HIV-1 INFECTS MULTIPOTENT PROGENITOR CELLS CAUSING CELL DEATH AND ESTABLISHING LATENT CELLULAR RESERVOIRS

Christoph C. Carter[1,2**], Adewunmi Onafuwa-Nuga[4**], Lucy A. McNamara, James Riddell IV[4], Dale Bixby[4], Michael R. Savona[4*], and Kathleen L. Collins[1,2,3,4†]

[1]Graduate Program in Cellular and Molecular Biology, [2]Medical Scientist Training Program, [3]Department of Microbiology and Immunology, [4]Department of Internal Medicine, University of Michigan, Ann Arbor, MI 48109 USA

HIV causes a chronic infection characterized by depletion of $CD4^+$ T lymphocytes. Despite the development of drugs that inhibit viral spread, HIV has been difficult to cure because of uncharacterized reservoirs of infected cells that are resistant to highly active antiretroviral therapy and the immune response. We used *in vitro* studies of wild type HIV as well as $CD34^+$ cells from infected people to demonstrate infection and killing of $CD34^+$ multipotent hematopoietic progenitor cells (HPCs). In some HPCs, we detected latent infection that stably persisted in cell culture until viral gene expression was activated by differentiation factors. A novel reporter HIV that directly detects latently infected cells *in vitro* confirmed the presence of distinct populations of active and latently infected HPCs. These findings have important implications for understanding HIV bone marrow pathology and the mechanisms by which HIV causes a persistent infection.