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Gut-associated plasmacytoid dendritic cells display an immature phenotype and upregulated granzyme B in subjects with HIV/AIDS

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Abstract

© 2015 Boichuk, Khaiboullina, Ramazanov, Khasanova, Ivanovskaya, Nizamutdinov, Sharafutdinov, Martynova, DeMeirleir, Hulstaert, Anokhin, Rizvanov and Lombardi. Plasmacytoid dendritic cells (pDCs) in the periphery of subjects with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) decrease over time, and the fate of these cells has been the subject of ongoing investigation. Previous studies using animal models as well as studies with humans suggest that these cells may redistribute to the gut. Other studies using animal models propose that the periphery pDCs are depleted and gut is repopulated with naive pDCs from the bone marrow. In the present study, we utilized immunohistochemistry to survey duodenum biopsies of subjects with HIV/AIDS and controls. We observed that subjects with HIV/AIDS had increased infiltration of Ki-67+/CD303+ pDCs, a phenotype consistent with bone marrow-derived pre-pDCs. In contrast, Ki-67+/CD303+ pDCs were not observed in control biopsies. We additionally observed that gut-associated pDCs in HIV/AIDS cases upregulate the proapoptotic enzyme granzyme B; however, no granzyme B was observed in the pDCs of control biopsies. Our data are consistent with reports in animal models that suggest periphery pDCs are depleted by exhaustion and that naive pDCs egress from the bone marrow and ultimately infiltrate the gut mucosa. Additionally, our observation of granzyme B upregulation in naive pDCs may identify a contributing factor to the gut pathology associated with HIV infection.

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Keywords

Granzyme B, Gut, HIV/AIDS, PDC, Plasmacytoid dendritic cell