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Editorial A SCITECHNOL JOURNAL

A Potential Role for Host-Microbe Dysbiosis in Enteropathy Associated with HIV Infection

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Human immunodeficiency virus (HIV) infection progressively depletes CD4+ T-lymphocytes from the immune system and, in the absence of treatment, leads to acquired immune deficiency syndrome (AIDS). Gut associated lymphoid tissue (GALT) harbors a majority of the body's lymphocytes and is an early and important mucosal target of HIV infection [1-3]. The massive and rapid depletion of CD4+ T cells from GALT in primary HIV infection is presumed to be an underlying cause of a progressive deterioration of intestinal immune and digestive functions collectively termed "enteropathy". The most common clinical manifestations of HIV-associated enteropathy, diarrhea and malnutrition, have a devastating impact on the day-to-day lives of millions of patients world-wide [4-6]. Immunologically, the loss of CD4+ T helper cell function in GALT is believed to contribute to HIV-associated enteropathy through disruption of homeostatic communication between adaptive and innate immunity. Although the molecular details of this communication breakdown have not yet been characterized, it is clear that HIV infection transforms the intestinal mucosa from a balanced homeostatic system to a chronically activated inflammatory environment [7], leading to disruption of epithelial barrier integrity [8,9] and microbial translocation [10-13].

The human gastrointestinal (GI) tract is colonized by up to 100 trillion bacterial cells [14] and the collective genome of the microbiome contains more than 100 times as many genes as our own. It is a delicately balanced polymicrobial community that provides important metabolites to the body [15] and modulates the expression of host genes involved in maintaining epithelial integrity [16-18] and mediating inflammatory and antimicrobial responses [19,20]. In health, a homeostatic balance between tolerogenic responses to resident microbes and an activated defense response to incoming pathogens is maintained through coordinated trialogue between the epithelial barrier, GALT, and the microbiome [21]. Recent studies indicate that lamina propria CD4+ T cells play an important role in maintaining intestinal homeostasis by inducing epithelial cell differentiation, polarization, and barrier function [22]. Massive CD4+ T cell loss from the GI mucosa in primary HIV infection therefore has the potential to disrupt homeostatic trialogue (dysbiosis) and thereby contribute to the epithelial deterioration that defines enteropathy.

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An intriguing hypothesis that has gained attention in recent years is that epithelial deterioration and enteropathy may contribute to the chronic immune activation associated with HIV disease progression by providing a mechanism for translocation of microbes and bacterial products across the epithelial barrier. A new investigative focus to test this hypothesis has been fueled by an enlightened appreciation, stemming largely from the Human Microbiome Project [23], of the role that the microbiota plays in health and disease. Early investigations have shown correlations between the levels of immune activation in HIV infected patients and modulations of gut bacterial populations [24] as well as a potential for therapeutic intervention with probiotics [25,26]. Ongoing and future investigations are expected to reveal novel paradigms about the kinetics and molecular mechanisms of dysbiosis in HIV infection and develop strategies for reducing its role in mucosal pathogenesis and disease progression.

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