ABSTRACT #25 [1] **Pathogenic SIV infection leads to rapid mobilization and death of plasmacytoid dendritic cells** Simon M. Barratt-Boyes, Kevin N. Brown[2], Viskam Wijewardana[1], Xiangdong Liu[11] Center for Vaccine Research, University of Pittsburgh, Pittsburgh, PA 15261, Experimental Immunology Branch, National Institutes of Health, National Cancer Institute, Bethesda, MD 20892 Plasmacytoid dendritic cells (pDC) are essential innate immune system cells that are lost from the circulation in HIV-infected individuals associated with CD4 T cell decline and disease progression. It has been hypothesized that pDC depletion from blood is caused by migration to inflamed lymph nodes and that chronic pDC activation within lymph nodes culminates in immune activation that is central to AIDS pathogenesis. We used precise methods of enumeration and in vivo labeling with 5-bromo-2'-deoxyuridine to track recently divided pDC in blood and tissue compartments of rhesus macaques with acute pathogenic SIVmac251 infection. We show that pDC are lost from blood and peripheral lymph nodes within 14 days of infection despite a normal frequency of pDC in bone marrow. Paradoxically, pDC loss masked a highly dynamic response characterized by rapid pDC mobilization into blood and a 10 to 20-fold increase in recruitment to lymph nodes relative to uninfected animals. Within lymph nodes pDC had increased levels of apoptosis and necrosis, were uniformly activated and were infected at frequencies similar to CD4 T cells. Nevertheless, remaining pDC had essentially normal functional responses to stimulation through Toll-like receptor 7, with half of lymph node pDC producing both TNF-a and IFN-a . These findings reveal that cell migration and death both contribute to pDC depletion in acute pathogenic SIV infection. We propose that the rapid recruitment of pDC to inflamed lymph nodes brings them into close contact with virus, virusinfected cells and pro-apoptotic factors leading to pDC death. The declining number of pDC together with their normal function suggests that chronic pDC activation in lymph nodes is not a critical mediator of immune activation in pathogenic SIV infection. [2]