a result of LF's numerous health-promoting properties and several practical uses.

A protein called lactoferrin (LF) binds iron and may aid in the absorption of iron. In addition to being a food additive, it can be present in human milk. Because LF binds to iron in breast milk, it may facilitate newborns' small intestine iron absorption. Iron is firmly bound by LF, which can continue to do so even after heating. Anemia-

differentiation is aided by LF. Gut nerve fiber development is aided by LF. Immune cell maturation and development are aided by LF. LF contributes to the synthesis of cytokines that inhibit inflammatory processes. By regulating the expression of tight junction proteins and having anti-inflammatory effects within the intestinal lining, lactoferrin helps to maintain the integrity of tight junctions between intestinal epithelial cells, which in turn prevents harmful substances from leaking from the gut lumen into the bloodstream. This effectively acts as a protective barrier against pathogens and toxins (Liu et al., 2021).

Lactoferrin, a protein naturally found in bodily secretions like breast milk and produced by neutrophils, is an important component of the body's innate immune system. It primarily regulates iron homeostasis, interacts directly with immune cells, and modulates the inflammatory response through pathways like NF-κB. This helps to reduce inflammation at sites of infection or injury by limiting the activity of inflammatory mediators like cytokines. By depriving bacteria of iron and rupturing their cell walls, lactoferrin (LF) has antibacterial effects. A glycoprotein called LF is present in milk and other body fluids. Because LF binds to iron, bacteria are deprived of this vital mineral. LF interacts with lipoteichoic acids in the cell wall of Gram-positive bacteria and lipopolysaccharides (LPS) in the outer membrane of Gram-negative bacteria. Without triggering cell lysis, LF can depolarize the cell membrane (Conesa et al., 2023).

Conclusion

An iron-binding protein called LF, which is present in the majority of bodily fluids, has been shown to be a strong antibacterial, anti-inflammatory, and immunomodulatory substrate that can strengthen the intestinal mucosal immune system and shield the intestine from illnesses like ulcerative colitis. It is difficult to comprehend the mechanisms of action of LF in intestinal mucosal immunology and ulcerative colitis because of its diverse microbial and host targets. As a result, more research is required to fully understand the underlying mechanisms.

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