CENTER FOR RNA BIOMEDICINE

RNA Innovation Seminar

Monday, November 19th at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109 Zina Pitcher

Mark Painter, PhD Candidate

I attended the University of St. Thomas in Saint Paul, Minnesota, where I graduated Summa cum laude with a B.S. in Biology in May 2014. I came to the University of Michigan as a PIBS student in August 2014, and joined both the Graduate Program in Immunology and Kathy Collins's lab in May 2015, where I am currently conducting my dissertation research.

"Contributions of the hematopoietic stem and progenitor cell HIV reservoir to persistent viremia in treated HIV patients"

Keywords: RNA virus, HIV, Latency, Viremia, Reverse transcription, RNA secondary structure, tRNA priming

Abstract: Long-lived reservoirs of persistent HIV are a major barrier to a cure. Thus, it is important to develop a better understanding of the cell types that contribute to persistent, low level residual viremia in HIV-infected people on anti-retroviral therapy. CD4 + hematopoietic stem and progenitor cells (HSPCs) have the capacity for life-long survival, self-renewal and the generation of daughter cells. Recent evidence shows they are also susceptible to HIV infection in vitro and in vivo. Whether HSPCs harbor infectious virus or contribute to plasma viremia is unknown. Here, we provide strong evidence that clusters of identical proviruses from HSPCs and their likely progeny often match PV. A higher proportion of these sequences matched residual PV than proviral genomes from bone marrow and peripheral blood mononuclear cells that did not form these clusters. A virus containing a signature deletion that renders the virus non-infectious was identified in several cellular compartments, including HSPCs, and PV. Thus, the virus must have spread to the various cellular compartments via cellular proliferation and differentiation from the initially-infected HSPC. Furthermore, an analysis of near full-length genomes isolated from HSPCs provided evidence that HSPCs harbor functional HIV proviral genomes that often match PV. These results support the conclusion that HIV-infected HSPCs form a distinct and functionally significant reservoir of persistent HIV in infected people.