

Session: 264. HIV: Pathogenesis
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Background. HIV-associated neurocognitive disorders cause significant morbidity and mortality despite the advent of antiretroviral therapy. An understanding of fundamental mechanisms underlying HIV infection and transmission events in the central nervous system (CNS) is needed. Microglia are resident myeloid cells that are readily infected by HIV and may constitute a CNS reservoir. We evaluated and compared existing microglial cell lines and primary cell-derived microglia as potential model systems for studying HIV-microglia interactions.

Methods. We cultured two immortalized human microglial lines (HMC3, C20) and developed two primary microglial models: induced microglia (iMG) derived from primary human monocytes; and microglial-like cells (iMGL) differentiated from induced pluripotent stem cells (iPSCs). We compared these four microglial cell types to commercially available fetal microglia (PM) for a microglial comparator, and monocyte-derived macrophages as a non-microglial comparator cell. Each cell type was evaluated for the presence of typical myeloid and microglia-specific markers by flow cytometry and immunofluorescence microscopy. HIV infection was performed using macrophage-tropic HIV or VSV-G-pseudotyped HIV.

Results. After differentiation, the iMG and iMGL displayed characteristic microglial morphology: a spindle shape and a reduction in the central body, along with ramified cell processes. Flow cytometry revealed significant differences in surface markers among the cell types. iMG and iMGL displayed CD11b, CD45, CXCR4, CCR5 and lack of expression of CD4 and CX3CR1. In contrast, HMC3, C20, and PM were negative for CD11b, CD45, CX3CR1, CD4, CXCR4. Immunostaining showed that iMG and iMGL were positive for microglial markers TMEM119 and P2RY12. RNA Seq analysis is currently underway to determine gene expression differences between the microglial cell lines and our microglia models. In preliminary results, iMG and iMGL were both readily infected with HIV, and comparison with other lines is ongoing.

Conclusion. There is no standard model available for defining the molecular and cellular events involved in HIV infection of microglia. Significant differences in microglial markers and in HIV receptor and coreceptor levels were noted in this study. iMG and iMGL appear to be viable microglial models susceptible to HIV infection.

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2519. Urban vs Rural HIV-infected Persons Have Differential Gene Expression for Estrogen Signaling, Inflammation, and Cytokine Production Pathways

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Background. People aging with HIV (PAWH) are living longer with effective antiretroviral therapy and new HIV diagnoses are rising in older populations. Concurrent with trends in age, the epidemiology of HIV infection in the United States has shifted geographically and racially; the Southeast and African Americans now have the highest HIV incidence and prevalence. Although there are marked health disparities for rural and African American PAWH, limited data exist comparing aging phenotypes between rural and urban PAWH, and no data exist comparing mechanistic pathways between these populations. Among African American PAWH, we hypothesize that rural PAWH will be more likely than urban PAWH to have a molecular profile of advanced aging associated with chronic disease burden and shorter health span.

Methods. Demographics, clinical data, and RNA were collected from 14 matched pairs from rural (Wake Forest University, Winston-Salem, NC) and urban cohorts (ALiVE cohort, Johns Hopkins University, Baltimore, MD) matched on age, sex, Short Physical Performance Battery score, smoking status, and sample collection date. Raw sequences were examined for quality, aligned using STAR, and normalized using DESeq2. DESeq2 tested matched pair differential gene expression. Genes with an average read count threshold > 5, a genomic control adjusted P-value < 0.01 and a fold change > 1.3 were retained for further analysis using STRING, MCODE, and IPA to find functional and biological patterns.

Results. Of the 399 genes meeting significance criteria, 212 showed higher expression in the rural group; the remaining 187 genes showed lower expression in the rural group. Top enriched canonical pathways in the IPA analysis identified differential estrogen signaling ($P < 0.0001$), inflammation ($P < 0.001$), and cytokine production ($p = 0.005$). Protein-protein interactions involved in cell-cell signaling and intracellular trafficking were also differentially identified between the 2 populations.

Conclusion. Urban and rural PAWH have differential gene expression, particularly centered around estrogen signaling and inflammatory cytokine production. These findings merit further investigation to determine clinical significance, including correlation with phenotypes and healthspan between rural and urban PAWH.

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2520. Resource utilization in adolescents and young adults with HIV in the HIV Research Network

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Background. Adolescents and young adults (AYA) with HIV experience worse health outcomes than adults with HIV in the United States. Little is known about AYA patterns of utilization of costly healthcare resources.

Methods. We estimated utilization of outpatient, emergency department (ED), and inpatient care among 13–30 year-olds from 2006–2015. We stratified outpatient visits, ED visits and inpatient days per person-year (PY) by transmission mode (perinatal (PHIVY), non-perinatal (NPHIVY)), age (13–17, 18–23, 24–30 years), CD4 strata (< 200, 200–499, ≥ 500 cells/μL) and presence or absence of viral load (VL) suppression (< , ≥ 400 copies/mL[c/mL]) combined with antiretroviral (ARV) use. We also quantified outpatient, ED, and inpatient care associated with specific AIDS-defining conditions.

Results. Among 4,450 AYA (PHIVY: 15%; NPHIVY: 85%), mean (SD) follow-up was 2.8 years (2.5) [PHIVY: 4.2 years (3.1); NPHIVY: 2.5 years (2.3)]. Mean age was 21.4 years (PHIVY: 16.9 years; NPHIVY: 22.3 years) and female sex was 28% (PHIVY: 52%; NPHIVY: 23%). Among PHIVY, most person-time (PT) was spent between ages 13–23 years (13–17 years: 43%; 18–23 years: 45%), CD4 ≥ 500/μL (61%), and VL < 400 c/mL (69%). Among NPHIVY, most PT was spent between ages 24 and 30 years (56%), CD4 ≥ 500/μL (54%), and VL < 400 c/mL (66%). PT spent while prescribed ARVs and VL ≥ 400 c/mL was 30% (PHIVY) and 24% (NPHIVY). For both PHIVY and NPHIVY, outpatient visit rates were higher at younger ages (13–17 years and 18–23 years), lower CD4 (< 200, 200–499/μL), and among those prescribed ARVs (Figure 1). Rates of ED visits and inpatient days were higher during PT spent at older ages (18–23 years, 24–30 years), lower CD4 (< 200, 200–499/μL), and VL ≥ 400 c/mL (Figures 2 and 3). Overall, utilization was higher among PHIVY than NPHIVY (outpatient: 12.1 vs. 6.0/PY; ED: 0.4 vs. 0.3/PY; inpatient: 1.5 vs. 0.8/PY). The overall rate of AIDS-defining conditions was 4.5/100 PY (Figure 4).

Conclusion. Among AYA with HIV, more ED visits and inpatient days were observed during time spent at older ages, lower CD4 counts, and VL ≥ 400 c/mL. While AIDS-defining conditions were rare, associated resource utilization was substantial. Interventions to improve retention in care, virologic suppression, and immune response may improve outcomes, and thus decrease costly resource utilization, for AYA with HIV as they transition to adulthood.

