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Microbial translocation is a cause of systemic immune activation in chronic HIV infection

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Chronic activation of the immune system is a hallmark of progressive HIV infection and better predicts disease outcome than plasma viral load, yet its etiology remains obscure. Here, we show that circulating microbial products, likely derived from the gastrointestinal tract, are a primary cause of HIV-related systemic immune activation. Circulating lipopolysaccharide, an indicator of microbial translocation, is significantly increased in chronically HIV-infected individuals and SIV-infected rhesus macaques. We show that monocytes are chronically stimulated in vivo by increased lipopolysaccharide, which also correlates with measures of innate and adaptive immune activation. Effective antiretroviral therapy appears to reduce microbial translocation. Furthermore, in non-pathogenic SIV infection of sooty mangabeys, microbial translocation does not seem to occur. These data establish a mechanism for chronic immune activation in the context of a compromised gastrointestinal mucosal surface and provide novel directions for therapeutic interventions that modify the consequences of acute HIV infection.